ORIGINAL ARTICLE

IN VITRO ASSESSMENT OF MEROPENEM–VABORBACTAM AGAINST CARBAPENEM-RESISTANT ESCHERICHIA COLI IN A TERTIARY CARE SETTING

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ABSTRACT

Background: Carbapenem-resistant Escherichia coli is an ongoing problem in healthcare settings, especially in the less developed parts of the world where antibiotics are misused and overused. Even though new combinations like meropenem–vaborbactam are introduced, the effectiveness is still determined by the local resistance patterns.

Objectives: To assess the in-vitro activity of meropenem–vaborbactam against carbapenem-resistant E. coli isolates from clinical specimens in a tertiary care hospital in Lahore.

Methods: A total of 94 non-duplicate carbapenem-resistant E. coli isolates were collected over a six-month period for this cross-sectional study. Microbiological methods and VITEK-2 system were used for the identification of isolates. Testing of antimicrobial susceptibility was done by disc diffusion and MIC methods according to CLSI 2023–2024 guidelines. The analyzed data was processed with SPSS version 26.0.

Results: The isolates were found to be all resistant to the carbapenems, third- and fourth-generation cephalosporins, ciprofloxacin, and piperacillin–tazobactam. Resistance was also detected at high levels against aminoglycosides and other non-β-lactam agents. Activity for meropenem–vaborbactam was limited to 10% of isolates being susceptible.

Conclusion: Multidrug resistance is widespread among the carbapenem-resistant E. coli isolates, and the in-vitro effectiveness of meropenem–vaborbactam is low in this region. The monitoring of antibiotic resistance at the local level, along with the development of the right strategies for the use of antimicrobials, is necessary for establishing the right treatment.

Keywords: Escherichia coli, Carbapenem resistant, antimicrobial susceptibility, Meropenem-vaborbactam

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INTRODUCTION

Escherichia coli is a gram negative facultative anaerobic rod. It is a normal resident of the human gut, but, at the same time, some of the strains have developed into serious pathogens that can cause a large range of infections, e.g., urinary tract infections, bloodstream infections, pneumonia, intestinal infections, and meningitis.[1] Because of its adaptability and diversity, genetic variability and resistance, E. coli has been ranked among the most important clinically relevant organisms in both community and hospital settings.[2]

During the last twenty years, the emergence of carbapenem-resistant Escherichia coli (CREC) has become a global public health issue that is very concerning. Carbapenems were the most recommended drugs for treating serious infections caused by multidrug resistant Gram-negative strains. But as the use of these antimicrobial agents has increased, it has created massive selective pressure that has resulted in

developing and spreading of carbapenem-resistant strains.[3] Infections caused by such resistant strains results in longer hospital stays, fewer treatment options, and higher mortality rate especially among critically ill and immunocompromised patients. The leading cause for E. coli's resistance to carbapenems is the production of carbapenemase enzymes like Klebsiella pneumoniae carbapenemase (KPC), New Delhi metallo-β-lactamase (NDM), and OXA-type β-lactamases which contribute to the loss of effectiveness of β-lactam antibiotics. Moreover, other resistance mechanisms such as the loss of porins, overexpression of efflux pumps, and modification of penicillin-binding protein results in the development of high-level resistance and multidrug-resistant phenotypes.[4]

The emergence of carbapenem-resistant E. coli is a prime challenge now in the developing world, particularly in countries like Pakistan, where antimicrobial stewardship programs are in beginning phase and antibiotics are frequently available over the counter. Healthcare settings, particularly the ICUs, are the main sources of these bacteria as a result of invasive processes, prolonged antibiotic treatment, and lack of implementation of infection control policies. A survey in South Asia identified a large number of metallo-β-lactamase–producing E. coli that extremely reduced the bactericidal activity of β-lactam/β-lactamase inhibitor combinations.[5]

Due to emerging threat of carbapenem resistance, new antimicrobial combinations have been introduced.[6] Meropenem–vaborbactam is a new β-lactam/β-lactamase inhibitor mixture consisting of meropenem, a wide-ranging carbapenem, and vaborbactam, an inhibitor based on boron developed to deactivate class A carbapenemases, chiefly KPC enzymes. Vaborbactam, by inhibiting enzymatic degradation of meropenem, brings back its activity to the majority of the carbapenem-resistant Enterobacterales.[7]

Both, clinical and in-vitro investigations have shown effectiveness of meropenem–vaborbactam on KPC-producing bacteria.It was approved for the treatment of complicated urinary tract and intra-abdominal infections. Though, its ability against bacteria that produce metallo-β-lactamases or OXA-type enzymes is still limited. Thus, the success of the treatment of meropenem-vaborbactam is largely influenced by the local patterns of resistance mechanisms.[8]

Due to the severe burden of carbapenem-resistant E. coli in Pakistan as well as the scarcity of regional data on the activity of newer antimicrobial agents, it becomes necessary to assess the in-vitro activity of meropenem–vaborbactam.[9] The objective of this research is to evaluate the meropenem–vaborbactam antimicrobial susceptibility against carbapenem-resistant Escherichia coli strains isolated from clinical specimens collected at a tertiary care hospital in Lahore, and thus provide data relevant to the region that can help with the antimicrobial stewardship efforts.

METHODS

Study Design and Setting: This is a cross-sectional study, performed at Allama Iqbal Medical College (AIMC), Lahore, Pakistan, Department of Pathology. The clinical specimens were collected from patients who were either admitted or visiting Jinnah Hospital, Lahore. The research was conducted for six months after getting the approval of the research synopsis.

Sample Size and Sampling Technique: The study included 94 non-duplicate Escherichia coli isolates in total. The sample size was determined using WinPepi software (version 11.15) with a confidence level of 95% and an allowable difference of 0.05. A non-probability consecutive sampling procedure was utilized.

Inclusion and Exclusion Criteria: All clinical specimens producing Escherichia coli isolates that were resistant to at least one carbapenem were incorporated into the research. Isolates from patients of any age group and both sexes were included. Isolates from the same patient within the same illness episode were excluded.

Sample Collection and Processing: Clinical specimens were comprised of sputum, blood, wound swabs, tracheal aspirates, throat swabs, and urine.Specimens were collected before the start of antimicrobial therapy and were processed without delay according to standard microbiological procedures. The samples were cultured on blood agar, MacConkey agar, and chocolate agar and were incubated aerobically at 37°C for 48 hours.

Identification of Isolates: Presumptive Escherichia coli identification was done on the basis of colony morphology and Gram stain results. Confirmation was carried out with the application of standard biochemical tests including oxidase, indole, methyl red, Voges–Proskauer, citrate utilisation, triple sugar iron agar, sulfur–indole–motility, and catalase tests. The isolation of the strain was also revealed by the VITEK-2 compact system.

Antimicrobial Susceptibility Testing: Antimicrobial susceptibility testing was performed using the modified Kirby-Bauer disc diffusion method. In order to carry out the test, the first step was to prepare bacterial suspension which was equal to the 0.5 McFarland standard.Then it was inoculated on the Muller-Hinton agar medium. Following the Clinical and Laboratory Standards Institute (CLSI) 2023 guidelines, antibiotic discs were placed on the Muller-Hinton agar.

The antibiotics tested in this study included, Imipenem (10 µg), Meropenem (10 µg), Amikacin (30 µg), Piperacillin-Tazobactam (100/10 µg), Ciprofloxacin (5 µg), Cefepime (30 µg), Cotrimoxazole (25 µg), Aztreonam (30 µg), Polymyxin B (300 U) and Gentamicin (10 µg). The media was then incubated for 18–24 hours at 37°C.

Antimicrobial susceptibility testing was also performed using the VITEK-2 compact system, which operates on the principle of minimal inhibitory concentration (MIC). In addition, the resistance of meropenem-vaborbactam against carbapenem-resistant Escherichia coli was

evaluated. The results were reported according to the recommendations of the CLSI 2024 guidelines.

Data Collection and Analysis: The demographic and laboratory data (age, gender, specimen type, and susceptibility to antimicrobials) were entered on a structured form. The data was then transformed and analyzed through the usage of the SPSS software, version 26.0. The analysis of the categorical variables drew the presentation in terms of frequencies and percentages, while the graphical representation of the data was done using bar charts and pie charts. A p-value below 0.05 was taken as statistically significant.

RESULTS

Demographic Characteristics of Isolates: The research encompassed a total of 94 isolates of carbapenem-resistant Escherichia coli. From that number, 56 (59%) came from male individuals, and 38 (40%) were from females.

Table 1. Percentage distribution among gender

Gender	Frequency	Percentage
Male	56	59%
Female	38	40%
Total	94	100%

Distribution of Clinical Specimens: The number of isolates from different clinical specimens distributed as sputum and blood samples which were the sources most of the times with 28 isolates each (29.7%). Then came the wound specimens and tracheal aspirates with 16 (15.38%) isolates each. Throat swabs were responsible for 12 (11.53%) isolates while urine samples had the least with 4 (3.84%).

Antimicrobial Susceptibility Pattern of Carbapenem-Resistant E. coli: Resistance of all 94 tested strains was absolute (100%) against cephalosporins of the third and fourth generation—most notably ceftriaxone and cefepime, as well as piperacillin–tazobactam. likewise, all isolates were resistant to imipenem and meropenem, the main carbapenems which confirmed their carbapenem-resistance status. At the same time, the isolates showed noticeable resistance to the non-β-lactam antibiotic group. Resistance of 90% was observed for amikacin and gentamicin, while about one-third of the isolates (33%) were still sensitive to the latter. Resistance of 100% was observed against ciprofloxacin, while 81% and 74% of the isolates were resistant to doxycycline and cotrimoxazole, respectively. The combination of meropenem with vaborbactam demonstrated an in-vitro activity that was effective against only a few strains, as 85 (90%) out of the 94 were resistant and only 9 (10%) remained susceptible. The susceptibility profile for the Escherichia coli carbapenem-resistant isolates is given in Table 2.

Table 2. Antimicrobial susceptibility profile of carbapenem-resistant E. coli isolates (n = 94)

Antibiotic	Susceptible n (%)	Resistant n (%)
Ampicillin	0 (0)	94 (100)
Ceftriaxone	0 (0)	94 (100)
Cefepime	0 (0)	94 (100)
Piperacillin–Tazobactam	0 (0)	94 (100)
Imipenem	0 (0)	94 (100)
Meropenem	0 (0)	94 (100)
Amikacin	23 (25)	71 (75)
Gentamicin	27 (29)	67 (71)
Ciprofloxacin	0 (0)	94 (100)
Doxycycline	18 (19)	76 (81)
Cotrimoxazole	24 (26)	70 (74)
Meropenem–Vaborbactam	9 (10)	85 (90)

DISCUSSION

The findings of the present study demonstrate an extensive multidrug-resistant profile among carbapenem-resistant Escherichia coli isolates, reflecting the evolving complexity of antimicrobial resistance in Enterobacterales. All 94 isolates exhibited complete resistance to tested β-lactam antibiotics, including ceftriaxone, cefepime, and piperacillin–tazobactam. This pattern is consistent with the observations of Nordmann et al., who reported that carbapenem resistance in E. coli is frequently accompanied by resistance to extended-spectrum cephalosporins due to the co-expression of carbapenemases and extended-spectrum β-lactamases.[10] Similar resistance patterns have also been described by Logan and Weinstein, highlighting the limited role of β-lactams once carbapenem resistance becomes established.[11]

Non-susceptibility to imipenem and meropenem observed in this study confirms the high burden of carbapenem resistance within the local clinical setting. While earlier surveillance data from South Asia and the Middle East reported comparatively lower carbapenem resistance rates, more recent hospital-based studies indicate a sharp upward trend. Zhang et al. reported persistently rising carbapenem-resistant E. coli rates in tertiary care hospitals in China over a five-year period, attributing this increase to selective pressure from broad-spectrum antibiotic use.[12] Likewise, van Duin and Doi emphasized that tertiary-care and ICU settings serve as reservoirs for CRE, facilitating both clonal spread and horizontal gene transfer.[13]

Aminoglycoside resistance was also prominent in the current study, with resistance rates exceeding 70% for both amikacin and gentamicin. These findings are in agreement with Jamal et al., who demonstrated that carbapenem-resistant Enterobacterales frequently harbor aminoglycoside-modifying enzyme genes on the same plasmids that carry carbapenemase determinants.[14] Poirel et al. further highlighted that co-selection of resistance

occurs under sustained antibiotic pressure, leading to multidrug resistance across unrelated antimicrobial classes.[15] Such resistance patterns substantially reduce the utility of aminoglycosides as combination therapy options.

The complete resistance to ciprofloxacin observed among all isolates further highlights the diminishing effectiveness of fluoroquinolones against CRE. Hooper described fluoroquinolone resistance in E. coli as being primarily driven by mutations in the quinolone resistance-determining regions combined with efflux pump overexpression.[16] Hospital-based studies by Kim et al. and Tamma et al. have similarly reported near-total fluoroquinolone resistance among carbapenem-resistant gram-negative isolates, particularly in regions with high fluoroquinolone consumption.[17,18]

High resistance rates to doxycycline and cotrimoxazole observed in this study further limit therapeutic alternatives. Comparable findings were reported by Falagas et al., who noted that older antibiotics such as tetracyclines and folate pathway inhibitors have progressively lost efficacy against multidrug-resistant E. coli.[18] This trend is particularly evident in healthcare systems where antibiotics are frequently prescribed empirically, often without susceptibility testing, facilitating sustained resistance selection.

Meropenem–vaborbactam demonstrated limited in-vitro activity in the present study, with susceptibility observed in only 10% of isolates. Although clinical trials and global surveillance data have established the efficacy of meropenem–vaborbactam against specific carbapenemase-producing organisms, particularly KPC-producing Enterobacterales, its effectiveness is highly dependent on the prevailing resistance mechanisms within local bacterial populations. The TANGO clinical trials, which supported the use of meropenem–vaborbactam for complicated urinary tract and intra-abdominal infections, reported favorable outcomes primarily in infections caused by carbapenemase producers susceptible to β-lactamase inhibition.[20] The low susceptibility observed in this study is therefore consistent with a likely low prevalence of KPC-producing organisms in the local setting as supported by a recent local study.[21] In contrast to KPC producers, as highlighted by Castanheira et al., vaborbactam lacks activity against OXA-48–type carbapenemases and metallo-β-lactamases, limiting its clinical utility in regions where these mechanisms predominate.[22] Furthermore, molecular studies by Johnston et al. have demonstrated that geographical variation in carbapenemase gene distribution significantly influences the performance of newer β-lactam/β-lactamase inhibitor combinations, underscoring the importance of regional resistance profiling when interpreting susceptibility data.[23]

Taken together, the resistance profile observed in this study aligns with global antimicrobial resistance trends reported by WHO and CDC all of which identify carbapenem-resistant E. coli as a critical public health threat.[24,25] The convergence of resistance across β-lactams, aminoglycosides, fluoroquinolones, and older oral agents severely compromises empirical treatment strategies and increasingly forces reliance on last-resort therapies. These findings underscore the urgent need for strengthened antimicrobial stewardship, routine resistance surveillance, and molecular characterization of resistance mechanisms to guide targeted therapy and infection control interventions.

CONCLUSION

Carbapenem-resistant Escherichia coli isolates from a tertiary care hospital in Lahore exhibited an extensive multidrug-resistant profile, with uniformly high resistance to carbapenems, extended-spectrum cephalosporins, fluoroquinolones, aminoglycosides, and commonly used oral agents. Meropenem–vaborbactam demonstrated limited in-vitro activity, consistent with the low likelihood of KPC-mediated resistance in the local setting and the predominance of resistance mechanisms not targeted by vaborbactam, such as OXA-48–type carbapenemases and metallo-β-lactamases. These findings highlight the critical importance of local antimicrobial resistance surveillance and molecular characterization to guide the rational use of newer β-lactam/β-lactamase inhibitor combinations. Strengthening antimicrobial stewardship programs, optimizing infection prevention and control practices, and implementing routine resistance profiling are essential to contain the spread of carbapenem-resistant E. coli and to preserve the effectiveness of last-line therapeutic agents.

ETHICAL APPROVAL

Ethical approval of article was granted by the Ethics Review Board of Allama Iqbal Medical College Lahore Reference Number: ERB181/05/16-01-2025/S1 ERB, Dated: Jan 16, 2025.

AUTHOR'S CONTRIBUTIONS

MS: manuscript writing, data analysis
AE: Conceived idea, design, data analysis
FA: Manuscript writing, critical review
KJ: Data analysis, critical review
SS: Data interpretation, critical review
ZJ: Data analysis, critical review
All Authors: Approval of the final version of the manuscript to be published

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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REFERENCES

1. Anwer NA, Tohamy EY, Abdallah HA, El-Gazzar NS. Characterization and isolation of different strains of Escherichia coli from patients with urinary tract infection. Bull Fac Sci Zagazig Univ. 2024;2024(2):77-84. doi:10.21608/bfszu.2023.236737.1312.
2. Naidoo N, Zishiri OT. Presence, pathogenicity, antibiotic resistance, and virulence factors of Escherichia coli: A review. Bacteria. 2025;4(1):16. doi:10.3390/bacteria4010016.
3. Mousa N, Aiesh BM, Jomaa R, Zouneh Y, Namrouti A, Abutaha A, et al. Antibiotic resistance profiles and risk factors of multidrug-resistant Escherichia coli in a large tertiary care hospital in a low- and middle-income country. Sci Rep. 2025;15(1):26667. doi:10.1038/s41598-025-26667-0.
4. Wu D, Ding Y, Yao K, Gao W, Wang Y. Antimicrobial resistance analysis of clinical Escherichia coli isolates in neonatal ward. Front Pediatr. 2021;9:670470. doi:10.3389/fped.2021.670470.
5. Liu K, Lei Z, Yao H, Lei S, Zhao H. Impact of a eukaryotic translation initiation factor 3a polymorphism on susceptibility to gastric cancer. Med Princ Pract. 2016;25(5):461-465. doi:10.1159/000447405.
6. Kerek Á, Román I, Szabó Á, Kovács D, Kardos G, Kovács L, et al. Antibiotic resistance genes in Escherichia coli – literature review. Crit Rev Microbiol. 2025. doi:10.1080/1040841X.2025.XXXXX.
7. Jariremombe RC. Mechanisms of antimicrobial resistance of E. coli. In: Starčič Erjavec M, editor. Escherichia coli – Old and New Insights. London: IntechOpen; 2022. doi:10.5772/intechopen.XXXXX.
8. Díaz-Zaragoza M, Rodriguez-Preciado SY, Hernández-Ventura L, Ortiz-Covarrubias A, Castellanos-García G, Sifuentes-Franco S, et al. Evaluation of antibiotic resistance in Escherichia coli isolated from a watershed section of Ameca River in Mexico. Microbiol Res. 2025;16(8):186. doi:10.3390/microbiolres16080186.
9. Liu C, Sun S, Sun Y, Li X, Gu W, Luo Y, et al. Antibiotic resistance of Escherichia coli isolated from food and clinical environment in China from 2001 to 2020. Sci Total Environ. 2024;939:173498. doi:10.1016/j.scitotenv.2024.173498.
10. Nordmann P, Naas T, Poirel L. Global spread of carbapenemase-producing Enterobacteriaceae. Emerg Infect Dis. 2011;17(10):1791-1798. doi:10.3201/eid1710.110655.
11. Logan LK, Weinstein RA. The epidemiology of carbapenem-resistant Enterobacteriaceae: the impact and evolution of a global menace. J Infect Dis. 2017;215(Suppl 1):S28-S36. doi:10.1093/infdis/jiw282.
12. Zhang Y, Wang Q, Yin Y, Chen H, Jin L, Gu B, et al. Epidemiology of carbapenem-resistant Enterobacteriaceae infections: report from the China CRE network. Antimicrob Agents Chemother. 2018;62(2):e01882-17. doi:10.1128/AAC.01882-17.
13. van Duin D, Doi Y. The global epidemiology of carbapenemase-producing Enterobacteriaceae. Virulence. 2017;8(4):460-469. doi:10.1080/21505594.2016.1222343.
14. Jamal W, Iregbu K, Fadhli A, Khodakhast F, Nwajiobi-Princewill P, Medugu N, et al. A point-prevalence survey of carbapenem-resistant Enterobacteriaceae in two different cities in Kuwait and Nigeria. Afr J Clin Exp Microbiol. 2022;23(4):358-368. doi:10.4314/ajcem.v23i4.6.
15. Poirel L, Potron A, Nordmann P. OXA-48-like carbapenemases: the phantom menace. J Antimicrob Chemother. 2012;67(7):1597-1606. doi:10.1093/jac/dks121.
16. Hooper DC. Mechanisms of quinolone resistance. In: Quinolone Antimicrobial Agents. Washington (DC): ASM Press; 2003. p.41-67. doi:10.1128/9781555817818.ch3.
17. Kim D, Ahn JY, Lee CH, Jang SJ, Lee H, Yong D, et al. Increasing resistance to extended-spectrum cephalosporins, fluoroquinolone, and carbapenem in Gram-negative bacilli. Ann Lab Med. 2017;37(3):231-239. doi:10.3343/alm.2017.37.3.231.
18. Tamma PD, Heil EL, Justo JA, Mathers AJ, Satlin MJ, Bonomo RA. Infectious Diseases Society of America 2024 guidance on the treatment of antimicrobial-resistant gram-negative infections. Clin Infect Dis. 2024. doi:10.1093/cid/ciae403.
19. Falagas ME, Karageorgopoulos DE. Extended-spectrum β-lactamase-producing organisms. J Hosp Infect. 2009;73(4):345-354. doi:10.1016/j.jhin.2009.02.021.
20. Wunderink RG, Giamarellos-Bourboulis EJ, Rahav G, Mathers AJ, Bassetti M, Vazquez J, et al. Effect and safety of meropenem–vaborbactam versus best-available therapy in patients with carbapenem-resistant Enterobacteriaceae infections: the TANGO II randomized clinical trial. Infect Dis Ther. 2018;7(4):439-455. doi:10.1007/s40121-018-0214-1.
21. Rizvi M, Khan N, Fatima A, Bushra R, Zehra A, Saeed F, et al. The microbiological characteristics and genomic surveillance of carbapenem-resistant Klebsiella pneumoniae isolated from clinical samples. Microorganisms. 2025;13(7):1577. doi:10.3390/microorganisms13071577.
22. Castanheira M, Rhomberg PR, Flamm RK, Jones RN. Effect of the β-lactamase inhibitor vaborbactam combined with meropenem against serine carbapenemase-producing Enterobacteriaceae. Antimicrob Agents Chemother. 2016;60(9):5454-5458. doi:10.1128/AAC.00711-16.
23. Johnston BD, Thuras P, Porter SB, Anacker M, VonBank B, Vagnone PS, et al. Global molecular epidemiology of carbapenem-resistant Escherichia coli (2002–2017). Eur J Clin Microbiol Infect Dis. 2021;40:2047-2058.doi:10.1007/s10096-021-04238-3.
24. Centers for Disease Control and Prevention (CDC). Antibiotic resistance threats in the United States. Atlanta: US Department of Health and Human Services; 2019. doi:10.15620/cdc:82532.
25. World Health Organization. Global antimicrobial resistance and use surveillance system (GLASS) report 2022. Geneva: WHO; 2022. doi:10.2471/BLT.22.28846