



**Prevalence of carbapenemase producing Enterobacterales at a tertiary care centre in South India**

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**Abstract**

Carbapenem resistant Enterobacterales (CRE) have emerged as a major public health threat. The resistance to carbapenem is mainly due to the production of carbapenemases, that hydrolyze the carbapenem & other beta lactam agents. In this study, prevalence of carbapenemase producing Enterobacterales is 11.3% by mCIM (modified carbapenem inactivation method) and eCIM (EDTA carbapenem inactivation method) methods as per CLSI guidelines. 2% of CRE isolates were resistant to colistin by disc elution method.

**Keywords:** CRE, mCIM, eCIM.

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**Introduction**

Carbapenem resistant Enterobacterales (CRE) have emerged as a major public health threat. The resistance to carbapenem is mainly due to the production of carbapenemases, that hydrolyze the carbapenem & other beta lactam agents. Other mechanisms include increased efflux pump action, blocking of specific bacterial porins in the bacterial cell membrane.

The major risk factors for CRE colonization include underlying comorbid conditions, prior antibiotic exposure, prior hospitalization or residence in a long-term care facility, invasive devices & extended stay in an ICU. Patients with CRE colonization or infection can

serve as reservoirs & can transmit CRE to healthcare personnel, other patients, family members & the environment.

The challenges of a Carbapenem resistant Enterobacterales (CRE) infections are limited treatment options which is expensive (fosfomycin, tigecycline, minocycline, polymyxin & combination therapy such as ceftazidime avibactam), longer hospital admissions, higher healthcare costs, increased mortality rate. Hence, this study was conducted to assess the prevalence rate of CRE in our hospital.

#### Aim:

To study the prevalence of carbapenemase producing Enterobacterales in a tertiary care centre.

#### Objectives

- To determine the proportion of carbapenem resistant Enterobacterales from clinical isolates in a tertiary care centre.
- To determine the proportion of resistance due to carbapenemase production amongst the CRE.
- To determine the susceptibility of carbapenemase producing CRE to colistin.

#### Materials and methods

**Study Design:** Cross sectional observational study

**Study Location:** Department of Microbiology, Pushpagiri Institute of Medical Sciences & Research Centre, Thiruvalla, Kerala

**Inclusion criteria:** All isolates belonging to Family Enterobacterales from various clinical samples between October 2022 to January 2023 were selected.

**Exclusion criteria:** Duplicate samples from the same patients were excluded.

**Methodology:** All clinically significant isolates belonging to Family Enterobacterales from various

clinical samples between October 2022 to January 2023 were selected.

**Screening for resistance to carbapenems:** Isolates showing zones as 'intermediate or resistant' to Imipenem(10ug) and/or Ertapenem (10ug) in disk diffusion test.

**Confirmation of Carbapenemase production:** Modified carbapenem inactivation method (mCIM) & EDTA – carbapenem inactivation methods (eCIM) (CLSI M100, 2022)

#### Results

Of the 924 isolates, belonging to Enterobacterales family, 218 isolates (24 %) showed resistance to carbapenem during screening. 105 (11% of the total & 48% of CRE) were carbapenemase producers. (Fig.1)

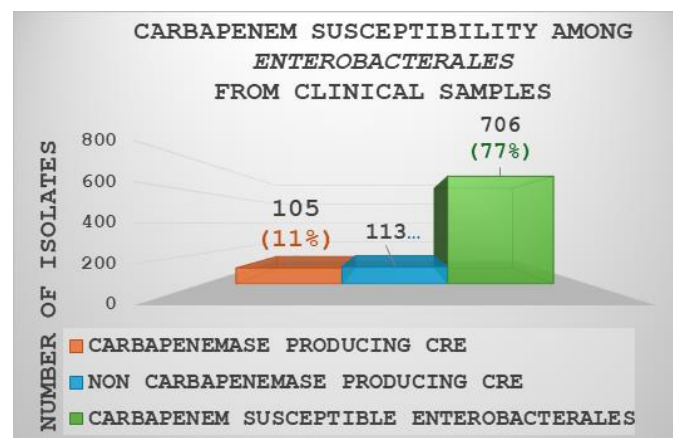


Figure 1

105 (11%) isolates were carbapenemase producers. 72 (69%) isolates were Metallo-beta lactamase (MBL) producers (Fig 2)

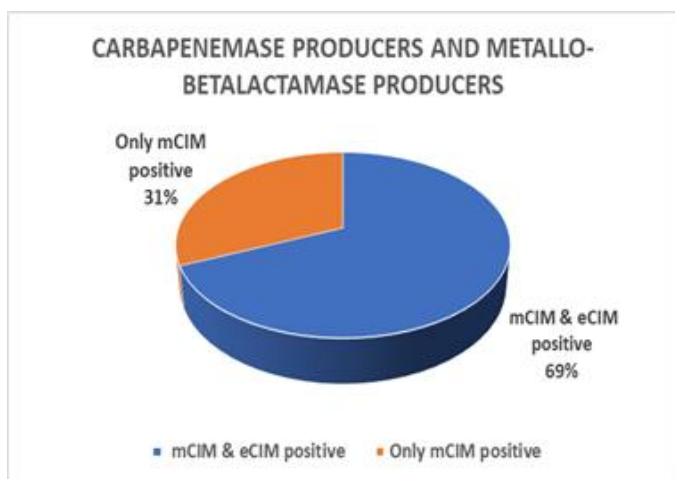


Figure 2

*Klebsiella pneumoniae* (62%) was found to be the predominant organism followed by, *Escherichia coli* (26%)

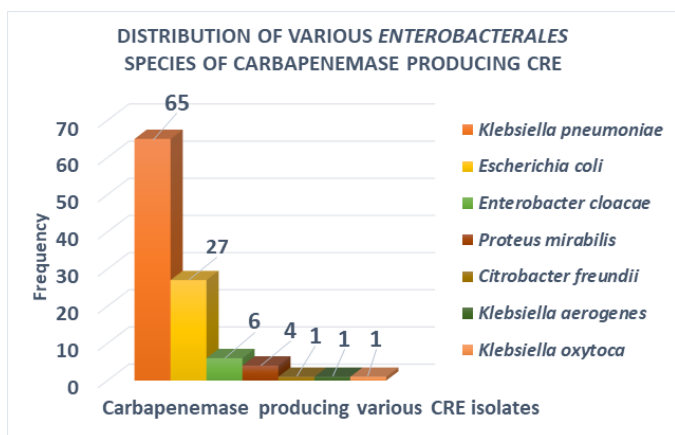


Figure 3

Out of 105 carbapenemase producing CRE isolates, 90 (86%) were isolated from hospitalized patients, remaining 15 (14%) isolates were from OP samples. Carbapenemase producing CRE were most frequently isolated from urine samples (43%) followed by sputum (22%), pus (21%) & blood (14%). Of 45 carbapenemase producing CRE isolates from urine, 21 were Catheter associated UTI (CAUTI).

Of 23 carbapenemase producing CRE isolates from sputum, 2 were ventilator associated pneumoniae (VAP). Of 22 carbapenemase producing CRE isolates from pus samples, 3 were surgical site associated infection (SSI).

Of 15 carbapenemase producing CRE isolates from blood, 4 were central line associated bloodstream infection (CLABSI).

Additionally, colistin susceptibility of the 105 carbapenemase producing CRE isolates were also tested by Colistin broth disk elution method, 103 (98%) of the carbapenemase producing CRE isolates were susceptible to colistin.

## Discussion

The prevalence of Carbapenemase producing Enterobacterales isolates in this study was found to be 11%, similar to a study by Gupta et al (8) which was 12%. 69% of the Carbapenemase producing CRE isolates were metallo-beta lactamase producers.

*Klebsiella pneumoniae* was found to be the predominant organism 62% followed by, *Escherichia coli* 26%, similar to a study by Wattal et al.

Carbapenemase producing CRE isolates was most frequently isolated from urine samples 43%, similar findings were obtained from Roopa et al where 42% were isolated from urine samples.

2 % of the carbapenemase producing CRE isolates were resistant to colistin. Colistin is used as a monotherapy or in combination with other antibiotics to treat CRE infections. Over the last few years, the usage of colistin has increased by about 10-fold & hence rise in resistance. Hence, this drug should be used judiciously.

## Limitations

Molecular testing for detection of genes responsible for carbapenemase production has not been done. Hence, serine and metallo-beta lactamase co-production could not be determined.

## Conclusion

Prevalence of CRE was 24% & carbapenemase producing Enterobacterales was found to be 11% in this

study. 14% of the carbapenemase producing CRE isolated were community acquired. In a country like India with huge population, this translates to alarming numbers.

Contracting a resistant strain, such as CRE, can lead to prolonged patient stay in the hospital. Therefore, maintaining good infection control practices is vital for reducing transmission.

This includes patient cohorting, the correct choice of treatment modalities, choosing newer BL-BLIs over colistin to conserve susceptibility to colistin. This is crucial as 2% of the isolates already showed resistance to colistin.

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