

Prevalence of Carbapenem-Resistant Enterobacterales, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* in a Tertiary Care Hospital in Eastern India: A Pilot Study

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Abstract

In recent years, a wide range of clinical infections are being caused by carbapenem-resistant Enterobacterales, *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. This is a matter of great concern, as carbapenem-resistant infections have fewer treatment options. The Enterobacterales comprises a large group of bacterial species commonly causing infections in healthcare settings. The most common bacteria are *Escherichia coli* and *Klebsiella pneumoniae*, which can cause both nosocomial and community-acquired infections. This study aimed to determine the prevalence of carbapenem-resistant Enterobacterales, *P. aeruginosa*, and *A. baumannii*, in a tertiary care center in India. The study was conducted over a period of seven months, from May 2022 to November 2022. The specimens were processed at the Microbiology Laboratory of Kalinga Institute of Medical Sciences- Pradyumna Bal Memorial Hospital, Bhubaneswar. Standard procedures were used to process the clinical specimens brought to the laboratory. Carbapenem-resistant isolates were screened according to the CLSI 2022 guidelines. This study included 3,006 isolates of Enterobacterales, *A. baumannii*, and *P. aeruginosa*. Of these, 29.40% (n = 844) were found to be carbapenem resistant. The breakup is as follows: 689 (77.94%) were Enterobacterales, 108 (12.21%) were *A. baumannii*, and 87 (9.84%) were *P. aeruginosa*. Thus, our investigation revealed an overall prevalence of carbapenem-resistant Enterobacterales, *A. baumannii*, and *P. aeruginosa* of 29.40%, which corresponds to previous studies in India. Early patient screening, isolation, and contact prevention measures will help reduce infection transmission. Further, larger multi-centric studies are required to obtain a wider perspective regarding this issue.

Keywords: Carbapenem Resistant, Enterobacterales, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*

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INTRODUCTION

Antimicrobial resistance has become a serious problem for human health in recent decades. The main reasons for antibiotic resistance are the excessive use and improper handling of antibiotics and lack of regulatory constraints. Five main mechanisms are responsible for antibiotic resistance, namely, enzyme modification and inactivation, antibiotic target site modification, target site replacement, efflux pumps and reduced permeability.¹ The members of the order Enterobacterales are the prominent causative agents of gram-negative bacterial infections and are resistant to several classes of antibiotics.² Historically, only the most difficult-to-treat infections have been treated with carbapenems. As multidrug organisms are common in seriously ill patients in intensive care units and other critical areas, carbapenems are being used to treat infections in these locations.^{3,4} However, there is growing concern regarding the increase in carbapenem-resistant Enterobacterales, resulting in increased mortality and global spread.⁵

Organisms that test resistant to at least one of the carbapenem antibiotics (imipenem, meropenem, ertapenem or doripenem) are known as carbapenem-resistant organisms.⁶ The most common carbapenem-resistant organisms are Enterobacterales (CRE; carbapenem-resistant Enterobacterales), *Acinetobacter baumannii* (CRAB; carbapenem-resistant *Acinetobacter baumannii*), and *Pseudomonas aeruginosa* (CRPA; carbapenem-resistant *Pseudomonas aeruginosa*).⁷

The most prominent members of the order Enterobacterales responsible for community-acquired and healthcare-associated infections are *Escherichia coli* and *Klebsiella pneumoniae*. These are among the most prevalent pathogens associated with CRE infections worldwide.⁵ The production of the enzyme carbapenemase, which hydrolyzes carbapenem and other β -lactam compounds, is the primary cause of resistance to carbapenems.¹ In CRE, it is also typical for carbapenemase-encoding genes to move between and within species by horizontal plasmid-mediated transfer.⁷ The overexpression of bacteria-induced efflux pumps, absence of porins in the cell membrane of bacterial cells, and poor binding of

carbapenem to *Penicillin-binding proteins* (PBPs) constitute other mechanisms of resistance.⁸

Patients with infections caused by CRE, CRAB, or CRPA have few treatment options. Therefore, early detection of carbapenem resistance is essential for implementing suitable infection prevention strategies to prevent the spread of carbapenem resistance. In addition, it is important to understand the epidemiology and bacteriology of CRE, CRAB, and CRPA to establish guidelines for realistic therapy, isolation of infectious patients, and contact tracing to stop further spread in healthcare facilities.

The aim of this study is to determine the prevalence of carbapenem-resistant Enterobacterales (CRE), *Acinetobacter baumannii* (CRAB) and *Pseudomonas aeruginosa* (CRPA) in a tertiary care set-up in Odisha.

MATERIALS AND METHODS

Study design and place

A cross-sectional prospective study was performed at the Department of Microbiology, Kalinga Institute of Medical Sciences, KIIT University, Odisha, India.

Ethical approval was obtained from IEC-KIMS (reference no. KIIT/KIMS/IEC/1346/2023) before the study.

Inclusion criteria

Non-repetitive strains and isolates from various clinical specimens were used in this study.

Exclusion criteria

Repetitive isolates from the same patient and microorganisms deemed as colonizers were excluded from the study.

This study took place over a period of seven months (May 2022 to November 2022). All clinical specimens received in the Microbiology Laboratory of PBMH, KIMS, were processed, and identification and antibiotic susceptibility tests (ASTs) were performed according to standard guidelines.

Antimicrobial susceptibility testing

Standard biochemical testing methods were used to identify the clinical isolates.⁹ ASTs

resistant isolates across different areas is shown in Figure 2.

The highest number of carbapenem resistant isolates were collected from the 56-65 age group 183 (20.70%), followed by 66-80 age group 179 (20.24%). A detailed description of distribution of carbapenem resistant isolates among different areas is shown in Figure 3.

DISCUSSION

Serious infections such as ventilator-associated pneumonia, bloodstream infections, community-acquired infections, hospital-

acquired pneumonia, urinary tract infections, and complicated intra-abdominal infections are often associated with the order Enterobacterales. Compared to CREs, carbapenem-resistant *P. aeruginosa* and *A. baumannii* are mainly responsible for mortality and disease. Research on novel antibiotics should focus on carbapenem resistant-non lactose fermenters (CR-NLFs) such as *P. aeruginosa* and *A. baumannii* along with CREs. The clinical and social implications of antibiotic resistance in the Enterobacterales are significant. The emergence of carbapenemase-producing Enterobacterales is an important issue and a consequence of the increasing use of carbapenems

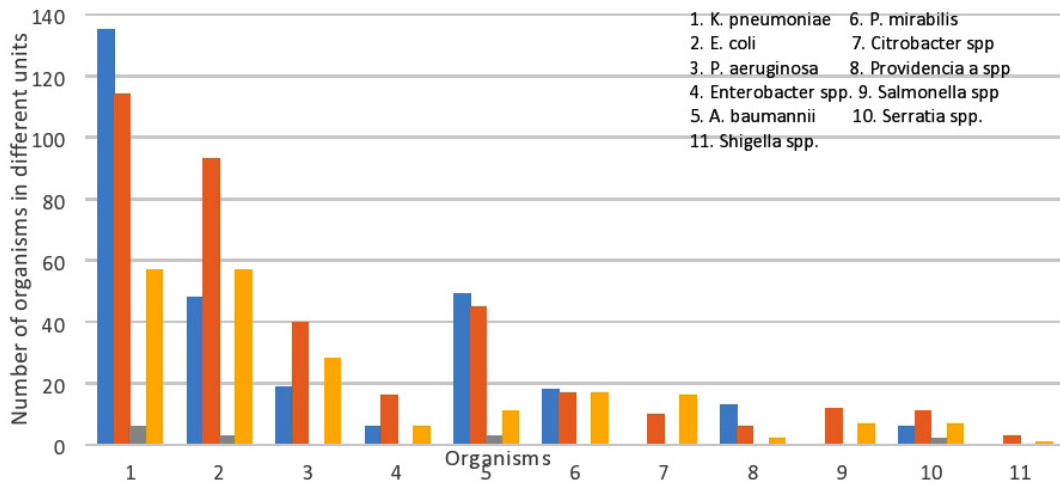


Figure 2. Area wise distribution of CRE, CRAB, and CRPA isolates

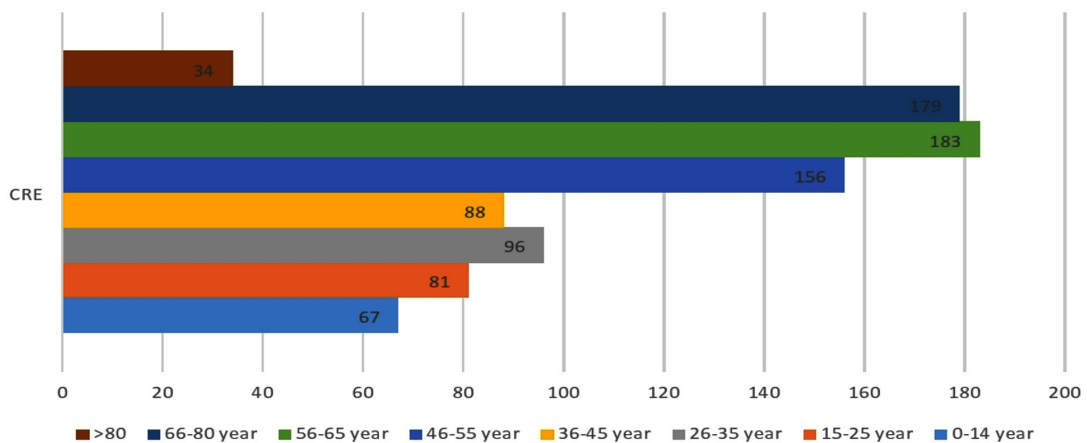


Figure 3. Age wise distribution of CRE, CRAB, and CRPA isolates

in suspected extended-spectrum beta-lactamase infections.¹¹

Carbapenemases are β -lactamases that can hydrolyze carbapenems, monobactams, cephalosporins and penicillins.¹² When it comes to treating infections caused by multidrug-resistant gram-negative bacteria, the drug of choice is carbapenems, leading to the steady increase in the incidence of CRE, CRPA, and CRAB over the last decade.¹³ Accurate and early diagnosis of carbapenem-resistant isolates is important for proper patient care and the prevention of the further spread of resistance within the community. This study determined the prevalence of CRE, CRPA, and CRAB in the tertiary care center to be 29.40%. This is similar to the prevalence of carbapenem resistance in Enterobacterales reported in other studies conducted in India. Srivastava *et al.* reported a prevalence rate of 29.35% in a study conducted in a hospital in North India,¹⁴ while Gupta *et al.*¹⁵ reported carbapenem resistance of 17% to 22% in Northern India. Nair and Vaz¹⁶ reported 26% carbapenem-resistant isolates from Mumbai. In a tertiary care facility in Delhi, Wattal *et al.* reported high carbapenem resistance in Enterobacterales, with a prevalence ranging from 13% to 51%.¹⁷

In our study, the prevalence of CRAB (9.84%) and CRPA (3.16%) which is similar to previous studies by Grewal *et al.*¹⁸ and Bandyopadhyay *et al.*¹⁹ According to Benachinmardi, *et al.*,²⁰ *P. aeruginosa* infections were more common, indicating a recent trend towards an increase in *A. baumannii* infections.

In a sentinel research investigation by CDC, the prevalence of CRPA was 9.1% in several parts of USA.²¹ A survey conducted by the WHO (2015) found that European nations and USA had a CRPA prevalence of 17.8% and 19.2%, respectively.²² According to a study by Gonnalves *et al.*, Brazil's CRPA prevalence was 43.9%.²³ According to a research conducted throughout Asia, the prevalence CRE infections constitute between 0.6-0.9% of all culture-positive infections. Although there is no consistent data on CRE from India, published papers reveal that carbapenem resistance in Enterobacteriaceae ranges between 18-31%.²⁴

In 2014, Chauhan *et al.*¹¹ reported a carbapenem resistance rate of 20.72% in

Enterobacterales, whereas in 2015, Modi *et al.* reported a carbapenem resistance rate of 25.44% in Enterobacterales.¹² Rao and Indumati¹³ reported 13.95% resistance in 2016, and Thomas and Sarwat²⁵ reported a prevalence of 18.54% in 2019. Pawar *et al.*²⁴ reported the rate to be 31.77% for Maharashtra. Kumarasani *et al.*²⁶ reported a prevalence of 23.7% in CRE isolates from Haryana. When distributed by sample, the highest number of carbapenem-resistant isolates were from urine samples, followed by blood, pus and wound swabs, tissues, ET, sputum, and other samples (e.g., vaginal swabs, bronchoalveolar lavage, throat swabs). Our findings are similar to those of a study carried out in India that also showed that urine samples (29, 26.36%) had the highest number of CRE, followed by pus samples (27, 24.54%) and blood samples (22, 20%).²⁷ In another study conducted in northern India as well, the majority of carbapenem-resistant organisms were found in urine (20, 47.1%), followed by pus (13, 27.1%).²⁸ Further, Mohamudha *et al.* observed that urine accounted for 39 (37%) of resistant isolates, followed by blood (23, 22.3%) and wound discharge (12, 11.7%).²⁹

In the present study, the majority of carbapenem resistant isolates were obtained from general wards (367, 41.5%) followed by ICU (294, 33.2%), NICU/PICU (14, 1.5%) and OPD (209, 23.6%). According to a study by Nair & Vaz, the majority of CRE isolates were found in hospitalized patients (42%), followed by OPD (32%) and ICU (26%).³⁰ Chauhan *et al.*³¹ made similar observations as well.

In our study, male dominance (537 patients, 60.75%) was observed, consistent with the reports of Parimala (50.90%),³² and Pawar *et al.* (65.3%).⁴ Among the different age groups included in the study, 427 (48.30%) of those in the 36–65 age group had the most CRAB, CRPA, and CRE, followed by 0–33 years (244, 24.60%) and 66–95 years (213, 24.09%), similar to the reports of Thomas (21–40 years, 33.25% with the most CRE, followed by 41–65 years, 30%).²⁵

CONCLUSION

This study focuses on the prevalence of carbapenem resistance among commonly isolated gram negative bacteria, which is a major

concern not only for treating physicians but also for infection control professionals. The prevalence of CRE, CRPA, and CRAB in this study was 29.40%, which corresponds with the prevalence reported in most previous studies in India. Our study also highlights the urgent need for proper surveillance and the introduction of appropriate infection control measures in this sector, as well as the need for the limited use of carbapenem antibiotics to stop the spread of carbapenem resistance. The number of drug-resistant microorganisms can be reduced by adherence to antimicrobial stewardship programs and antibiotic guidelines, including those for carbapenem antibiotics. Because patients with carbapenem-resistant infections require more antibiotic treatments and have longer hospital and intensive care stays and higher mortality rates, carbapenem-resistant infections are likely to be more costly to the healthcare system. More importantly, CR-NLFs such as *P. aeruginosa* and *A. baumannii* should be considered in the development of new antibiotics, in addition to CREs.

Limitations

Genotypic study for genes responsible for carbapenem resistance is further required to know the accurate results.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

FUNDING

None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

This study was approved by the Institutional Ethics Committee, Kalinga Institute of Medical Sciences, Bhubaneswar, India, with reference no. KIIT/KIMS/IEC/1346/2023.

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