

Carbapenem Resistance among Enterobacteriaceae, a New Challenge

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ABSTRACT

Objective: To identify the commonest organism encountering carbapenem resistance among *Enterobacteriaceae* in indoor as well as outdoor patients irrespective of age and sex at Shaikh Zayed hospital, Lahore.

Study design: Cross sectional analytical study.

Place of study: Study was carried out at Shaikh Zayed Hospital, Lahore,

Sample size: Fifty carbapenem (meropenem) resistant strains of *Enterobacteriaceae* were included in this study.

Material and methods: Initially 50 carbapenem (meropenem) resistant isolates of *Enterobacteriaceae* were collected from samples received from in-door as well as out-door patients. The organisms were identified by routine laboratory tests including biochemical methods and API 20E system (bioMerieux).

Results: Largest numbers of isolates, 44% (22/50), were found to be *E. coli*, 26% (13/50) isolates were *K. pneumoniae*, 14% (7/50) *Citrobacter species*, 12% (6/50) *Enterobacter species*, 2% (1/50) *Providentia rettgeri* and 2% (1/50) *Morganella morganii* (Fig 1).

Conclusion: Carbapenem resistance in *Enterobacteriaceae* is emerging as a new challenge to health care settings as there is no drug in pipeline to treat carbapenem resistant isolates.

Key words: Carbapenem resistance, carbapenem resistant *Enterobacteriaceae*, *K. pneumoniae* carbapenemase.

INTRODUCTION

Introduction of carbapenem in clinical practice represents a great advance to treatment of β -lactam resistant bacteria. Due to their broad spectrum of activity and stability to hydrolysis by most β -lactamases, the carbapenems have been the drug of choice for treating infections caused by penicillin or cephalosporin resistant gram negative bacilli¹. Carbapenems are commonly used to treat infections caused by multidrug-resistant *Enterobacteriaceae*². Carbapenem resistance among *Enterobacteriaceae* particularly among *K. pneumoniae* and *E. coli* is an emerging problem worldwide³.

Carbapenems are the drugs of choice for the treatment of infections caused by ESBL producing organisms but carbapenemases (Metallo β -lactamases or MBLs) have emerged and spread from *P. aeruginosa* to *Enterobacteriaceae*⁴.

Resistance to carbapenems develops when bacteria acquire or develop structural changes within their PBPs, when they acquire metallo-beta-

lactamases that are capable of rapidly degrading carbapenems, or when changes in the membrane permeability arise as a result of loss of specific outer membrane porins⁵. Several resistance mechanisms occur to circumvent the efficacy of carbapenem and the carbapenemases are the most prominent enzymes that neutralize carbapenem⁶.

The rapid global spread of *K. pneumoniae* that produces *K. pneumoniae* carbapenemase (KPC) is of major concern⁷. KPC beta-lactamases belong to the family of serine carbapenemases and are usually found in *K. pneumoniae* and *E. coli*. KPC hydrolyzes beta-lactam agents, thereby reducing their action⁸. KPC activity has been reported, albeit less frequently, in other members of family *Enterobacteriaceae* (*K. oxytoca*, *Enterobacter spp.*, *Salmonella spp.*, *Citrobacter freundii*, and *Serratia spp.*) as well as in *Pseudomonas aeruginosa*⁹.

MATERIAL AND METHODS

A cross sectional analytical type of study was carried out at Shaikh Zayed Hospital, Lahore for duration of 9 months. A total of 50 non-repetitive isolates of carbapenem resistant *Enterobacteriaceae* were collected from different indoor as well as outdoor units of Shaikh Zayed Hospital, Lahore.

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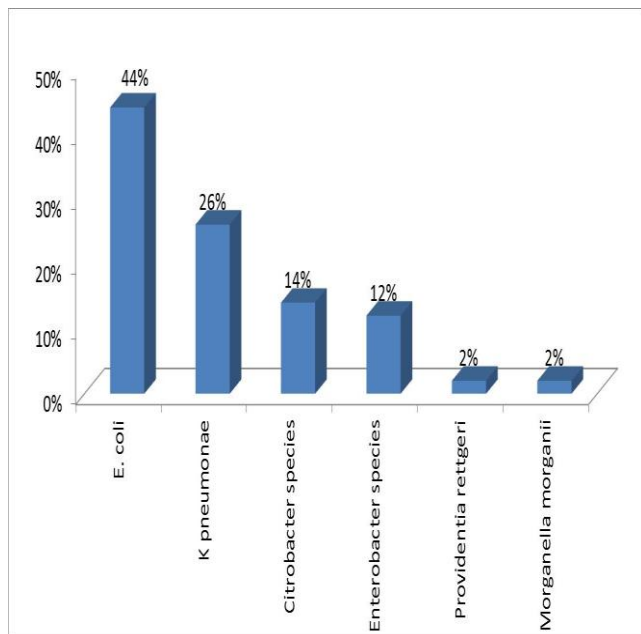
A brief record of the isolate number, laboratory number, patient identification code, date of collection of the sample, location of the patient, body site from where the isolates had been taken and the isolate (as was initially identified in the laboratory) was noted. The isolates were allocated serial numbers from 1-50.

The isolates were sub cultured on a suitable differential medium like MacConkey or CLED. The isolates were stored on a holding medium i.e. nutrient agar slope for the required period of time. For long time storage the specimen were held in a 10/50 (20% v/v) glycerol/tryptic soya broth (TSB Oxoid).

A suitable colony from differential medium was taken with a sterilized wire loop. It was homogenized in normal saline and compared with 0.5 McFarland standard turbidity. It was then inoculated and spread as per routine on Mueller-Hinton medium for antimicrobial sensitivity¹⁰. The organisms were identified by routine laboratory tests and by API 20 E system.

RESULTS

The identity of the isolates was reconfirmed by routine laboratory test and full identification was carried out by API 20 E identification system. Repeat susceptibility testing showed resistance to meropenem uniformly. Largest numbers of isolates, 44% (22/50), were found to be *E. coli*, followed by 26% (13/50) isolates of *K. pneumoniae*, 14% (7/50) *Citrobacter species*, 12% (6/50) *Enterobacter species*, 2% (1/50) *Providentia rettgeri* and 2%(1/50) *Morganella morganii* (Fig 1).



The source of largest number of isolates was urine i.e 50% (25/50) samples were from urine followed by pus 16% (8/50), fluid 14% (7/50), blood 10% (5/50), sputum 6%(3/50), CVP tip 2% (1/50) and PD catheter tip 2% (1/50) (Table1).

Table1: Distribution profile according to source of specimen

No of isolates	Source of Specimen
25	Urine
08	Pus
07	Fluids
05	Blood
03	Sputum
01	CVP catheter tip
01	PD catheter tip

DISCUSSION

The commonest organism found in our study was *E. coli* followed by *K. pneumoniae*¹¹. The *Escherichia* genus comprises a large group of organisms, many of which reside as normal commensals in the intestinal tracts of animals and humans while others serve as important intestinal and extraintestinal pathogens¹². Transmission of resistance genes from normally nonpathogenic species to more virulent organisms within the animal or human intestinal tract may be an important mechanism for acquiring clinically significant antimicrobial-resistant organisms. *E.coli* may serve as an important reservoir for these transmissible resistances, since it is clear that this organism has developed a number of elaborate mechanisms for acquiring and disseminating plasmids, transposons, phage, and other genetic determinants¹³.

The second commonest organism found in our study was *k.pneumoniae*. Carbapenem-resistant *K. pneumoniae* (CRKP) is the species of carbapenem resistant *Enterobacteriaceae* (CRE) most commonly encountered worldwide. CRKP is resistant to almost all available antimicrobial agents, and infections with CRKP have been associated with high rates of morbidity and mortality, particularly among persons with prolonged hospitalization and those who are critically ill and exposed to invasive devices (e.g., ventilators or central venous catheters)¹⁴⁻¹⁵.

Urine was the most frequent sample received during our study. The reason for this was that the most common hospital-acquired infection is urinary tract infection (UTI), which accounts for almost 40% of all nosocomial infections¹⁶.

CONCLUSION

Carbapenem resistance in *Enterobacteriaceae* is increasing in our setting. Infection with carbapenem-resistant *Enterobacteriaceae* (CRE) or

carbapenemase-producing *Enterobacteriaceae* is emerging as an important challenge in health-care settings and is associated with high degree of morbidity and mortality. Resistance to carbapenems is becoming a global problem leaving the physicians with a limited choice of antibiotics.

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