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Microbiological epidemiology and clinical outcomes of carbapenem-resistant Enterobacterales and *Pseudomonas aeruginosa* infections in adult patients admitted to intensive care in India: A multicenter observational study

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BACKGROUND & METHODS

Introduction

There is a scarcity of studies understanding the epidemiology and management of carbapenem-resistant Enterobacterales (CRE) and *P. aeruginosa* (CRPA) infections in India. This study assessed the microbiological epidemiology, treatment patterns and clinical outcomes of patients with confirmed CRE/CRPA infections across Indian tertiary care centres.

Study setting and population

This observational feasibility study enrolled patients between April 2023 to April 2024 from tertiary care referral hospitals across five states in India, namely Kasturba Medical College, Manipal, Karnataka; Christian Medical College, Vellore, Tamil Nadu; Tata Medical Center, Kolkata, West Bengal; P.D. Hinduja Hospital & Medical Research Centre, Mumbai, Maharashtra; and Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh.

Part A enrolled severely ill adult patients (≥ 18 years-old) admitted to the intensive care unit (ICU) who were diagnosed with infections due to CRE/CRPA. Types of infections included complicated urinary tract infection (cUTI), complicated intra-abdominal infections (cIAI), acute bacterial skin and skin structure infections (ABSSSIs), hospital-acquired and ventilator-associated bacterial pneumonia (HAP/VAP), and bloodstream infections (BSIs).

The study was approved by the Health Ministry's Screening Committee and Institutional Ethics Committees.

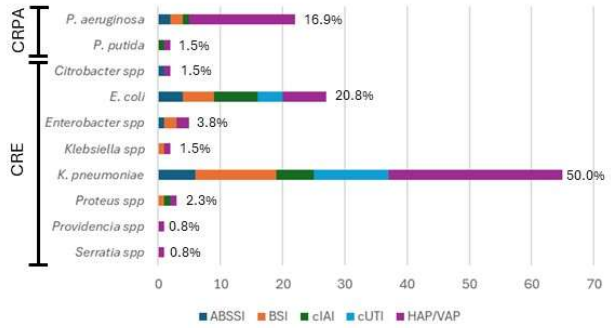
Procedures and Assessments

Determination of initial eligibility of CRE/CRPA isolates was performed in local microbiology laboratories following standard operating procedures. Non-duplicate bacterial isolates, isolated from any clinically relevant site, underwent identification through biochemical methods (e.g. Vitek) or MALDI-TOF MS technique. *In vitro* susceptibility testing (AST) was conducted following Clinical and Laboratory Standard Institute (CLSI) guidelines and interpretive breakpoint values[2]. Tigecycline and colistin susceptibility was interpreted according to the relevant or appropriate breakpoints, FDA[3] and EUCAST[4], respectively. If susceptibility to a particular antibiotic was not reported, the organism susceptibility was coded as "not available".

Management of patients was according to the site's standard of care. Retrospective demographic, medical history, and clinical management data were collected from before the confirmation of the CRE/CRPA infection and prospective data was collected for the acute phase of treatment. Patients were followed for 28 days from the day the specimen that confirmed CRE/CRPA infection was collected or until death/discharge, whichever was earlier.

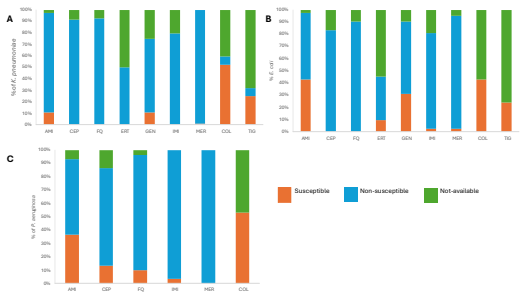
RESULTS

Figure 1- Microbial diagnosis in India according to organism with site of infection defined by colour



Dark blue = Acute bacterial skin and skin structure infections, Orange = blood stream infection, Green = Complicated intra-abdominal infection, Light blue = Complicated urinary tract infection, Purple = Hospital acquired/Ventilator associated pneumonia. The rates of each organism are indicated by the percentage.

Figure 2- *in vitro* susceptibility of *Klebsiella pneumoniae* (A), *Escherichia coli* (B) and *P. aeruginosa* (C) isolates to antibiotics routinely tested in the sites.



*AMI=amikacin; CEP= cefepime; FQ= fluoroquinolone; ERT=ertapenem; GEN=gentamicin; IMI=imipenem; MER= meropenem; COL= colistin; TIG= tigecycline.

Main Findings:

- A total of 106 patients were enrolled, and the most common diagnosis was hospital/ventilator associated pneumonia (51 patients; 48.1%)(Figure 1).
- Among 130 isolates, *Klebsiella pneumoniae* was the most prevalent species (65), followed by *Escherichia coli* (26) and *P. aeruginosa* (23).
- In addition to carbapenem resistance, resistance to fluoroquinolones (97%) was very high among 105 isolates tested (Figure 2).
- Susceptibility to Amikacin was low in *K. pneumoniae* (7/64 tested; 10.9%), but modest for *E. coli* (11/25 tested; 44%). Resistance to colistin was observed in 13% *K. pneumoniae* (4/30 tested) isolates (Figure 2).
- The most commonly administered treatment was meropenem (n=68), predominantly administered empirically.
- The next most common were polymyxin B (n=50), ceftazidime/avibactam +/- aztreonam (n=49) and teicoplanin (n=35).
- The 28-day mortality rate was 34.9% and clinical success at test of cure (7 days after end of treatment) was 60.8%.

CONCLUSIONS

CRE/CRPA infections are an increasing problem in India. Despite the introduction of new therapies, treatment options remain limited. Development of and access to novel treatments are urgently needed.

References:

1. Antimicrobial Resistance Collaborators (2022)
2. CLSI, 2018. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 11th ed. CLSI standard- M07. Wayne, PA 19087-1898 USA
3. https://www.fda.gov/drugs/development-resources/tigecycline-injection-products
4. eucast: MIC determination

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