Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 12, pp.44353-44355, December, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

PREVALENCE OF CARBAPENEM-RESISTANT ENTEROBACTERIACEAE IN A TERTIARY CARE REFERRAL CENTRE: KERALA, SOUTH INDIA

***,[1]Rohey Jan, [1]Nita George, [1]Mohan Mathew, [2]Waseem Raja, [3]Molly Johny, [1]Vipin Lal and [1]George, P.**

[1]Department of Critical Care Medicine & Anesthesiology, Lakeshore hospital & Reserch Centre Kochi-Kerala, India
[2]Department of Gastroenterology & Hepatology, Medical Trust Hospital Kochi-Kerala, India
[3]Department of Microbiology, Lakeshore Hospital & Reserch Centre Kochi-Kerala, India

ARTICLE INFO

Article History:
Received 20th September, 2016
Received in revised form
22nd October, 2016
Accepted 25th November, 2016
Published online 30th December, 2016

Key words:

Carbapenem Resistant
Enterobacteriaceae (CRE),
Klebsiella pneumonia,
ET aspirates,
Antimicrobial Stewardship.

ABSTRACT

Objective: The emergence of Carbapenem Resistant *Enterobacteriaceae* (CRE) in recent times has become a serious threat to public health due to the high mortality, potential dissemination rates and limited availability of effective treatment options.
Aims/objective: The aim of the study was to determine the prevalence rate of CRE in ICU settings at Lakeshore hospital & research centre Kochi –Kerala.
Methods: A Retrospective study was conducted in Critical care department over a period of 1 year from January 2015 – December 2015, following its approval by the institutional ethical committee. A total of 1035 susceptible isolates were retrieved from the electronic medical records (EMR) of the hospital. The study sample includes patients from all ICU, s and specimens tested for culture sensitivity were blood, urine, endotrachial aspirate, sputum, wound pus/abscess and others.
Results : The total number of Enterobacteriace isolates were 624 (60.3%), out of which CRE isolates were 50, with CRE Prevelance rate of 8.0 %, (50/624). The most common organisms identified were Klebsella pneumoniae 82% followed by E. Coli 18% & the most common sources of CRE isolates were ET aspirates (22%), followed by urine culture (18%). Majority of the CRE isolates were found in age group of 61-75 years (42%), followed by 46-60 yrs (24%) with male prepondance (2.1:1). CRE isolates were mainly sensitive to Tigecycline (70%), Colistin (50%) and amikacin (40%).
Conclusion: This study provides a baseline data of current scenario of CRE in our set up. A strict antibiotic policy should be addressed especially with observed emergence of carbapenem resistance. Continuous review of need to invasive devices and strict compliance with basic infection control measures are mandatory to limit the spread of CRE.

Citation: Rohey Jan, Nita George, Mohan Mathew, Waseem Raja, Molly Johny, Vipin Lal and George. P. 2016. "Prevalence of carbapenem-resistant enterobacteriaceae in a tertiary care referral Centre: Kerala, South India", *International Journal of Current Research*, 8, (12), 44353-44355.

INTRODUCTION

Carbapenem-resistant Enterobacteriaceae (CRE) have emerged as a cause of nosocomial infections in several regions around the world. Because of their progressive geographic dissemination and limited therapeutic alternatives, they are now considered an important public health threat classified as urgent by the Centers for Disease Control and Prevention (Nordmann, 2012 and Solomon *et al*., 2014). Carbapenems are a group of β-lactam antimicrobial agents with an exceptionally broad spectrum of activity (Zhanel *et al*., 2007). They are used as a last resort against many multi drug resistant, gram negative bacteria, and in cases of infections due to Extended spectrum beta lactamase (ESBL) and Amp C enzyme producing *Enterobacteriaceae* (Deshpande, 2010 and Datta, 2012). The emergence and dissemination of carbapenem resistant bacteria in recent times represents a serious threat to public health. Resistance has been observed in several *Enterobacteriaceae*, as well as in members of the *Pseudomonas* and *Acinetobacter* genera. (Deshpande *et al*., 2010) These organisms are associated with high mortality rates and have the potential to spread widely. (CRE Toolkit, 2012) Resistance to carbapenems can be brought about by various mechanisms, the most common being the production of carbapenemases, a class of enzymes capable of hydrolyzing carbapenems and other β-lactams. (Datta *et al*., 2012) Resistance to carbapenems can also be due to the poor binding of carbapenems to penicillin-binding proteins present in the bacteria, the over-expression of multidrug efflux pumps by the bacteria or lack of porins

****Corresponding author: Rohey Jan***
Department of Critical Care Medicine & Anesthesiology, Lakeshore hospital & Reserch Centre Kochi-Kerala, India

present in the bacterial cell membrane. However, for significant resistance to emerge, it is thought that a combination of resistance mechanisms is required (Baldwin, 2008). Carbapenem Resistant *Enterobacteriaceae* (CRE) can be defined as *Enterobacteriaceae* that are resistant to one or all of the following carbapenems: imipenem, meropenem, ertapenem or doripenem; and resistant to all of the following third-generation cephalosporins: ceftriaxone, cefotaxime and ceftazidime. *Klebsiella* species and *Escherichia coli* that meet the CRE definition are a priority for detection; however, other *Enterobacteriaceae* (e.g. *Enterobacter species*) are also of significant importance. CRE have been associated with high mortality and morbidity rates of up to 40-50% recorded in some studies. (CRE Toolkit, 2012) Also, CRE are found to carry genes that confer high levels of resistance to many other antimicrobials, often leaving very limited therapeutic options (CRE, 2012 and Clinical and Laboratory Standards Institute, 2012). In 2007, the overall worldwide susceptibility to carbapenems was 98% among the *Enterobacteriaceae*.

Presumably this is caused due to a number of factors, including antibiotic usage, dosing regimens, and local hospital practices concerning isolation of patients with multiresistant pathogens. (Queenan and Bush, 2007) With the increasing incidence of CRE in hospitals, a rapid and accurate routine protocol for CRE screening and detection is required. Appropriate detection of CRE is vital in patient care and infection control in order to institute correct, targeted treatment and to reduce the escalation of resistance (Datta, 2012). The primary objective of the study was to determine the prevalence of CRE in ICU settings at Lakeshore hospital & research centre Kochi Kerala, South India. To the best of our Knowledge the studies on CRE prevalence in our part of world are very limited, and this is the first of its kind from our state Kerala, south India to determine the prevalence of CRE in our ICU settings, as our hospital is a large 800 beded tertiary referral & research centre.

Methods: A Retrospective ICU- based study, was conducted in Critical care department & Anesthesiology Lakeshore hospital kochi-Kerala south India, which is a 800-beded, tertiary-care teaching hospital with approximately 10,000 annual admissions and 4,500 clinical microbiological cultures processed annually. The study was conducted over a period of 1 year, from January 2015 – December 2015, following its approval by the Institutional ethical committee. A total of 1035 susceptible isolates were retrieved from the electronic medical records (EMR) of our hospital. The study sample includes patients from all ICU,s and various specimens tested for culture sensitivity were blood, urine, endotrachial aspirate, bronchial washing, central line tip, wound pus / abscess, sputum, drain fluids and others. CRE isolates were identified using the Vitek 2 - Compact system (Bio Mérieux, France).

RESULTS

Over a period of one year, the total number of bacterial isolates were 1035, out of which number of Enterobacteriace isolates were 624 (60.3%), (Table 1). The number of CRE isolates among 624 enterobacteriace isolates were 50, with CRE Prevelance rate of 8.0 %, (50/624). The most common organisms identified were Klebsella pneumoniae 82% (41/50) followed by E. Coli (18%), (Table 2). The most common source of infection were ET aspirates (22%), 11/50 followed by urine culture (18%), 9/50, drain fluid (18%), 9/50, blood (10%), 5/50, wound pus / abscess (10%), 5/50 and Sputum (8%),4/50 (Table 3). Out of 50 CRE isolates, Males were 34 and females 16 with (M: F ratio = 2.1: I), (Table 4)

Maximum number of CRE isolates were found in age group of 61-75 years (42%), (21/50), followed by 46-60 yrs (24%) (Table 5), Majority of CRE isolates were sensitive to Tigecycline (70 %), Colistin (50%) and Amikacin (40%), (Table 6).

Table 1. Distribution of Enterobacteriacea isolates according to species

Species	Number	Percentage (%)
Klebsiella pneumonia	309 /624	49.4%
E Coli	155/624	24.8%
Pseudomonas	88/624	14.1%
Acinetobacter	72/624	11.5%
Total	624/1035	60.2%

Table 2. Distribution and Prevalence of CRE (Carbepenum Resistant Enterobacteriace) according to species

CRE Species	Number	Prevalance (%)
Klebsella pneumonia	41/50	82 %
E Coli	9/50	18 %
Pseudomonas	0/50	0 %
Acinetobacter	0/50	0 %
Total	50/624	8.0%

Table 3. CRE distribution according to source of samples for culture

Sample source	Number	Percentage (%)
Blood	5/50	10%
Urine	9/50	18%
Sputum	4/50	8%
Endotracheal aspirates	11/50	22%
Bronchial washings	3/50	10%
Drain Fluid	9/50	18%
Wound pus/Abscess	5/50	10%
Others	4/50	8%

Table 4. Gender distribution in CRE patients (n = 50)

Gender	Number	Percentage (%)
Male	34	68%
Females	16	32%

Table 5. Age distribution of CRE patients (n=50)

Age group (years)	Number (n)	Percentage (%)
< 15	1	2%
15 - 30	5	10%
31 - 45	6	12%
46 - 60	12	24%
61- 75	19	38%
>75	7	14%
TOTAL	50	100 %

Table 6. Antimicrobial Susceptibility of Carbapenem-Resistant Enterobacteriaceae (CRE) Isolates

Antimicrobial Agent	Number of susceptible isolates / total number of CRE isolates	Percentage (%)
Tigecycline	35	70%
Pipercillin tazobactum	8	16%
colistin	25	50%
Amikacin	2o	40%
Aztreonam	5	10%
Any Fluoroquinolone (L/M/C)	2	4%

DISCUSSION

The prevalence of CRE in our study was found to be 8.0 % (50/624). This is similar to the CRE prevalence rates obtained in similar studies from other parts of India. Datta *et al*. reported a CRE prevalence rate of 7.87% from a study conducted in a tertiary care hospital in North India (Datta, 2012), while Gupta *et al* reported carbapenem resistance varying from 17 to 22% among *Enterobacteriaceae* strains. (Gupta *et al*., 2006) Wattal *et al* reported a high CRE prevalence rate ranging from 13 to 51% in a tertiary care hospital in Delhi. (Wattal *et al*., 2010) Thus, the significant CRE prevalence rates recorded in different parts of India emphasize the need for controlling the further dissemination of CRE. The most common CRE isolate found in our study was Klebsiella Pneumonae 82% (41/50) followed by E Coli 18% (18/50). Similar results were found in studies done by Allice *et al*. (2012-2013). And Gupta *et al*. (2006), where Klebsiella Pneumonia and E coli was the common findings. Majority of CRE isolates in our study were in age group of 61-75 years (38%) followed by 46- 60 years (24%) and most of the CRE isolates in our study were sensitive to Tigecycline (70%), 35/50 followed by colistin (50 %) and Amikacin (40%), Similar results were found in study done by Allice *et al*. (Alice, 2015). *Enterobacteriaceae* majorly contribute to the intrinsic human gut flora. They are also capable of colonizing the gut of patients and spreading through the community via the faeco-oral route. Thus the spread of CRE is deeply disconcerting in a country such as India with a reservoir of more than 1.4 billion people (Deshpande, 2010; Nagaraj *et al*., 2011). The first step in dealing with the problem of CRE is the identification of infected patients. Appropriate detection of CRE is vital in patient care and infection control in order to institute correct, targeted treatment and to reduce the escalation of resistance. Although molecular techniques are regarded as the gold standard for detection of carbapenem resistance, it becomes impractical in a routine diagnostic laboratory setup due to cost factors.

Thus, the need of the hour is the rapid, practical and cost effective phenotypic detection of CRE (Zhanel, 2007). CRE infected patients serve as reservoirs for spreading infection and contaminating the environment. Thus, identified CRE infected/ colonised patients must be contact isolated. (Nagaraj *et al*., 2012) Antimicrobial stewardship may be the most effective in the control of CRE through targeted specific antimicrobial usage. Limited use of invasive procedures is also an important intervention in CRE prevention in hospital settings (Gupta, 2011). The limitation of our study was that a significant risk of CRE has been observed but since it was a retrospective study, the exact rate and mechanism of this resistance could not be confirmed. We also recommend that carbapenem resistance should be thoroughly investigated by further research to know the magnitude and mechanism of such resistance. In conclusion, this study shows a significant rate of carbapenem resistance among *Enterobacteriaceae* isolated in ICU patients, as reported in similar studies from other parts of India. It provides a clearer picture of the current CRE scenario in our settings which can be attributed to unrestricted use of antibiotics, prolonged mechanical ventilation, previous hospitalization, long duration of hospital stay, indewelling catheterization, advanced age, multiple comorbidities (CLD, ESRD, COPD, CHF, Diabetes, Malignancy), immunosuppression and plasmid mediated MDR pathogens. These isolates pose a special therapeutic challenge especially with the growing resistance to carbapenems. Therefore, strict antibiotic policy, continuous review of the need to invasive devices, minimizing duration of hospital stay together with strict compliance to infection control precautions would serve as the most efficient way of preventing the spread of these organisms. The need of the hour would be to have a strong antimicrobial stewardship program, which is followed by all concerned Doctors, with further emphasis on better cost effective, logical infection control measures to prevent the dissemination of such multidrug resistant bacteria.

Disclosure: The authors report no conflicts of interest in this work.

REFERENCES

Alice Y. Guh, MD, MPH; Sandra N. Bulens et al. Epidemiology of Carbapenem-Resistant Enterobacteriaceae in 7 US Communities, 2012-2013. JAMA 2015

Baldwin CM, Lyseng-Williamson KA, Keam SJ. Meropenem-A review of its use in the treatment of serious bacterial infections. Drugs 2008; 68:803-838.

Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing: 22th informational supplement. CLSI publication 2012; M100-S22. Clinical and Laboratory Standard Institute, Wayne, Pennsylvania.

CRE Toolkit, CDC-Guidance for Control of Carbapenem-resistant *Enterobacteriaceae* (CRE), 2012. http://www.cdc.gov/ hai/organisms/cre/cre-toolkit/f-level-prevention.html

Datta P, Gupta V, Garg S, Chander J. Phenotypic method for differentiation of carbapenemases in *Enterobacteriaceae*: Study from north India. Indian J Pathol Microbiol 2012; 55:357-360.

Deshpande P, Rodrigues C, Shetty A, *et al*. New Delhi Metallo-b lactamase (NDM-1) in *Enterobacteriaceae*: Treatment options with Carbapenems Compromised. J Assoc Physician India 2010; 58:147-149.

Gupta E, Mohanty S, Sood S, *et al*. Emerging resistance to carbapenems in a tertiary care hospital in north India. Indian J Med Res 2006;124:95-98.

Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem resistant *Enterobacteriaceae:* epidemiology and prevention. Healthcare Epidemiol 2011; 53:60-67.

Nagaraj S, Chandran SP, Shamanna P, Macaden R. Carbapenem resistance among Escherichia coli and *Klebsiella pneumoniaeae* in a tertiary care hospital in south India. Indian J Med Microbiol 2012;30:93-95.

Nordmann P, Dortet L, Poirel L. Carbapenem resistance in Enterobacteriaceae: here is the storm! Trends in molecular medicine. 2012; 18(5):263–72

Nordmann P, Naas T, Poirel L. Global Spread of Carbapenemase-producing *Enterobacteriaceae*. Emerg Infect Dis 2011;17:1791-1798.

Queenan AM, Bush K. Carbapenemases: the versatile β- Lactamases. Clinical Microbiology Reviews 2007;20:440-458.

Solomon SL, Oliver KB. Antibiotic resistance threats in the United States: stepping back from the brink. American family physician. 2014; 89(12):938–41

Wattal C, Goel N, Oberoi JK, *et al*. Surveillance of multidrug resistant organisms in tertiary care hospital in Delhi, India. J Assoc Physicians India 2010; 58:32-36.

Zhanel GG, Wiebe R, Dilay L, *et al*. Comparative Review of the Carbapenems. Drugs 2007; 67:1027-1052.

****