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Research article

# Epidemiological and clinical characteristics of patients with carbapenem-resistant Enterobacterales in a university hospital of Colombia: Enzyme coproductions in rise

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ABSTRACT

The distribution of carbapenemases in Carbapenem-Resistant Enterobacterales (CRE) has recently undergone a change in our region. According to the Colombian National Institute of Health, there is an increasing prevalence of NDM and NDM-KPC co-producing strains. We carried-out an ambispective cohort study of adult inpatients from Hospital Universitario San Ignacio (2021–2023), infected or colonized with CRE, in which carbapenemases immunochromatographic assay was performed. Out of the 150 patients included in the study, 71.3 % presented with an infection, and carbapenemases were detected in 92.7 % of these cases. Among them, KPC predominated (54 %), while 16.7 % demonstrated enzyme coproductions, mainly KPC-NDM. CRE infected patients had an 18.7 % 30-days mortality, but we could not demonstrate an association between type of carbapenemase and mortality rate ($p = 0.82$). Logistic regression analysis suggested that ICU admission was independently correlated to fatality (OR 5.08; CI 1.68–16.01). NDM and KPC-NDM presence in CRE poses a public health threat and a therapeutic challenge, with unknown mortality differences according to the carbapenemases pattern. Nevertheless, there was not an association between enzyme type and mortality.

## 1. Introduction

Despite antimicrobial resistance is naturally expected, the advent of antimicrobials and their non-rational use in both clinical and agricultural contexts has amplified this phenomenon. In the case of Enterobacterales, the most important mechanism of resistance is enzymatic, for which enzymes such as extended-spectrum beta-lactamases (ESBL), AmpC cephalosporinases, and more recently carbapenemases, are becoming increasingly important [1,2]. In recent years, there has been a suggestion to designate certain pathogens,

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including carbapenem-resistant Enterobacterales (CRE), as critical priorities [3,4]. However, not all carbapenemases are equivalent, considering the existence of both serine-carbapenemases (including class A, such as KPC, and class D, such as OXA-48, in the Ambler classification) and metallo-betalactamases (class B, such as NDM, in the Ambler classification) [5].

Epidemiological events of worldwide interest have been described in the presence of CRE, ranging from sporadic reports and small outbreaks to the establishment of endemic circulation of these microorganisms. Special interest has arisen in countries such as India, Pakistan, Italy, the United States of America, and Colombia, where endemicity is now established (NDM in the first two countries, KPC in the remaining three). The high 30-day mortality rates (around 30–60 %) described in these countries, in the presence of CRE infections, make the situation even more worrisome [6–8].

According to the CRACKLE-2 cohort, which included data from Colombia, infections caused by carbapenem-resistant *Klebsiella pneumoniae* are associated to a 28 % 30-day mortality, in contrast to the United States and China, where it reaches 23 % and 12 %, respectively [9]. In a recent Colombian study in which our institution participated, the 30-day mortality rate was 38.17 % [10]. In infections caused by Enterobacterales that produce metallo-carbapenemases, a trial showed a 30-day mortality rate of 19 % in those who received Ceftazidime/Avibactam + Aztreonam, compared to 44 % in those assigned to standard therapy [11]. To date, no studies have compared mortality rates in patients with infections caused by metallo-carbapenemase-producing Enterobacterales against those caused by serine-carbapenemases or enzyme-coproducing bacteria. The most recent national carbapenem resistance technical report illustrates an increasing proportion of NDM-producing or KPC-NDM co-producing Enterobacterales [12]. According to the Latin American Network for Antimicrobial Resistance Surveillance (ReLAVRA) [13], several countries in the region have recently reported outbreaks of Enterobacterales with carbapenemases co-production, being the KPC + NDM combination among the most interesting. Unfortunately, there is scarce information on their clinical impact and best therapeutic approach [13].

Considering this panorama, we present an ambispective cohort of Colombian inpatients of a third level university hospital. Our purpose was to identify the demographic, clinical, microbiological, and outcome features of patients with colonization and infection by CRE, which were detected by automated tests and enzymatic identification by immunochromatography. Likewise, we aimed to evaluate the relationship between the type of enzyme production and mortality rate in infected patients.

## 2. Methods

This is an ambispective cohort of patients with CRE colonization and infection hospitalized at Hospital Universitario San Ignacio de Bogotá, Colombia, from October 2021 to June 2023. Sample collection started when our institution introduced NG-Test Carba-5 V2.0 (NG Biotech) within the clinical decision algorithms. We included patients with CRE isolates, defined as MIC $\geq$1 for ertapenem and/or MIC $\geq$2 for meropenem (according to the institutional automated antimicrobial susceptibility testing) and who underwent immunochromatography testing for enzyme detection. We excluded patients aged less than 18 years, non-fermenting gram-negative bacilli isolates, results from rectal swab sampleing, patients who died during the first 48 h of in-hospital stay or who were referred to other institutions.

Patients were classified as infected or colonized. To consider a patient as infected, antimicrobial therapy should had been prescribed due to the diagnosis of an infectious clinical syndrome, in which the isolated CRE was considered to be directly responsible; this diagnosis was established by the treating physician and occurred during the study period. Meanwhile, a patient was considered to be colonized by a CRE if the isolate was interpreted as non-responsible from the clinical state of the patient, meaning the absence of an infectious syndrome diagnosis. Therefore, antimicrobial therapy was not prescribed, or was withdrawn previous to completion. Infections were also classified as hospital-acquired or community-acquired, taking into account the institutional epidemiological surveillance committee evaluation, as well as the National Healthcare Safety Network (NHSN) [14] and National Institute of Health criteria.

We implemented the institutional microbiology laboratory register to identify patients of interest for this study. This registry includes all the institutional isolates in which CRE cases are suspected, and is periodically sent to the infectious diseases unit. We also reviewed the microbiology laboratory database, which includes all patients, isolates and antimicrobial susceptibilities profiles from the emergency department, hospitalization floors, and intensive care units.

Data about demographic characteristics, comorbidities, clinical manifestations and therapeutic interventions was collected from institutional medical records, using a standardized database. To avoid misinterpretation or typing errors, and to ensure full completion of data fields, the main investigator reviewed all the records, and a fifth was reviewed in duplicate. Date of infection onset was defined from the date of index culture collection, and the type of infection was defined according to the origin of the culture sample and clinical interpretation. Empirical antibiotic therapy was defined based on the initiation of antimicrobials for suspected infection, prior to the identification of the microorganism and its phenotypic resistance profile.

Targeted antibiotic therapy was defined as antimicrobial agents' administration guided by microbiological identification and susceptibility pattern. Empirical or targeted antibiotic therapy was considered adequate if the isolate responsible from infection was susceptible, according to the MIC values reported by the automated antimicrobial susceptibility system. Mortality outcome was measured 30 days after the diagnosis of infection, and information related to each patient's vital state was retrieved from subsequent electronic medical records. If the patient did not have additional records, it was obtained from the national public database of affiliation to the General System of Social Security in Health (ADRES), that allowed us to verify whether the patient survived at the time of consultation.

### 2.1. Microbiological tests

Microorganisms' identification was made using the VITEK®-MS V3.2 mass spectrometry system (Biomeriéux), and antimicrobial resistance evaluation was performed by automated broth microdilution, using the commercial VITEK® 2 system (Biomeriéux). In our institutional protocol, the suspicion of carbapenemase-producing Enterobacterales begins with the detection of microorganisms showing carbapenems MIC in the intermediate or resistant range, according to the cut-off points established by CLSI, update 2023 (intermediate MIC ≥1 for ertapenem and/or MIC ≥2 for meropenem). Strains that complied with this criterion were evaluated by phenotypic carbapenemase capture test (CarbaNP), and in case of a positive result, the immunochromatographic phenotypic capture-differentiation test (NG-Test Carba-5 V2.0, NG Biotech), a tool with sensitivity and specificity of >96 % for the enzymes included, was performed [15].

### 2.2. Statistical analysis

Before describing the cohort, an exploratory analysis of the variables was performed, discarding missing data and evaluating outliers. A descriptive analysis of the population was performed using measures of central tendency and dispersion, according to the data distribution; results were presented with means and standard deviations for normally distributed data, and medians and inter-quartile ranges (IQR) for non-normally distributed variables. Subsequently, a Kaplan Meier analysis was performed on data from CRE infected patients to explore the potential association between the type of carbapenemase enzyme and all-cause mortality rate. We determined an administrative censoring of 30 days after microbiological isolation and computed a Log-rank test to compare the survival curves. Furthermore, a multivariate logistic regression was also fitted to evaluate the association between enzyme type andfatality, controlling for age, sex, bacteremia, and ICU admission; odds ratios (OR) and their 95 % confidence intervals (CI) were calculated. All analyses were made in R software version 4.1. (R CRAN, Vienna, Austria). We used the *survival, survminer* statistical packages.

## 3. Results

Out of a total of 181 eligible patients, 31 (17.1 %) were excluded. Most frequent reasons for exclusion were: samples obtained from

**Table 1**
Characteristics of infected and colonized patients with CRE at HUSI (2021–2023).

| Characteristics | Total | Colonized | Infected |
|---|---|---|---|
| Variables | N = 150 | N = 43 | N = 107 |
| Demographics | | | |
| Male sex, n (%) | 104 (69.3 %) | 32 (74.4 %) | 72 (67.3 %) |
| Age in years, median (IQR) | 61 (46.25–61) | 61 (41.5–72) | 62 (49.5–69.5) |
| Underlying conditions | | | |
| Diabetes mellitus, n (%) | 40 (26.7 %) | 11 (25.5 %) | 29 (27.1 %) |
| Chronic kidney disease, n (%) | 36 (24 %) | 14 (32.6 %) | 22 (20.6 %) |
| Haematologic neoplasm, n (%) | 26 (17.3 %) | 9 (20.9 %) | 17 (15.9 %) |
| Solid organ neoplasm, n (%) | 35 (23.3 %) | 9 (20.9 %) | 26 (24.3 %) |
| HIV infection, n (%) | 7 (4.7 %) | 4 (9.3 %) | 3 (2.8 %) |
| Other immunosuppression[a], n (%) | 15 (10 %) | 5 (11.6 %) | 10 (9.3 %) |
| Recent hospital stay[b], n (%) | 83 (55.3 %) | 20 (46.5 %) | 63 (58.9 %) |
| Previous antibiotics use[c], n (%) | 52 (34.7 %) | 13 (30.2 %) | 39 (36.4 %) |
| Charlson index, median (IQR) | 4 [2–6] | 5 (2.5–6) | 4 [2–6] |
| Type of microorganisms | | | |
| *Klebsiella pneumoniae* | 62 (41.3 %) | 14 (32.6 %) | 48 (44.9 %) |
| *Enterobacter cloacae complex* | 28 (18.7 %) | 13 (30.2 %) | 15 (14 %) |
| *Klebsiella oxytoca* | 18 (12 %) | 6 (14 %) | 12 (11.2 %) |
| Other Enterobacterales | 42 (28 %) | 10 (23.3 %) | 32 (29.9 %) |
| Enzymatic characteristics | | | |
| KPC, n (%) | 81 (54 %) | 22 (51.2 %) | 59 (55.1 %) |
| NDM, n (%) | 30 (20 %) | 10 (23.3 %) | 20 (18.7 %) |
| VIM, n (%) | 1 (0.7 %) | 0 (0 %) | 1 (0.9 %) |
| IMP, n (%) | 0 (0 %) | 0 (0 %) | 0 (0 %) |
| OXA, n (%) | 2 (1.3 %) | 1 (2.3 %) | 1 (0.9 %) |
| Coproductions, n (%) | 25 (16.7 %) | 8 (18.6 %) | 17 (15.9 %) |
| KPC-NDM | 23 | 6 | 17 |
| Abscence of enzymatic detection, n (%) | 13 (8.7 %) | 3 (7 %) | 10 (9.3 %) |
| Clinical outcomes | | | |
| Mortality at 30 days, n (%) | 23 (15.3 %) | 3 (7.0 %) | 20 (18.7 %) |

[a] Corticosteroids use defined as prednisolone> 20 mg/day for >3 weeks, or equivalents.
[b] Hospital stay during previous six months.
[c] Broad-spectrum antibiotics, including carbapenems, fluoroquinolones, third or fourth generation cephalosporins, aminoglycosides, polymyxins or Ceftazidime/Avibactam during previous three months.

patients who were not hospitalized (n = 16, 51.5 %), strains with unavailable immunochromatography (n = 7, 22.6 %), sensitive strains (n = 4, 12.9 %), age <18 years (n = 2, 6.5 %), co-infection with non-fermenting gram-negative bacilli (n = 1, 3.2 %), and discharge within 48 h of hospitalization (n = 1, 3.2 %).

A total of 150 patients were considered in the analysis, who were definitively classified as infected (n = 107, 71.3 %) or colonized (n = 43, 28.7 %). Median age was 61 years (IQR 46.2–70); the sample was mostly represented by men (69.3 %), and subjects exhibited a median Charlson index of 4 (IQR 2–6). Sociodemographic, clinical, and microbiological characteristics of the population are presented (Table 1).

Among 43 colonized patients, previous exposure to broad-spectrum antibiotics occurred in 13 (30.2 %), a similar proportion when compared to infected patients. Most frequent isolates were *Klebsiella pneumoniae* (n = 14,32.6 %), *Enterobacter cloacae complex* (n = 13, 30.2 %) and *Klebsiella oxytoca* (n = 6, 14 %). Main samples were urine cultures (n = 28 patients, 65.1 %).

For the 107 infected patients, most frequently detected microorganisms were *Klebsiella pneumoniae* (n = 48, 44.9 %), *Enterobacter cloacae complex* (n = 15, 14 %), and *Klebsiella oxytoca* (n = 12, 11.2 %). In descending order, these were followed by *Escherichia coli*, *Citrobacter freundii*, *Proteus mirabilis*, and other Enterobacterales. Isolates were retrieved from blood (n = 45, 42.1 %), urine (n = 43, 40.2 %), orotracheal secretions (n = 4, 3.7 %) and other samples (n = 15, 14 %). Main definitive diagnoses were urinary tract infection (n = 46, 43 %), intra-abdominal/gastrointestinal infection (n = 23, 21.5 %), lower respiratory infection (n = 14, 13.1 %), febrile neutropenia (n = 10, 9.3 %), and skin and soft tissue infection (n = 7, 6.5 %). The remaining cases were attributed to other infectious foci, while the origin of infection could not be determined in 3 (2.8 %).

Among patients infected by KPC-producing Enterobacterales, a MIC≥16 for meropenem was reported in 69 (90.8 %), and a MIC≥8 for meropenem was informed in 54 (71.1 %). CRE infections attributable to NDM-producing microorganisms had a MIC≥16 for meropenem in 35 (94.6 %) and a MIC≥8 for ertapenem in 34 (91.9 %). In the case of infections caused by KPC-producing microorganisms, the most frequently indicated antibiotic was ceftazidime/avibactam in 45 (76.2 %), while monotherapy was prescribed in 36 (80 %). In infections with Enterobacterales-producing NDM, combined therapy with ceftazidime/avibactam and aztreonam was used in 6 (30 %), while monotherapy was used in 12 (60 %), with urinary tract infection being the most frequent diagnosis in the latter. In those infected with Enterobacterales that caused KPC-NDM coproduction, combined therapy was prescribed in 13 (76.4 %), among which 9 received ceftazidime-avibactam and aztreonam.

Admission to the intensive care unit (ICU) was required in 25 (23.4 %) patients. Complication with septic shock occurred in 17 (15.9 %), and acute respiratory failure in 15 (14 %). Of those admitted to the ICU, invasive mechanical ventilation was initiated in 10 (40 %) and vasoactive agents in 7 (28 %). All-cause mortality at 30 days after isolation was 18.7 % (n = 20), and 30-day hospital readmission occurred in 8 (7.5 %). Infected patients who survived were younger, were less likely to demonstrated bacteremia and had

**Table 2**
Clinical and microbiological characteristics of patients infected by CRE, according to fatality.

| Characteristics | Survivors n = 87 | Deceased | Multivariate analysis, OR (CI95 %) |
|---|---|---|---|
| Male sex, n (%) | 60 (69 %) | 12 (60 %) | |
| Age in years, median (IQR) | 61 (49–68) | 66 (55.5-77-5) | 1.02 (0.99–1.06) |
| Underlying conditions | | | |
| Diabetes mellitus, n (%) | 26 (89.6 %) | 3 (10,3 %) | |
| Chronic kidney disease, n (%) | 19 (86.4 %) | 3 (13.7 %) | |
| Haematologic neoplasm, n (%) | 11 (64.7 %) | 6 (35.3 %) | |
| Solid organ neoplasm, n (%) | 18 (69.2 %) | 8 (30.8 %) | |
| Charlson index, median (IQR) | 3 [2–5] | 5 [2–7] | |
| Bloodstream infection | 33 (73.3 %) | 12 (26.7 %) | 2.71 (0.92–8.46) |
| INCREMENT-CPE, median (IQR) | 5 [5–8] | 8 (6.75–11.5) | |
| Source of infection | | | |
| Urinary tract infection, n (%) | 41 (89.1 %) | 5 (10.9 %) | |
| Intraabdominal/gastrointestinal infection, n (%) | 18 (78.3 %) | 5 (21.7 %) | |
| Lower respiratory infection, n (%) | 7 (50 %) | 7 (50 %) | |
| Hospital acquired infection, n (%) | 31 (75.6 %) | 10 (24.4 %) | |
| Type of microorganisms | | | |
| *Klebsiella pneumoniae* | 38 (79.2 %) | 10 (20.8 %) | |
| *Enterobacter cloacae complex* | 13 (86.7 %) | 2 (13.3 %) | |
| *Klebsiella oxytoca* | 8 (66.7 %) | 4 (33.3 %) | |
| Other Enterobacterales | 28 (82.3 %) | 6 (17.7 %) | |
| Enzyme characteristics | | | |
| KPC, n (%) | 47 (79.7 %) | 12 (20.3 %) | |
| NDM, n (%) | 16 (80 %) | 4 (20 %) | 0.88 (0.18–3.74) |
| VIM, n (%) | 1 (100 %) | 0 (0 %) | |
| IMP, n (%) | 0 (0 %) | 0 (0 %) | |
| OXA, n (%) | 1 (100 %) | 0 (0 %) | |
| Coproductions, n (%) | 13 (76.5 %) | 4 (23.5 %) | 0.89 (0.19–3.5) |
| KPC-NDM | 13 | 4 | |
| ICU admission, n (%) | 15 (17.2 %) | 10 (50 %) | 5.08 (1.68–16.01) |
| Inappropriate empiric therapy, n (%) | 78 (89.7 %) | 19 (95 %) | |
| Empiric therapy duration in days, median (IQR) | 4 (2.25–6) | 3 (2.75–5) | |

Percentages are presented according to files distribution.

lower INCREMENT-CPE scores than those who died (Table 2).

### 3.1. Relationship between type of enzyme and all-cause mortality

Kaplan-Meier curves were used to assess the relationship between enzyme type and all-cause mortality rate at 30 days after hospital isolation. The Log-rank test indicated no significant difference between the curves (p = 0.82). (Fig. 1). A multivariate logistic regression analysis was conducted to examine the association between carbapenemase enzyme type and all-cause mortality. This analysis was adjusted for several potential confounding factors, including age, sex, Charlson index, length of stay in the intensive care unit (ICU), and bloodstream infection status. No association was found between the presence of an NDM enzyme (OR 0.88; CI 0.18–3.74), nor the enzyme co-production (OR 0.89; CI 0.19–3.5), when compared to KPC production. We found an association of admission to the ICU with all-cause fatality (OR 5.08; CI 1.68–16.01).

## 4. Discussion

Although 30-day mortality rate was high in our study, it was lower compared to previous publications focused on KPC-producing microorganisms [9,10,16], and similar to findings from a clinical trial with infections caused by NDM or VIM-producing strains [11]. So far, there are still very few studies evaluating mortality associated to CRE infections according to the enzyme type. A study from Thailand describes a 43.75 % 14-day mortality in the presence of NDM-producing Enterobacterales (including NDM/OXA-48 co-productions) and 0 % in the presence of OXA-type serine-carbapenemases [17]. However, therapeutic regimens were mainly polymyxin-based combinations, and we hypothesize this might play a role, at least partial, in the observed mortality differences. Another work describes 30-day mortality of 35 %, 50 % and 37 % in strains with KPC, OXA-48 or a metallobetalactamase production (mainly NDM), respectively [18]. To our knowledge, this is the first publication to compare the mortality from KPC-producing Enterobacterales infection against KPC-NDM co-productions infection.

ICU admission was the only variable in our study that showed an association with in-hospital fatality at 30 days. This is consistent with previous studies in which sepsis and septic shock, (frequently observed in critically ill patients), have been associated with fatal outcomes [19,20]. Specific researches evaluating risk factors for mortality in critically ill patients have found associations with severity scores such as SAPS-II [21,22]. It is also worth noting that the observed change in mortality, compared to previous publications, cannot definitively be attributed solely to the introduction of new antimicrobials. It cannot be overlooked that admission to the ICU may also be influenced by the severity of the infection (as occurs in patients with septic or septic shock), as well as by underlying comorbidities.

Recent national data indicated that among CRE, the distribution of carbapenemases was predominantly KPC (70 %), followed by NDM (7 %), VIM (2.8 %), and co-production of enzymes in up to 6 % of cases [23]. Compared to our findings, it is evident that, although KPC (54 %) remains the most prevalent carbapenemase enzyme, the contribution of NDM (20 %) and co-productions (16.7 %) is also markedly relevant in both colonized and infected patients. Co-productions in this study are aligned with the most recent national resistance report, which indicates that carbapenemase co-productions in CRE reach 16.9 %, being KPC-NDM the most prevalent [12]. Despite the limited literature on KPC-NDM co-productions, it has been described that resistance determinants might originate from different plasmids. Alternatively, they could be acquired concomitantly from hybrid plasmids, mediated by the 6100-insertion sequence [24–26]. Although there is a growing body of literature guiding the therapeutic approach of infections caused by KPC- or metallobetalactamase-producing CRE, the absence of recommendations and trials for infections with carbapenemase co-producing strains is still a major evidence gap [27].

Limitations in our study include the inability to rule out an association between mortality and the type of enzyme, in spite of not reporting any differences in mortality rates according to enzyme type. The possibility of type II statistical error does exist, given that

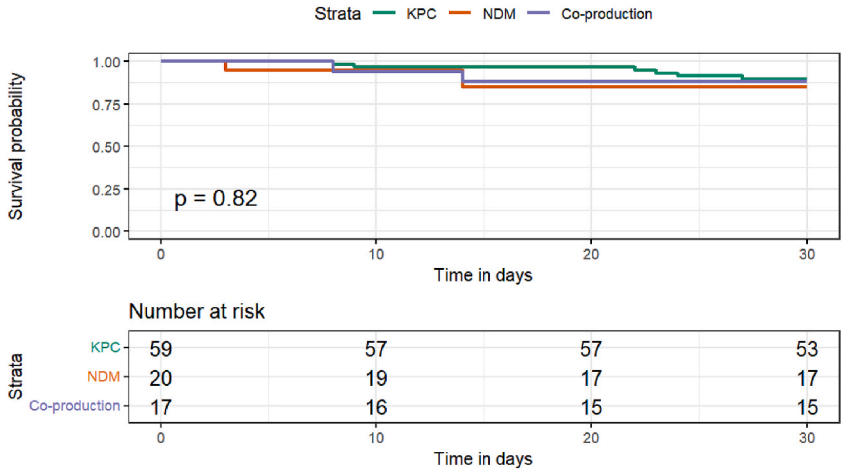


**Fig. 1.** Survival curve for CRE infection at 30 days from isolation, according to carbapenemase enzyme.

power of our sample was limited, since it depended on the maximum number of cases collected. This publication encourages the formulation of hypotheses that could guide the design of multicenter studies with larger samples. Such studies could help clarify current issues, including the most relevant associations with mortality rates and potential therapeutic interventions that may offer better outcomes.

Another important limitation arises from the MICs yielded by the automated VITEK2 system as the first step in the diagnostic algorithm of CRE. While certain studies have reported a very high capture rate of KPCs using this methodology, others have shown false susceptibilities of up to 23 % when compared to molecular tests. IMP capture has shown drawbacks related to false resistance, rather than false susceptibility, and for the case of OXA-48, it is well known that all automated systems, including VITEK2, have variable performance [28–31].

A relevant aspect from our study is that we used immunochromatography for the detection of carbapenemases, and there is the possibility, although very low, of failing to detect enzymes not considered by this tool. This represents an inherent bias related to the measuring instrument, which sensitivity and specificity is high for Enterobacterales (>96 %) [15,32]. Furthermore, immunochromatography provides results in approximately 15 min, leading to its adoption in multiple institutions. Our study is pertinent for medical practice in real-life situations and encourages the use these tools in clinical care in low-to middle-income countries. Indeed, this diagnostic test has shown improved time to results and patient outcomes and could be a cost-effective strategy [33]. Finally, it would have been ideal to implement a genotypic tool for resistance detection, or strains sequencing, especially for those in which immunochromatography failed to detect enzymes.

## 5. Conclusions

Infections caused by carbapenem-resistant Enterobacterales, producers of NDM and KPC-NDM enzymes, are increasingly relevant in our environment, pose a public health threat, represent a challenge in terms of therapeutic approach. Although we did not find an association between the pattern of carbapenemases in CRE infections and mortality rate or fatality, it is relevant to conducted further studies to confirm or rebate the results.

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## Ethics statement

The study complies with all current regulations. It was approved by both the Research Committee and the Institutional Ethics Committee, code 2023–079 (May 3rd, 2023), and was conducted according the principles set in the Declaration of Helsinki. Informed consent was waived since data was encrypted and due to the observational nature of the study.

## Data availability statement

Data is not publicly available. It will be made available on request.

## CRediT authorship contribution statement

**Juan Fernando Contreras-Valero:** Writing – original draft, Methodology, Investigation, Conceptualization. **Sandra Milena Gualtero-Trujillo:** Validation, Supervision, Conceptualization. **Gloria Cecilia Cortés-Fraile:** Validation, Resources, Conceptualization. **Sebastián Hernández-Garzón:** Investigation. **Natalia Manrique-Marín:** Investigation. **Miguel Ángel Narváez-Chaves:** Investigation. **Sandra Liliana Valderrama-Beltrán:** Writing – review & editing, Software, Methodology, Formal analysis, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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