RES-163

Genomic Epidemiology of Carbapenem-Resistant *Escherichia coli* From Hospitalized Patients From Five Public/Private Hospitals Across India

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BACKGROUND & METHODS

Introduction

The global increasing rates of carbapenem-resistance poses significant challenges to clinical management of patients[1]. In low- and middle-income countries (LMIC) this challenge is further complicated by weak surveillance systems and scarce clinical data. Local surveillance using hospital-level data is important to guide effective treatment for critical patients. GARDP conducted a 2-part, multicentre, prospective, observational study following patients treated for bacterial infections caused by carbapenem-resistant organisms (CROs) in public/private hospitals in India between April 2023 and May 2024. Here we present the genomic characterization of carbapenem-resistant *Escherichia coli* (CR *E. coli*) isolates that were isolated from patients with serious bacterial infections (SBI).

Material & Methods

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. The study consisted of two parts, part A enrolled severely ill adult patients (≥ 18 years-old) admitted to the intensive care unit (ICU) who were diagnosed with infections due to CROs. 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).

Part B enrolled adults diagnosed with complicated urinary tract infections (cUTIs) or acute pyelonephritis (AP) caused by CROs, who was in intravenous (IV) antibiotic regimen for at least 5 days as an inpatient but not admitted to ICU. Parts A and B ran concurrently.

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

Clinical isolates

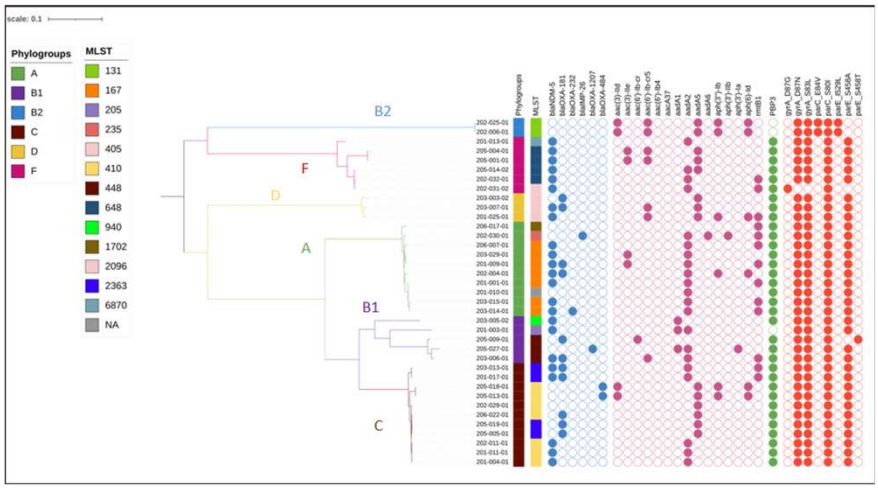
Non-duplicate CR *E. coli* isolates, isolated from any clinically relevant site had their initial eligibility performed in local microbiology laboratories following standard operating procedures. These isolates were shipped to a central laboratory for further characterization.

WGS and core genome analysis

The species identification was confirmed through MALDI-TOF MS technique, and they had their whole genome sequenced (WGS) on Illumina platform. DNA library was prepared using the Nextera XT kit; paired-end sequencing with a read length of 2 × 250 bp (base pairs) and a sequencing cycle of 2 × 501 was performed on the Illumina NovaSeq 6000 platform following sequencing protocol v1.5 chemistry provided by the manufacturer (Illumina Inc, San Diego, CA, USA). Identification of genes that confer antibiotic resistance was annotated using AMRFinderPlus and CARD. The multi-locus sequence types (MLST) was determined using mlst v2.22 (github.com/tseemann/mlst).

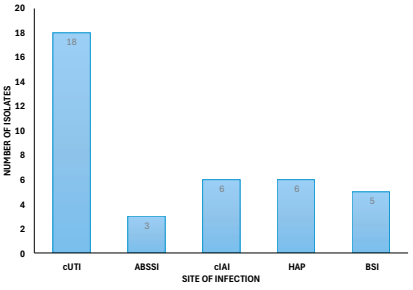
RESULTS

Figure 1- Phylogenetic tree for the CR *E. coli* isolates from five hospitals in India. Phylogroups, MLST and the main antibiotic resistance genes (ARG) are represented.



The *E. coli* phylogeny includes strain sequence type (MLST), phylogroups, ARGs for carbapenem (blue) and aminoglycosides (magenta), presence of the four amino acid insertion in the PBP3 protein (green) and mutations in the resistance-determining regions (QRDRs) of the *parC* and *gyrA* genes (orange). Filled boxes indicate the presence of the corresponding genes.

Figure 2- Distribution of 37 CR *E. coli* per infection



**cUTI= complicated urinary tract infection, ABSSI= acute bacterial skin and skin structure infection, cIAI=complicated intra-abdominal infection, HAP/VAP= hospital acquired pneumonia/ventilator acquired pneumonia , BSI= blood stream infection .*

Main Findings

1. The most frequent site of infection from where CR. *E. coli* was isolated was cUTI, followed by cIAI and HAP/VAP.
2. MLST analyses of the isolates showed high diversity of MLSTs distributed along the sites.
3. The most common STs were the globally dominant high risk ST167 and ST410.
4. All isolates carry multiple ARGs.
5. Among ARGs that confer resistance to carbapenems, NDM-5 was the most common carbapenemase (24/37), followed by OXA-181 (11/37).
6. Seven isolates were co-producing two carbapenemases (NDM-5 and OXA-48-like).
7. The four amino acid insertion in the PBP3 protein were present in all, except three isolates (ST131 and ST205).
8. All isolates harboured quinolone resistance-determining regions (QRDRs) of the *parC* and *gyrA* genes.
9. Among ARGs that confer resistance to aminoglycosides, 16S ribosomal RNA, encoded by *rmtB1* gene, was the most common enzyme.

CONCLUSIONS

High prevalence of genes conferring resistance to multiple classes of antibiotic in CR *E. coli* resulted in few therapeutic options for the clinical management of these patients. Access to new approved antibiotics with activity against carbapenem-resistant pathogens is critical for this region.

Reference:

1. Murray, Christopher J L et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet, **399**(10325): 629 – 655.

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