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Original Article

Microbiology Section

Comparison of Antimicrobial Activity between Ceftriaxone-Sulbactam-Disodium EDTA and Ceftazidime-Avibactam against Carbapenemase Producing Enterobacterales Isolates from a Tertiary Care Hospital: An In-vitro Study

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ABSTRACT

Introduction: The spread of Multidrug-Resistant (MDR) organisms worldwide poses a significant public health challenge, particularly in the South Asian region, including India. Infections caused by Metallo-β-Lactamase (MBL) producing Enterobacterales are a notable concern. The rising incidence of MBL-producing isolates underscores the urgent need for innovative therapeutic strategies and effective antimicrobial combinations to address these threats. Combination treatments such as Ceftriaxone Sulbactam-disodium Ethylenediamine Tetraacetate (EDTA) (CSE) and Ceftazidime-Avibactam (CZA) have emerged as promising alternatives to conventional antibiotics.

Aim: To compare the in-vitro efficacy of two antibiotic combinations, namely CSE and CZA, against Carbapenemase-producing Enterobacterales isolates.

Materials and Methods: An in-vitro study was conducted over a period of six months from June 2024 to November 2024 at the Department of Microbiology, SRM Medical College Hospital, Chengalpattu, Tamil Nadu, India. A total of 141 Enterobacterales isolates that were resistant to either Imipenem or Meropenem, obtained from various clinical samples, were included. Phenotypic differentiation was performed using the EDTA-modified Carbapenem Inactivation Method (eCIM) method in conjunction with the modified Carbapenem Inactivation Method (mCIM) method. Further in-vitro susceptibility testing was conducted using the Kirby-Bauer disk diffusion method to compare the two antibiotic combinations, namely CSE and CZA. Demographic parameters including age, gender, sample type, ward and organism-wise distribution were assessed throughout the course of this study. Data analysis was performed using percentage susceptibility and frequency distribution. The p-value was determined using Fisher's exact test, with a p-value <0.05 regarded as statistically significant.

Results: Among 141 Carbapenem-Resistant Enterobacterales (CRE) isolates, 39 (27.66%) were phenotypically identified as Carbapenemase producers using the mCIM-eCIM method. Antimicrobial susceptibility testing of these isolates, performed using the Kirby-Bauer disk diffusion method, revealed that all 39 (100%) Carbapenemase-producing isolates were susceptible to CSE. In contrast, only 9 (23%) serine carbapenemase-producing isolates were susceptible to CZA, while 30 (77%) MBL-producing isolates demonstrated resistance.

Conclusion: In this study, CSE emerged as a potent antibacterial agent against MBL-producing isolates. Therefore, it is strongly recommended to include CSE in the routine susceptibility panel and consider its use as a carbapenem and colistin-sparing drug against carbapenemase producers, especially MBL-producing Enterobacterales isolates.

Keywords: Carbapenem resistant enterobacterales, Ethylenediamine tetra acetic acid, Metallo-β-lactamase, Serine carbapenemase

INTRODUCTION

The global spread of MDR organisms represents a major public health issue, particularly in the South Asian region, including India, primarily due to infections linked to Enterobacterales that produce MBL [1]. These enzymes confer resistance against almost all β-lactam antibiotics, including carbapenems, which are frequently regarded as the last line of defence for treating severe infections. The occurrence of Extended-Spectrum Beta-Lactamases (ESBLs) and MBLs is on the rise throughout India, with reported prevalence rates varying from 8-78% [2-5]. This increasing incidence of MBL-producing isolates has underscored the urgent need for innovative therapeutic strategies and effective antimicrobial combinations to address these threats.

Combination treatments like CSE and CZA have emerged as promising alternatives to conventional antibiotics. CSE combines a third-generation cephalosporin with a β-lactamase inhibitor and a metal ion chelator to target MBL activity. The addition of sulbactam and EDTA with ceftriaxone broadens its antimicrobial spectrum, conferring enhanced efficacy against ESBL- and MBL-producing bacterial strains [6]. Conversely, CZA exhibits potent in-vitro activity against a broad range of resistant Gram-negative pathogens, including MDR, Extensively Drug-Resistant (XDR), and Pan-Drug-Resistant (PDR) isolates harbouring ESBLs, AmpC β-lactamases, *Klebsiella pneumoniae* Carbapenemases (KPCs), and class D serine β-lactamases [7]. CZA merges a third-generation cephalosporin with avibactam, a non β-lactam β-lactamase inhibitor effective against a wide spectrum of β-lactamase-producing bacteria, although its effectiveness against MBLs is limited. The eCIM serves as a reliable phenotypic test to detect MBL-producing organisms, facilitating targeted investigations into the efficacy of novel antimicrobial agents.

There are very few in-vitro studies comparing the susceptibility of CSE against Gram-negative isolates [2,8]. Moreover, this is the first study to conduct a comparative analysis of the in-vitro susceptibility profiles of CSE and CZA from Carbapenemase-producing Enterobacterales isolates characterised phenotypically based on the mCIM-eCIM method.

This study aims to perform an in-vitro comparison of the antimicrobial activity of CSE and CZA against Carbapenemase-producing Enterobacterales isolates. The primary objective was to phenotypically characterise CRE isolates using the mCIM-eCIM method, while the secondary objective was to test their in-vitro susceptibility by the disk diffusion method against CSE and CZA. By analysing the effectiveness of these two treatment options, this research seeks to provide valuable insights into combating these challenging pathogens and addressing the growing issue of antimicrobial resistance.

MATERIALS AND METHODS

This in-vitro study was conducted in the Department of Microbiology at SRM Medical College Hospital, Chengalpattu, Tamil Nadu, India, over a period of six months from June 2024 to November 2024. The study obtained clearance from the Institutional Ethics Committee (IEC No.: SRMIEC-ST0723-571) at SRM MCH&RC, dated 14.03.2024.

Inclusion criteria: All clinical isolates from patient samples, irrespective of age and gender, that showed resistance to carbapenems and Enterobacterales isolates showing resistance to either Imipenem or Meropenem, as determined by the Kirby-Bauer disk diffusion method, were included in the study.

Exclusion criteria: Gram-negative isolates other than Enterobacterales and isolates that were susceptible to either Imipenem or Meropenem were excluded from the study.

Sample size calculation: The required sample size for this study was estimated using the formula based on reference values from a study by Laolerd W et al., which compared the sensitivity and specificity of phenotypic methods for detection of Carbapenemase production in Enterobacterales isolates in which Carba NP test showed a Sensitivity, Specificity, Positive predictive value and negative predictive value of 84.75%, 100%, 100% and 65.31%, respectively [9]. Whereas mCIM showed both Sensitivity and Specificity of 100% [9].

Formula: $(z\propto/2+z1-\beta)^2\ (p1q1+p2q2)/(p1-q2)^2$

$p1=84.75\approx85$, $p2=65.31\approx65$, $z\propto/2=1.96$, $z1-\beta=0.84$

n=(1.96+0.84)2 (85×15+65×35)/(85–65)2

n=7.84×3550/400

n=69.5≈70

Total sample size=n1+n2=70+70

Total sample size=140.

Sample collection: A total of 835 gram-negative isolates were obtained from 1,160 clinical samples, which included blood, Cerebrospinal Fluid (CSF), sputum, urine, tissue and pus from infected wounds, collected from inpatients, encompassing both ICU and ward patients, during standard culture procedures.

Antimicrobial susceptibility testing: Antimicrobial susceptibility testing was performed using the Kirby–Bauer disk diffusion technique, in accordance with Clinical Laboratory Standards Institute (CLSI) guidelines (2025) [10]. Antimicrobial disks containing Meropenem 10 µg (Lot No. MRP10-2408) and Imipenem 10 µg (Lot No. IPM10-2429) were sourced from Hi-Media in Maharashtra, India. The antibiotic disks for CSE (Lot No. CSE-2303) and Ceftazidime-Avibactam (Lot No. CZA30-20-2308) were acquired from the Microxpress® division of Tulip Diagnostics Pvt. Ltd., Goa, India.

From 24-hour incubated 5% blood agar plates that had developed isolated pathogen colonies, a suspension was prepared with a turbidity equivalent to 0.5 McFarland standards in nutrient broth. After a preparation time of 15 minutes, a sterile cotton swab was immersed in the suspension, rotated several times, and pressed against the inner wall of the tube above the liquid level. This swab was then used to streak the inoculum onto the dried surface of a Mueller–Hinton agar (MHA) plate. To achieve an even distribution, the swab was streaked an additional two times at 45° angles over the agar. Following a rest period of 3-5 minutes, antibiotic disks were placed on the agar and gently pushed down to ensure complete contact. The disks were arranged with a minimum distance of 24 mm apart (centre to centre). The plates were then inverted and incubated aerobically at 37°C for 16-18 hours, ensuring this was done within 15 minutes after placing the disks. The antibiotic susceptibility of the isolates was categorised based on zone diameter: ≥23 mm as sensitive (S), between 20-22 mm as intermediate (I), and ≤19 mm as resistant (R), according to CLSI breakpoints for Enterobacterales (excluding *Salmonella/Shigella*), after performing quality control with control strains (ATCC 25922 *Escherichia coli*, ATCC 700603 *Klebsiella pneumoniae*, and ATCC 35218 *Escherichia coli*) [10].

Characterisation of samples: Of the 835 gram-negative isolates obtained from various patient samples, 660 isolates were identified as Enterobacterales. Out of these, 141 isolates were found to be resistant to carbapenem drugs, namely Imipenem and Meropenem. These 141 carbapenem-resistant isolates were screened for carbapenemase production using the mCIM method, followed by phenotypic differentiation based on their enzymatic activity into Serine carbapenemase and MBL using eCIM, as per CLSI guidelines [10].

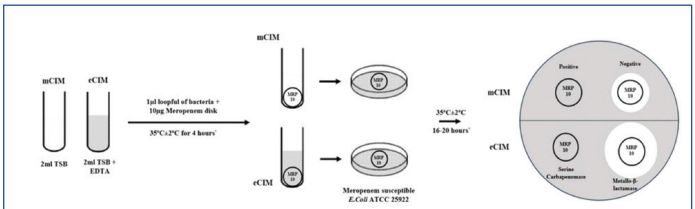
Phenotypic differentiation of samples: A 1-µL loopful of bacteria was suspended in a 2-mL tube containing Tryptone Soya Broth (Himedia SKU: LQ009A). Similarly, another 1-µL loopful of bacteria was suspended in a 2-mL tube of Tryptone Soya Broth supplemented with EDTA at a final concentration of 5 mM, achieved by adding 20 µL of 0.5 M EDTA to 2 mL of TSB. A meropenem disk was placed into each tube and the tubes were incubated at 35°C for 4 hours±15 minutes. After incubation, the disks were removed and transferred onto Mueller-Hinton Agar (MHA) plates freshly inoculated with a 0.5 McFarland suspension of carbapenem-susceptible *E. coli* ATCC 25922. The plates were then incubated at 35°C for 16 to 20 hours, and the results of the mCIM and eCIM tests were interpreted according to CLSI guidelines [10]. [Table/Fig-1] shows comparison of mCIM and eCIM in terms of advantages, disadvantages, clinical use and other features.

Feature	mCIM	eCIM
Purpose	Detects any carbapenemase (KPC, NDM, OXA, etc.,)	Detects metallo- beta-lactamase (MBL) production
Detection type	Phenotypic (enzyme activity)	Phenotypic (enzyme activity)
Sensitivity	High for all carbapenemases	High for MBL producers
Specificity	Detects all carbapenemases, but cannot differentiate types	Detects all MBLs, even unknown variants
Time required	18-24 hours	18-24 hours
Cost	Low (cheap reagents, basic lab setup)	Low (cheap reagents, basic lab setup)
Requirements	Tryptone soya broth, Meropenem disk (10 µg), inoculation loops, Normal saline, MHA plates, Meropenem susceptible indicator strain (*E.coli* ATCC 25922), incubator	Tryptone soya broth, Meropenem disk (10 µg), inoculation loops, Normal saline, MHA plates Meropenem susceptible indicator strain (*E.coli* ATCC 25922), 0.5 M EDTA, incubator

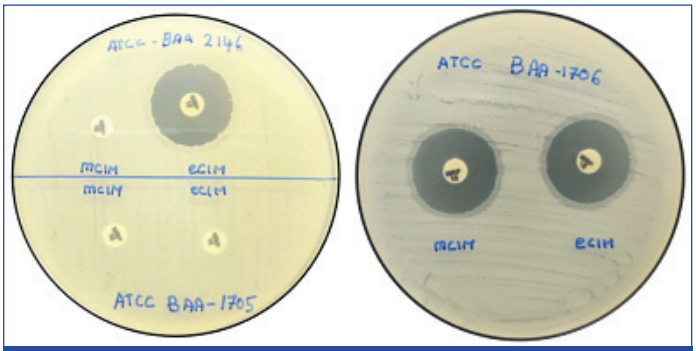
Advantage	Detects all carbapenemases, not just MBLs	Identifies actual enzyme activity, including unknown MBLs
Disadvantage	Cannot differentiate between carbapenemase types	Cannot detect non- MBL carbapenemases (e.g., KPC, OXA- 48)
Clinical use	Helps identify carbapenem-resistant infections	Helps guide treatment decisions for MBL infections

[Table/Fig-1]: Shows comparison between phenotypic tests namely mCIM (Modified Carbapenem Inactivation Method) and eCIM (EDTA modified Carbapenem Inactivation Method) [10].

For the mCIM, a zone size of ≥19 mm is considered negative, while a zone size of 6 to 15 mm is positive. A zone of 16 to 18 mm with pinpoint colonies is considered intermediate and defined as positive [11,12]. An isolate is deemed positive for MBL production if the eCIM zone size increases by ≥5 mm compared to the mCIM zone [Table/Fig-2]. An increase of ≤4 mm indicates a negative result for MBL production. As per CLSI guidelines, the following strains were used as internal controls for the mCIM and eCIM tests: *K. pneumoniae* ATCC BAA-2146 (*bla*$_{NDM}$-positive), *K. pneumoniae* ATCC BAA-1705 (*bla*$_{KPC}$-positive), and *K. pneumoniae* ATCC BAA-1706 (carbapenemase-negative) [Table/Fig-3].

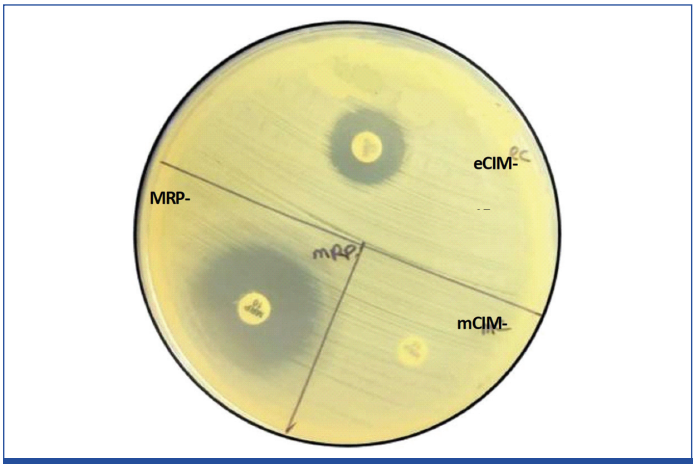


[Table/Fig-2]: Procedure and interpretation of mCIM and eCIM.



[Table/Fig-3]: QC results of mCIM and eCIM methods performed with internal controls ATCC BAA-2146 *Klebsiella pneumoniae bla*$_{NDM}$ (mCIM positive, eCIM positive), ATCC-1705 *Klebsiella pneumoniae bla*$_{KPC}$ (mCIM positive, eCIM negative) and ATCC BAA-1706 *Klebsiella pneumoniae* Carbapenemase (KPC) negative (mCIM negative, eCIM negative).

[Table/Fig-4] shows the zone diameters of eCIM, mCIM, and the meropenem disk against the meropenem-susceptible *Escherichia coli* ATCC 25922 strain. Note the zone diameter of meropenem (26 mm), mCIM (6 mm - positive), and eCIM (15 mm - positive). An increase of ≥5 mm in the zone diameter for eCIM compared to mCIM (15 mm - 6 mm=9 mm) indicates the inhibition of MBL in the presence of EDTA.



[Table/Fig-4]: Zone diameters of eCIM, mCIM and meropenem disk against meropenem susceptible *Escherichia coli* ATCC 25922 strain.
Result: Positive mCIM and eCIM; Report: Metallo-β-lactamase detected

STATISTICAL ANALYSIS

Data analysis involved calculating percentage susceptibility and analysing frequency distribution. The Fisher's exact test was performed using Statistical Package for the Social Sciences (SPSS) Statistics v29.0 to assess whether susceptibility patterns differed significantly between the two carbapenemase enzyme groups (Serine and MBL) when tested for CSE and CZA. A p-value of <0.05 was considered statistically significant.

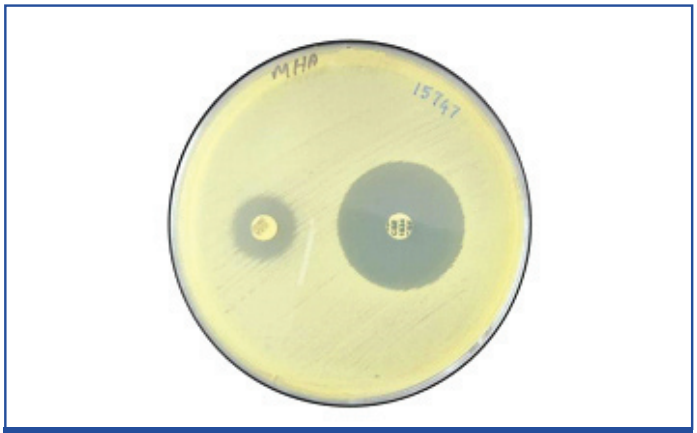
RESULTS

A total of 1,160 samples, including blood, Cerebrospinal Fluid (CSF), sputum, urine, tissue and pus from infected wounds, were collected from inpatients. Among these 1,160 clinical isolates, 835 (72%) were gram-negative isolates. The majority of these isolates were obtained from urine samples (510, 61.08%) and pus from wounds (279, 33.41%), followed by blood (38, 4.55%), sputum (4, 0.5%), tissue samples (3, 0.4%), and tracheal aspirate (1, 0.12%).

The predominant gram-negative pathogens identified were *Escherichia coli* (446, 53.41%) and *Klebsiella pneumoniae* (218, 26.07%), comprising 79% (660) of the total gram-negative isolates. This was followed by *Pseudomonas* spp. (99, 11.87%), *Citrobacter* spp. (49, 5.82%), and *Acinetobacter* species (23, 2.81%). Of these, 141 out of 713 Enterobacterales isolates were resistant to either Imipenem or Meropenem, accounting for 19.77% of Enterobacterales pathogens (*Citrobacter* spp. and Citrobacter spp.) isolated. All these carbapenem-resistant Enterobacterales (CRE) isolates were subsequently screened for carbapenemase production using the mCIM method, according to CLSI guidelines, followed by phenotypic differentiation of MBL from Serine carbapenemase-producing Enterobacterales isolates using eCIM [10].

Out of these 141 CRE isolates, 39 isolates (27.65%) were identified as carbapenemase producers by the mCIM method. Further differentiation using the eCIM method showed that 30 (76.92%) of the carbapenemase-producing isolates were eCIM positive, indicating MBL enzyme producers, while 9 (23.08%) were found to be Serine carbapenemase producers.

Comparison of antimicrobial susceptibility profile between CSE and CZA: Antimicrobial susceptibility testing was performed using the Kirby-Bauer disk diffusion method, according to CLSI guidelines [10]. Antimicrobial disks were placed alongside the CSE (30/15/20 µg) antimicrobial disk. Disk diffusion breakpoints were compared as per CLSI guidelines, which indicated susceptible breakpoints for CZA as ≥21 mm and resistant zone diameter as ≤20 mm [Table/Fig-5].



[Table/Fig-5]: Comparison of zone diameter between Ceftazidime-Avibactam (CZA) (13 mm) and Ceftriaxone Sulbactam-disodium EDTA (CSE) (29 mm) against eCIM positive Metallo-β-lactamase producing isolate.

As susceptibility breakpoints were not available for the CSE combination, Ceftriaxone breakpoints, as per CLSI guidelines for Enterobacterales, were used as reference breakpoints. These were derived based on corresponding Minimum Inhibitory Concentrations (MIC) values by Prabhu M et al., and mentioned in several other studies, including those by Yadav S et al., Gupta S et al., Sanghavi S et al., and Patil UN and Jambulingappa KL which were also similar to the susceptibility breakpoints provided by the manufacturer (Venus Remedies Pvt. Ltd.), indicating susceptible zone diameter as ≥23 mm, intermediate zone diameter between 20-22 mm, and resistant zone diameter as ≤19 mm [13-17].

Antimicrobial susceptibility testing revealed that all 39 carbapenemase-producing isolates were susceptible (100%) to CSE, whereas only 9 (23%) of the Serine carbapenemase-producing isolates were susceptible to CZA, with 30 (77%) of the MBL-producing Enterobacterales isolates showing resistance [Table/Fig-6].

Antimicrobial susceptibility testing	Ceftriaxone+Sulbactam+ Disodium EDTA		Ceftazidime+Avibactam	
	Susceptible	Resistant	Susceptible	Resistant
Metallo β-lactamase	30	0	0	30
Serine carbapenemase	9	0	9	0

[Table/Fig-6]: Comparison of antimicrobial susceptibility pattern between CSE and CZA against Serine Carbapenemase and Metallo-β-Lactamase (MBL) producing Enterobacterales isolates.

All 39 carbapenemase-producing isolates showed susceptibility to the CSE combination. As a result, no statistically significant difference in CSE efficacy was observed between the two groups (Fisher's exact test, p≈1.00), indicating that CSE retains broad-spectrum activity irrespective of the carbapenemase class. In contrast, marked variability was noted in the activity of CZA. All serine carbapenemase producers were susceptible to CZA, whereas none of the MBL producers were susceptible. This difference was statistically significant (Fisher's exact test, $p \approx 1.46 \times 10^{-9}$), underscoring a highly significant association between the type of carbapenemase enzyme produced and its susceptibility to CZA, exhibiting limited efficacy against MBL-producing isolates. These findings are consistent with known resistance mechanisms, as avibactam, a β-lactamase inhibitor in CZA, is ineffective against MBLs but retains activity against Serine carbapenemases [Table/Fig-7].

Antibiotic tested	Type of carbapenemase enzyme	Susceptible	Resistant	p-value	Statistical significance
Ceftriaxone+Sulbactam+Disodium EDTA (CSE)	Metallo β-lactamase	30	0	1.0	No statistically significant difference (all isolates susceptible)
	Serine carbapenemase	9	0		
Serine carbapenemase	Metallo β-lactamase	0	30	1.46×10^{-9}	Highly significant (p-value <0.05)
	Serine carbapenemase	9	0		

[Table/Fig-7]: Statistical analysis of susceptibility of two antibiotic combinations namely CSE and CZA against Metallo β-lactamase (MBL) and Serine Carbapenemase producing isolates by Fisher's exact test.

DISCUSSION

The establishment of precise techniques for identifying antimicrobial resistance is essential not only for treatment but also for monitoring the spread of resistant bacteria or resistance genes within healthcare settings and the wider community. In this study, the phenotypic characterisation of carbapenemase-producing Enterobacterales using the mCIM-eCIM method showed a sensitivity of 100% and specificity of 98.07%, which is almost identical to the study conducted by Tsai YM et al., which demonstrated a sensitivity of 100% and specificity of 100% [18]. In a similar study conducted by Sfeir MM et al., mCIM-eCIM indicated a sensitivity of 100% and a specificity of 90%, effectively distinguishing between serine- and metal-dependent carbapenemases, suggesting that the inhibition of MBL by EDTA is both specific and dependent on its concentration [11].

In another study conducted by Li J et al., the coincidence rate for the combined mCIM and eCIM was reported to be 97.5% when compared to gene detection methods. A high concordance was observed between mCIM and PCR tests in identifying carbapenemase enzymes, with the exception of one false-positive result from mCIM that failed to detect the five main carbapenemase genes through PCR. The sensitivity was recorded at 100%, specificity at 95.5%, and κ was 0.970 [19].

Moreover, due to limited therapeutic options, there is a need to assess the in-vitro activity of the combination of available antibiotics to guide the therapeutic management of MDR gram-negative bacilli, especially MBL producers. The widespread prevalence of MBLs among increasingly difficult-to-treat organisms underscores the importance of this novel CSE compound, which retains activity against a large number of carbapenemase-producing CRE isolates.

CSE is a Fixed-Dose Combination (FDC) that comprises ceftriaxone, sulbactam and the non antibiotic adjuvant EDTA. While sulbactam permanently binds to beta-lactamases, preventing ceftriaxone from degrading and restoring its action against resistant strains, ceftriaxone, a third-generation cephalosporin, kills bacteria by preventing the synthesis of their cell walls. By neutralising the key metal ions (Zn^{2+}, Ca^{2+}, and Mg^{2+}) needed for MBL activity, EDTA amplifies this action. Additionally, EDTA improves antibiotic penetration by breaking down the bacterial outer membrane. CSE is highly effective against MDR bacteria, including strains that produce MBL and ESBL, thanks to the combined action of these compounds. By eliminating biofilms, preventing curli formation, and lowering the expression of efflux transporters, CSE overcomes antibiotic resistance and provides advantages over ceftriaxone and sulbactam alone. CSE significantly lowers MICs by targeting multiple bacterial pathways, making it several times more effective than broad-spectrum antibiotics like cefoperazone-sulbactam, piperacillin-tazobactam, meropenem and ceftriaxone [20-22].

In this present study, CSE showed an in vitro susceptibility of 100% against both serine carbapenemase and MBL-producing Enterobacterales isolates [Table/Fig-6]. A study carried out in vitro by Naseema S et al., assessed the effectiveness of CSE against MDR strains isolated from ICU patients and confirmed by Vitek-II, revealing an overall susceptibility of 88% against CSE, with 12% resistance [23].

This study primarily focuses on comparing the in-vitro efficacy of CSE and CZA against carbapenemase-producing Enterobacterales isolates, categorised based on their phenotypic characterisation. However, it does not address their in-vivo efficacy or the clinical outcomes of the patients, which remains a gap to be addressed in future studies. Furthermore, future studies will also include antimicrobial susceptibility testing of non Enterobacterales isolates of clinical significance, such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, against the CSE combination.

Limitation(s)

This study had certain limitations, particularly regarding the comparison with other novel antibiotics such as CZA in combination with Aztreonam, Cefiderocol, Ceftolozane-Tazobactam, Meropenem-Vaborbactam-Aztreonam and Imipenem-Cilastatin-Relebactam. Additionally, the optimal effective dose of EDTA requires further clinical investigation. The sample size was relatively limited, which could sometimes lead to random variations in results, potentially causing inconsistencies in yielding more reliable and accurate

conclusions across multiple large-scale studies. Furthermore, there is a scarcity of research on the clinical efficacy, standardised reference breakpoints, safety profile, as well as Pharmacokinetic/Pharmacodynamic (PK/PD) indices of this novel CSE combination.

CONCLUSION(S)

The eCIM test offers several advantages, including its simplicity, cost-effectiveness and rapidity in detecting MBL-producing Enterobacterales. It does not require specialised equipment or molecular techniques, making it accessible to most clinical laboratories. This helps guide antimicrobial therapy by identifying resistant strains, ensuring more effective treatment and reducing the spread of resistance. Additionally, it can be integrated into routine microbiological practices, making it a valuable tool for both diagnostic use and surveillance of bacterial resistance. Based on the antimicrobial susceptibility testing performed in-vitro, this novel combination agent, CSE, displays potent activity against CREs, particularly NDM-producing isolates. It could also serve as a carbapenem-sparing drug for carbapenem-susceptible organisms and as a colistin-sparing drug for carbapenem-resistant organisms. Based on this study, it is highly recommended to add CSE to the routine susceptibility panel, as it shows potential as an effective treatment option against Serine and MBL producers.

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