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INVITRO BACTERICIDAL ACTIVITY OF CEFTAZIDIME- AVIBACTAM AGAINST CARBAPENEMASE PRODUCING ORGANISMS ISOLATED FROM PATIENTS ADMITTED AT A TERTIARY CARE CENTRE, TELANGANA.

Dr Chelumalla Rajitha[1], Dr Sanka Pavani[2], Dr V Sudha Rani[3], N. Sai Phani Vikas[4].

[1](Microbiology, Post Graduate, Osmania Medical College, Hyderabad, Telangana, 500095, India)

[2](Microbiology, Associate Professor, Osmania Medical College, Hyderabad, Telangana, 500095,India)

[3](Microbiology, Professor & HOD, Osmania Medical College, Hyderabad, Telangana, 500095, India)

[4](MBBS, Final year, Gandhi Medical College, Secunderabad, Telangana, 500003, India)

Correspondence:

Dr S Pavani

Associate Professor, Department of Microbiology, Osmania Medical College, Hyderabad,
Telangana, 500095,
India
pavanifh@gmail.com

ABSTRACT:

Background and Objectives: Incidence of Carbapenem – resistant Enterobacteriaceae infections are increasing rapidly. Clinical management has become a challenge as it is associated with high morbidity and mortality. Ceftazidime – Avibactam is a newer beta – lactamase inhibitor combination which inhibits peptidoglycan synthesis by inhibiting the Penicillin binding proteins and are found to be effective against Carbapenem – resistant organisms. This study aims to assess the invitro antimicrobial susceptibility patterns of clinically important Carbapenemase producing organism and to study the susceptibility patternof carbapenem – resistant organisms to Ceftazidime – Avibactam (CZA).

Materials and Methods: A cross sectional study conducted among patients admitted at a tertiary care centre, Hyderabad, Telangana from January to June 2023. A total of 50 carbapenem resistant isolates on screening were subjected for assessing susceptibility pattern to Ceftazidime– Avibactam by Kirby Bauer disc diffusion method.

Results: Of the 50 CRE isolates, 42 (84%) were sensitive to CZA and 8 (16%) isolates showed resistance to CZA.

Conclusion: This study indicated Ceftazidime – Avibactam as a new clinical therapeutic regimen in the treatment of Carbapenem – resistant Enterobacteriaceae.

Keywords: Enterobacteriaceae, Carbapenemase, Carbapenemase producing organisms, Ceftazidime – avibactam

INTRODUCTION:

Carbapenemase producing organisms (CPO) are emerging worldwide and causing significant morbidity and mortality. CPO are endemic in the Indian subcontinent and a major cause of both community acquired and health care associated infections. The major risk factors for patients infected with carbapenem resistant Gram-negative bacteria are serious underlying illness, long term care facility residence and exposure to carbapenem.[1]

The increasing prevalence of such organisms threatens to restrain treatment options after compromising carbapenems which is often regarded as “last resort” antimicrobials in hospitals and long-term care facilities. The incidence of carbapenem resistant Enterobacteriaceae (CRE) infections in recent years has increased rapidly. Since the CRE strainis usually resistant to most of antimicrobial agents and limiting the treatment options, the mortality rate in patients with this infection is high.[2]

Infections due to carbapenem – resistant organisms are increasingly reported and associated with higher morbidity and mortality rates than those infections caused by carbapenem susceptible organisms. To overcome these carbapenemases, beta lactamase inhibitors are being developed to combine with a beta lactam agent.

The currently available first-generation beta – lactamases have narrow spectrum and donot inhibit carbapenemases, diazabicyclooctane bases second generation beta – lactamase inhibitors have a broader spectrum.[3]

Because of concomitant co production of other enzymes by CPO, evaluating the impactof the combination of beta-lactam/beta-lactamase inhibitor is needed. Therefore, this

study aims to assess the invitro antimicrobial susceptibility patterns of clinically important CPO to Ceftazidime-avibactam (CZA) from patients admitted at a tertiary care centre, Hyderabad,Telangana.

MATERIALS AND METHODS:

Study Design: Cross Sectional Study

Study Setting: The study included 50 CRE isolates from patients admitted at a tertiary care centre, Hyderabad, Telangana.

Study Duration: The study was done from January 2023 to June 2023

Inclusion Criteria:

- Patients admitted at a tertiary care centre - Osmania general hospital.
- Both males and females of all age groups.
- Patients irrespective of co-morbidities.
- Patients willing to give consent.

Exclusion Criteria:

- Patients managed in outpatient departments.
- Patient not willing to give consent.

All types of samples from the patients admitted at a tertiary care centre were collected under strict aseptic conditions and cultured within 2 hours of collection. Organisms belonging to Enterobacteriaceae family were identified and susceptibility patterns were assessed by Kirby Bauer disc diffusion method. The isolates which showed resistant zones for any one of the carbapenem class drugs i.e., Imipenem, Meropenem, Doripenem or Ertapenem were screenedas CRE and subjected to confirmatory test – Modified Hodge test. All the clinical isolates that were resistant to carbapenems were subjected to Kirby Bauer disc diffusion method with Ceftazidime-avibactam (CZA).

RESULTS:

During the study period a total of 50 CRE isolates were collected. Of 50 CRE isolates, 42 (84%) showed susceptibility to ceftazidime-avibactam and 8 (16%) showed resistance.

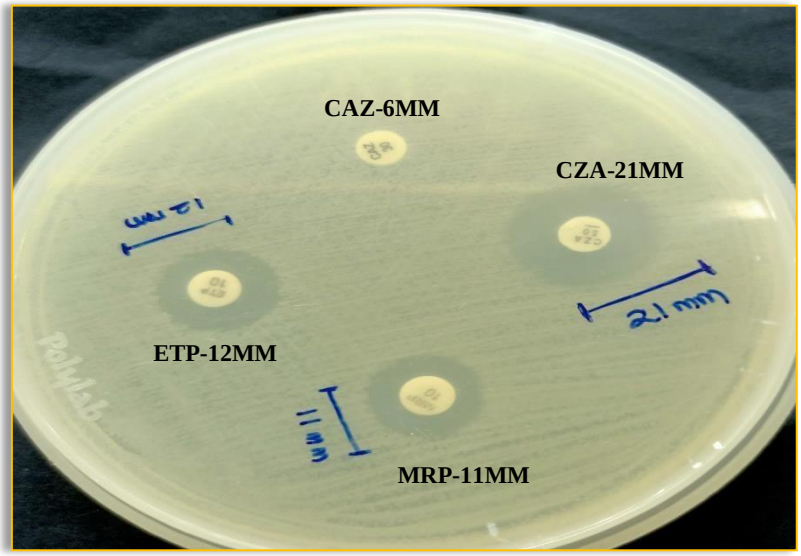

Fig:1 Isolate showing resistance to Ertapenem and meropenem (CRE) is susceptible to CZA

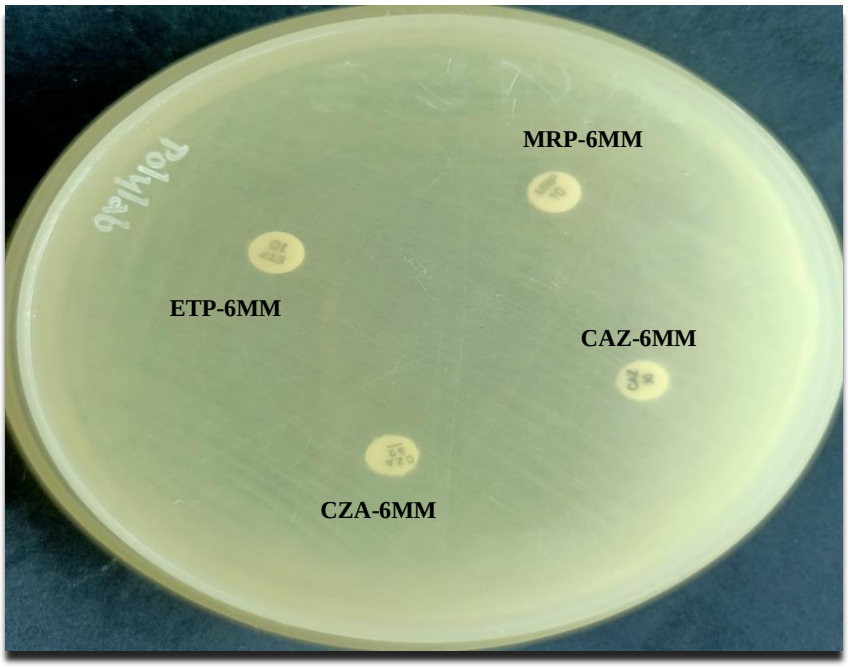

Fig:2 Isolate showing resistance to all the four discs – meropenem, ertapenem, ceftazidime andceftazidime-avibactam

DISCUSSION:

Antimicrobial resistance in Gram negative bacteria, particularly among those of the Enterobacteriaceae family has become a leading cause of morbidity and mortality and a serious public health concern worldwide. The increased prevalence of isolates carrying Carbapenemases in recent years constitute a greater challenge, leading to multidrug resistant (MDR), extensively drug resistant (XDR) and pandrug-resistant (PDR) bacteria.[5]

In India, high carbapenem resistance in Enterobacterales has been reported by the Indian council of medical research (ICMR) with resistance rates up to 30% for Escherichia

coliand 50% for Klebsiella pneumoniae. The increasing prevalence of infectious diseases caused by MDR Gram-negative bacteria places a hurdle in the selection of appropriate empiric antimicrobial therapy for seriously ill hospitalized patients.[6]

Among the 50 CRE isolates collected in the present study, 42 (84%) showed susceptibility to Ceftazidime-avibactam (CZA) and 8 (16%) showed resistant. The 84% of susceptibility to CZA in the present study was correlating with the studies conducted by DaliaM Ibrahim et al which showed 88% sensitivity to CZA[7], study by M.S.Nour and M.A.Kaffas showed 88.2% sensitivity to CZA[8].

The study by Renru Han et al showed 99.4% sensitivity to CZA [9] were as the study byA.M.Ahmed et al[10] showed 30% efficacy to CZA by Kirby Bauer disk diffusion method. The variation of sensitivity to CZA in various studies may be due to differences in the tested isolates features of different resistance mechanisms to carbapenems.

The shortage of active compounds and a deficiency of convincing clinical data have ledto controversy about antimicrobial treatment choices for infections caused by MDR and XDR Gram-negative bacilli.[11] The results in this study confirmed the potent in vitro and broad coverage of CZA against CRE indicates a valuable treatment option for infections caused by CRE.

CONCLUSION:

As a compound preparation of novel enzyme inhibitor, Ceftazidime-avibactam showed highest sensitivity (84%) against CRE indicating it as a new therapeutic regimen in managing infections caused by Carbapenem resistant Enterobacteriaceae.

LIST OF ABBREVIATIONS:

CRE: Carbapenem Resistant Enterobacteriaceae

CPO: Carbapenemase Producing Organisms

CZA: Ceftazidime-Avibactam

MDR: Multi-drug Resistant

XDR: Extensively-drug-Resistant

PDR: Pan-drug Resistant

CAZ: Ceftazidime

ETP: Ertapenem

MRP: Meropenem

ICMR: Indian Council of Medical Research

CONFLICTS OF INTEREST:

Authors declare that they have no conflict of Interest.

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Nil

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