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BRIEF REPORT

Prevalence of carbapenem resistant *Enterobacteriaceae* from a tertiary care hospital in Mumbai, India

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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 treatment options associated with these organisms. Thus, the present study was conducted in our tertiary care hospital in Mumbai, to retrospectively analyze the prevalence of CRE in the hospital.

Methods: The study was carried out in the microbiology department of the tertiary care hospital over a period of 12 months. The samples tested were clinical samples from hospitalized and Out-Patient Department (OPD) patients sent to the department for microbiological testing. CRE isolates were identified using the Vitek 2- Compact system (BioMérieux, France).

Results: A CRE prevalence rate of 12.26% was obtained from the study, from which the majority of the isolates were detected in urine samples (46%). Although most of the CRE isolates were detected in patient samples from the wards (42%) and the ICU (26%), a significant number of isolates was also detected from the OPD patients (19%).

Conclusion: Thus, the study shows a significant rate of carbapenem resistance among *Enterobacteriaceae* isolated from hospitalized and OPD patients. This emphasizes the urgent need for CRE control at the hospital and community level, and to rationalize the use of antibiotics. *J Microbiol Infect Dis 2013;3(4): 207-210*

Key words: Carbapenem Resistant *Enterobacteriaceae*, Antimicrobial Stewardship

Bombay'da bir üçüncü basamak hastanede Karbapenem dirençli Enterobacteriaceae sıklığı

ÖZET

Amaç: Karbapenem dirençli *Enterobacteriaceae* (CRE) enfeksiyonlarındaki artış halk sağlığı için önemli bir tehdit oluşturmaktadır çünkü bu bakterilerin enfeksiyonlarında kullanılabilecek sınırlı sayıda antibiyotik vardır ve mortalitesi yüksektir. Bu çalışma, Mumbai'de bulunan üçüncü basamak hizmet veren merkezimizde CRE prevalansını belirlemek amacıyla retrospektif olarak yapıldı.

Yöntemler: Çalışma mikrobiyoloji bölümünde 12 aylık bir sürede yapıldı. Hem hastane kökenli hem de toplum kaynaklı örnekler çalışmaya dahil edilmiştir. Örnekler Vitek 2- Compact System (BioMérieux, France) ile analiz edildi.

Bulgular: Çalışmamızda CRE sıklığı %12.26olarak bulunmuş olup örneklerin büyük bir kısmı idrar (% 46) örneklerinden elde edildi. Ancak CRE izole edilen örneklerin önemli bir kısmı yara örneklerinden (% 42) idi. Örneklerin % 26'sı yoğun bakım hastalarından izole edilirken %19'u da toplum kaynaklı örneklerden izole edildi.

Sonuç: Çalışmamızda *Enterobacteriaceae* üyelerinin önemli bir kısmında karbapenem direnci olduğu gösterilmiştir. CRE kökenlerinin toplumda ve hastanede kontrol edilmesini sağlayacak önlemlere ve akılcı antibiyotik kullanımı sağlayacak tedbirlere ihtiyaç vardır.

Anahtar kelimeler: Karbapenem Dirençli *Enterobacteriaceae*, Antibiyotik yönetimi

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INTRODUCTION

Carbapenems are a group of β-lactam antimicrobial agents with an exceptionally broad spectrum of activity.[1] 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*.[2,3] 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.[2] These organisms are associated with high mortality rates and have the potential to spread widely.[4]

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.[3] 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 present in the bacterial cell membrane. However, for significant resistance to emerge, it is thought that a combination of resistance mechanisms is required.[5]

Carbapenem Resistant *Enterobacteriaceae* (CRE) can be defined as *Enterobacteriaceae* that are resistant to one or all of the following carbapenems: ertapenem, meropenem, imipenem 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.[4] Also, CRE are found to carry genes that confer high levels of resistance to many other antimicrobials, often leaving very limited therapeutic options.[4,6]

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.[7] 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.[3]

The primary objective of this study was to evaluate the prevalence of CRE in a 330 bedded tertiary care hospital in Mumbai. This study is epidemiologically important since studies based on the emergence and spread of carbapenem resistance in India, are very limited, of which studies pertaining to CRE specifically are even fewer.

METHODS

The study was a retrospective study carried out in the Microbiology department of a tertiary care hospital, Mumbai, from January 2012 to December 2012. The clinical samples tested were those collected from patients hospitalized in the wards, the Intensive Care Unit (ICU), the Cardiac Care Unit (CCU), the Neonatal Intensive Care Unit (NICU), the Pediatric Intensive Care Unit (PICU), as well as from OPD patients coming to the hospital for treatment. These included blood, urine, stool, endotracheal secretions, sputum, pus, wound, and other samples. All samples were processed as per standard microbiology protocol. The identification and antibiotic susceptibility study of all clinical isolates was done using the Vitek 2 Compact System (BioMérieux, France). Isolates that showed elevated MICs to one or all of the following carbapenems-meropenem, imipenem and ertapenem; as well as resistance to ceftriaxone, cefotaxime and ceftazidime were considered to be carbapenem resistant. The resistance breakpoints used for detecting carbapenem resistance among *Enterobacteriaceae* was ≥4µg/ml for imipenem and meropenem, and ≥2µg/ml for ertapenem. The resistance breakpoints used for ceftriaxone and cefotaxime was ≥64µg/ml and for ceftazidime was ≥32 µg/ml. All resistance breakpoints were according to CLSI guidelines (document M100-S22).[3,4,6]

RESULTS

A total of 1282 bacterial isolates were obtained from the clinical samples tested over 12 months, of which 465 were *Enterobacteriaceae*. 57 isolates of the total 465 *Enterobacteriaceae* were found to be carbapenem resistant (12.26%).

The CRE isolates obtained are given in Table 1.

The area wise distribution of CRE identified from the samples in the hospital is given in Fig. 1, and the sample wise distribution is given in Fig. 2.

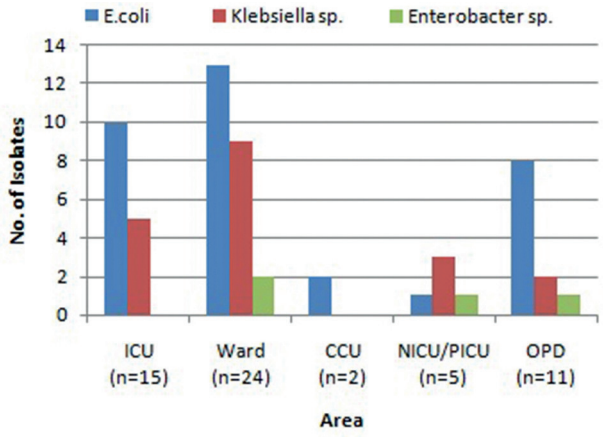

Figure 1. Area wise Distribution of CRE Isolates

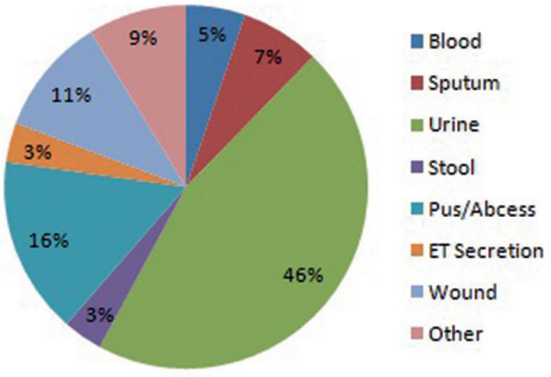

Figure 2. Sample wise Distribution of CRE Isolates

Table 1. Strain and sample distribution of Carbapenem Resistant *Enterobacteriaceae* isolates

	ICU/CCU		Ward			NICU/PICU			OPD		
Sample	*E. coli*	*Klebsiella sp.*	*E. coli*	*Klebsiella sp.*	*Enterobacter sp.*	*E. coli*	*Klebsiella sp.*	*Enterobacter sp.*	*E. coli*	*Klebsiella sp.*	*Enterobacter sp.*
Blood	1	-	-	-	-	-	1	1	-	-	-
Sputum	-	3	-	1	-	-	-	-	-	-	-
Urine	7	-	8	3	-	-	-	-	7	1	-
Stool	-	-	1	-	-	1	-	-	-	-	-
Pus/ Abscess	2	-	3	3	-	-	-	-	-	-	1
ET secretion	1	1	-	-	-	-	-	-	-	-	-
Wound	-	-	1	1	1	-	1	-	1	1	-
Other	1	1	-	1	1	-	1	-	-	-	-

DISCUSSION

The prevalence of CRE in the hospital was found to be 12.26%. 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[3] while Gupta et al reported carbapenem resistance varying from 17 to 22% among *Enterobacteriaceae* strains.[8] Wattal et al reported a high CRE prevalence rate ranging from 13 to 51% in a tertiary care hospital in Delhi.[9] Thus, the significant CRE prevalence rates recorded in different parts of India emphasize the need for controlling the further dissemination of CRE. Of the CRE identified in the hospital, maximum were from patient urine samples (46%). In addition, although most CRE isolates were obtained from patients admitted in the hospital wards (42%) and ICU (26%), a significant number of CRE isolates were also isolated from OPD patient samples (19%). This suggests that several CRE isolated in the study may have been community acquired.

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.[2,10] 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 up due to cost factors. Thus, the need of the hour is the rapid, practical and cost effective phenotypic detection of CRE.[3] CRE infected patients serve as reservoirs for spreading infection and contaminating the environment. Thus, identified CRE infected/ colonised patients must be contact isolated.[11] 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.[12]

The major limitation of our study was the lack of a confirmatory test for the carbapenem resistant *Enterobacteriaceae* identified by the Vitek 2 system. However, since this was a retrospective study of a routine diagnostic lab, the ability of the Vitek 2 system to identify >90% of *Enterobacteriaceae* that are resistant to or that have reduced susceptibility to one or more carbapenems was considered sufficient.[13]

In conclusion, this study shows a significant rate of carbapenem resistance among *Enterobacteriaceae* isolated from hospitalized and OPD patients as reported in similar studies from other parts of India. It provides a clearer picture of the current CRE scenario in the hospital setup of the country and thus further emphasizes the need for control of CRE dissemination within the community. 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. Would Antibiotic holiday, i.e. stopping the use of certain carbapenems, bring back organism sensitivity is another approach to be looked into.

REFERENCES

1. Zhanel GG, Wiebe R, Dilay L, et al. Comparative Review of the Carbapenems. Drugs 2007; 67:1027-1052.
2. 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.
3. 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.
4. 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
5. 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.
6. 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.
7. Queenan AM, Bush K. Carbapenemases: the versatile β- Lactamases. Clinical Microbiology Reviews 2007;20:440-458.
8. 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.
9. 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.
10. Nordmann P, Naas T, Poirel L. Global Spread of Carbapenemase-producing *Enterobacteriaceae*. Emerg Infect Dis 2011;17:1791-1798.
11. 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.
12. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem resistant *Enterobacteriaceae:* epidemiology and prevention. Healthcare Epidemiol 2011;53:60-67.
13. Woodford N, Eastaway AT, Ford M, et al. Comparison of BD Phoenix, Vitek 2, and microscan automated systems for detection and inference of mechanisms responsible for carbapenem resistance in *enterobacteriaceae*. J Clin Microbiol 2010;48:2999-3002.