



## ORIGINAL ARTICLE

# Detection of KPC-producing Enterobacteriaceae among Hospitalized patients with phenotypic method in Shahid Modarres Hospital, Tehran, Iran

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### ABSTRACT

*Enterobacteriaceae* spp. are an important part of agents that cause infection in health care facilities. Due to importance of monitoring and management of drug resistance in health care facilities, especially for preventing of dissemination of new resistances such as KPC producing enterobacteriaceae, in this study KPC producer Enterobacteriaceae in hospital departments detected and antibiotic resistance pattern of these isolates was determined. Enterobacteriaceae spp. that isolated from hospitalized patients in departments of the Shahid Modarres hospital was identified by routine biochemical tests. Susceptibility testing for these species was performed according to method that recommended with CLSI guidelines. For detection of KPC producers the phenotypic method, Modified Hodge Test, was used as CLSI recommendation. From 1000 isolated Enterobacteriaceae spp., 76 (7.6%) isolates were resistant to Ertapenem, 84 (8.4%) isolates were Imipenem resistant and fifteen (1.5%) isolates had positive results on Modified Hodge test. The emergence of KPC producer Enterobacteriaceae and multi drug resistant species in hospitals is a major healthcare challenge and could cause an increase in both mortality and morbidity among hospitalized patients.

**Key words:** KPC, *Klebsiella pneumoniae*, *Enterobacter* spp., *E. coli*, Iran

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### INTRODUCTION

The Enterobacteriaceae is common microbiota of the gastrointestinal tract of humans and other animals [1]. These organisms are a major cause of both community-acquired and health-care-acquired infections. In several past decades the spread of Enterobacteriaceae with resistance to broad-spectrum antimicrobials is a major concern of health care workers and many clinicians have relied on the carbapenems to treat infections caused by these resistant organisms. Unlike resistance in some type of resistant bacteria that resistance mediated by a single mechanism, carbapenem resistance is complex and can be mediated by producing enzymes that inactivate carbapenems (carbapenemase) [2].

According to the hydrolytic mechanism at the active site, carbapenemases were divided into two major families. The first described family contains at least one zinc atom at the active site and inhibited by EDTA [3]. The other family contain serine at their active site and EDTA do not inhibit the activity of these enzymes [4]. The pattern of carbapenemases dissemination was changed after identification of plasmid encoded carbapenemases such as IMP-1 [5] and KPC-1 [2].

KPC (*Klebsiella pneumoniae* carbapenemase), an enzyme encoded by a gene that is located on a highly transmissible plasmid, was first identified from a *Klebsiella* in 2001 in North Carolina [2] and has now become the most frequent carbapenemase around the world. KPC distinguished from other functional 2f group enzymes by two characteristics. Its location and substrate hydrolysis spectrum. KPC is located on transferable plasmid and its hydrolysis spectrum includes aminothiazoleoxime cephalosporins.

One of the most reliable phenotypic tests for detecting KPCs that currently endorsed by the CLSI, is the Modified Hodge Test (MHT) which has got acceptable sensitivity and specificity for the carbapenemase production[6]. KPC producer Enterobacteriaceae spp. are an important health care problem in Iran, due to the large distribution of ESBL producing Enterobacteriaceae spp. that carbapenems were considered to be one of the few treatment options. Our study was carried out to determine the prevalence of KPC producing Enterobacteriaceae, isolated from admitting patients in ShahidModarres hospital Tehran, Iran.

## METHODS AND MATERIALS

### Patients and specimens:

Our analysis was based on 1000 Enterobacteriaceae spp. culture isolates which originated from urine, trachea, Foley catheter, blood and exudates samples of patients from ICU, out-patient, transplant, Urology, Nephrology, CCU and general surgery departments of Shahid Modarres hospital in Tehran, Iran. Specimens were collected from patients during a period of one year.

### Isolates Identification and Antibiotic susceptibility:

In this study, all isolates were selected for special microbiology tests and subsequent antibiotic susceptibility testing was performed. Antibiotic susceptibility testing was done by disc diffusion method, recommended by the Clinical and Laboratory Standards Institute (CLSI) guideline, with antibiotic discs(Roscocompany, Copenhagen, Denmark). The tested antibiotics included: Cefotaxime, Cefepime, Imipenem, Ceftriaxone, Ceftazidime, Meropenem and Ertapenem. All Imipenem, Ertapenem and Meropenem resistant isolates were examined by Modified Hodge Test (MHT) which previously described and recommended with CLSI [7].

## RESULTS

In this study, 1000 isolates of Enterobacteriaceae spp. were obtained from clinical specimens and subsequently subjected to laboratory investigation for detecting KPC producers. The rates of Ertapenem and Imipenem resistance in the isolates were 76 (7.6%) and 84 (8.4%), respectively. From these resistant isolates 15 (1.5%) had positive MHT results.

This study presents infectious isolates with positive MHT results in patients from departments of the Shahid Modarres hospital. These isolates in addition to positive results in MHT, are multi drug resistance in susceptibility test.

Most of Enterobacteriaceae which were KPC positive were *Klebsiella pneumoniae* and other species of Enterobacteriaceae in this one-year project were Enterobacter spp. and E. coli. The most common source was urine followed by trachea, Foley catheter, exudates and blood. Most isolates cultured from specimens which were collected from acute-care departments such as ICU. Outpatient isolates cultured from patients with acute urinary tract infection.

## DISCUSSION

After recognition of carbapenemase enzymes, there has been a rapid increase in carbapenem resistant Enterobacteriaceae [8] worldwide. Carbapenem resistant Enterobacteriaceae has various types which have different distribution patterns in different areas. The KPC type of carbapenem resistant Enterobacteriaceae is predominant in USA [9], Greece[10], Puerto Rico[11], and Colombia[12]. The VIM type is most predominant in the southern Mediterranean region, e.g. Greece[13], and NDM-1 is frequently detected in the Indian subcontinent. Increasing carbapenemase producing organisms is of grave concern in Iran[14]. All types of these carbapenemases have been described in Enterobacteriaceae family, including *Klebsiella pneumoniae*, E. coli, *Serratiamarcescens*, *Citrobacter* spp. and *Enterobacter* spp.[15]. According to various studies in Europe, which represent a rise since 2005 in carbapenem resistance from invasive *Klebsiellapneumoniae* isolates [15], the importance of monitoring of these isolates grows increasingly.

There is strong evidence that the risk of introducing and spread of carbapenemase producing Enterobacteriaceae in health care facilities increases significantly when infected or colonized with carbapenemase producing Enterobacteriaceae patients, administered for medical purposes. Due to lack of certain optimal treatment for infections, caused by KPC-producing isolates, clinical data are necessarily needed in order to determine the suitable treatment of KPC infections. It's seems that a combination therapy is indispensable for infections caused by KPC-producing organisms. The worldwide emergence of KPC producing Enterobacteriaceae has become a serious concern, because these new emerging drug resistant bacteria may lead to an increase in mortality and morbidity of healthcare acquired infections. For the effective control management of health care facilities in countries such as Iran, which drug resistant bacteria are predominant, designing studies and reporting the rate of resistance in health care facilities, is needed.

**CONCLUSION**

There are a few reports of KPC producing bacteria in Iran and the presented study is one the first studies that report emergence and distribution of these organisms in departments of hospitals in Tehran, Iran. KPC producing Enterobacteriaceae emergence monitoring, and recommendations for controlling these bacteria in Iran are very important. It seems that there is need to organize a national committee for surveillance of these bacteria. The triumph against KPC producing Enterobacteriaceae, novel type of antimicrobial resistance, depends on some changes in health care policies: Increasing laboratories' capacities and infection control, in addition to, changing attitudes towards the use of antibiotics at a global level.

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