Research Article

Emerging Resistance to Commonly Used Carbapenem (Imipenem and Meropenem) among the Gram Negative Bacteria in A Tertiary Care Centre of Central India

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ABSTRACT

Carbapenems are well known for their broadest spectrum of clinical activity and utmost potency among the different β-lactam antibiotics. Unfortunately, the recent emergence of multidrug-resistant pathogens seriously threatens this class of lifesaving drugs. To evaluate the pattern and extent of resistance to carbapenem among gram negative bacteria isolated from blood culture at tertiary care centre. Method and material: A cross sectional observational study was conducted in a tertiary care centre. Data regarding culture and sensitivity was obtained from Microbiology department. Resistance to carbapenem was observed to be in 78.35% of gram negative isolates. Imipenem was found to be resistant in around 76.97% while meropenem was resistant in 79.74% of isolates. Terrific high level of resistance to the carbapenem is found among GNB, this is indeed is hazardous not only to patient but also to community.

Keywords: Carbapenems, Gram negative bacteria, Imipenem, Meropenem.

INTRODUCTION

Carbapenems is an important element of our antibiotic resources. Among the various β-lactams currently available, carbapenems has a unique status as it have broader spectrum and are relatively resistant to hydrolysis by most β-lactamases. In addition carbapenems diffuse easily in bacteria and hence it is more efficient. Out of different β-lactams, carbapenems possess the broadest spectrum of activity and great potency. As a result, they are considered as "last-line agents" or "antibiotics of last resort" to deal with serious infection and multi drug resistant strains. These versatile and potent antimicrobial agents had served the humanity for more than 3 decades. Unfortunately, multidrug-resistant (MDR) pathogens are developing resistance to this class of antimicrobial agents. Emergence of carbepenam resistance has seriously threatens health care sector as this class of lifesaving drugs will no more be effective as it was previously.[1]

Mechanisms of resistance to carbapenems occurs through production of β-lactamases, efflux pumps, and mutations that alter the expression and/or function of porins and PBPs. Combinations of these mechanisms can result in high levels of resistance to carbapenems in certain bacterial species, especially in Klebsilla p neumoniae, P. aeruginosa, and A. baumannii.[1,2]

Carbapenem resistance in Gram-positive cocci occurs as a result of substitutions in amino acid sequences of PBPs or production of a new carbapenem-resistant PBP. While among Gram-negative bacteria carbapenem resistance is due to expression of β-lactamases and efflux pumps, as well as porin loss and alterations in PBP.[3]

Carbapenemases belong to specific β-lactamases family. Expression of this enzyme seems to be the most common cause of carbapenem resistance. Some important classes of carbepenamases are class A carbapenemases (e.g., KPC and GES enzymes), class B metallo-β-lactamases (e.g., VIM, IMP, and NDM β-lactamases), and class D carbapenemases have recently reported. Although, class C β-lactamases, such as CMY-10 and PDC β-lactamases are not affective carbapenemses, but it can lead to carbapenem resistance, particularly when it is expressed in combination with other resistance mechanisms.[1,4] It is frightening that bacterial strain producing ESBL and carbapenemase are also being found in the food animals, various food animal species and food products.

These carbepenem resistant strains are threat to critical care management of infectious disease.[5] Carbapenemase producing bugs respond only to colistin, tigecycline, and fosfomycin, none of which is an 'ideal' antibiotic.[6] Hence present study was under taken to evaluate the extent up to which gram negative bacteria have developed resistance to carbapenem.

MATERIALS AND METHODS

A cross sectional observational study was conducted in a tertiary care teaching centre of central India, Gandhi Medical College and associated Hamidia Hospital. The study is approved by of institutional ethical committee. Blood specimens routinely submitted for cultures and sensitivity during the period of September to December 2013 to the microbiology laboratory of the hospital was analyzed. The positive cultures were identified and undergone the culture and sensitivity analysis as routinely

processed in department of Microbiology Laboratory. The antibiotic resistance patterns of the organisms were performed by Kirby- Bauer's disk diffusion method on Mueller Hinton agar plates. Data regarding type of bacterial isolates and antibiotic culture and sensitivity was obtained from bacteriology laboratory of microbiology department.

RESULTS

Total 1319 blood specimen was collected during period of September to December 2013. Out of 1319 blood sample received, 469 turn out to be positive for growth of gram negative bacteria. Among gram negative bacteria most commonly observed pathogen was Klebsiella 239(50.95%), followed by E. coli 92(19.61%), pseudomonas 62(13.21%), and the non lactose fermenting gram negative bacteria 40(8.52%), citrobacter 30(6.39%) and acinetobacter 6(1.27%).

The resistance to carbapenem was observed to be 78.35%. Around 361(76.97%) isolates was found to be non-susceptible to imipenem, while 374(79.74%) isolates were resistant to meropenem. The data of resistant isolates of individual gram negative bacteria are given in the table.

Table 1: Showing the frequency and percentage of different gram negative bacteria

Bacteria	No. of isolates	Percentage	95% confidence interval
Klebsiella	239	50.95%	0.4645 to 0.5546
E. Coli	93	19.82%	0.1646 to 0.2368
Pseudomonas	62	13.21%	0.1044 to 0.1660
NLFGNB	39	8.31%	0.0612 to 0.1119
Citrobacter	30	6.39%	0.0449 to 0.0901
Acinetobacter	6	1.27%	0.0052 to 0.0283

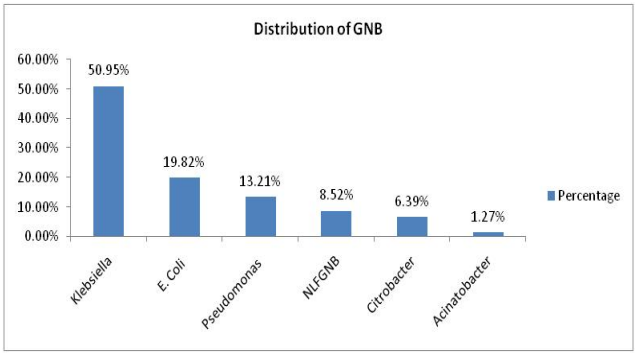

Figure 1: Distribution of various gram negative bacteria

Table 2: Showing the number, percentage and confidence interval of resistant isolates to imipenem

Bacteria	No. of resistant isolates	Percentage of resistant isolates	95% Confidence interval
Klebsiella	186	77.82%	0.7212 to 0.8265
E. Coli	74	79.56%	0.7020 to 0.8659
Pseudomonas	48	77.41%	0.6548 to 0.8616
NLFGNB	27	69.23%	0.5348 to 0.8153
Citrobacter	22	73.33%	0.5535 to 0.8602
Acinetobacter	4	66.66%	0.5535 to 0.8602

Table 3: Showing the number, percentage and confidence interval of resistant isolates to Meropenem

Bacteria	No. of resistant isolates	Percentage of resistant isolates	95% Confidence interval
Klebsiella	199	83.26%	0.7798 to 0.8749
E. Coli	69	74.19%	0.6442 to 0.8205
Pseudomonas	49	79.03%	0.6723 to 0.8745
NLFGNB	28	71.79%	0.5610 to 0.8358
Citrobacter	24	80.00%	0.6233 to 0.9086
Acinetobacter	4	66.66%	0.2957 to 0.9075

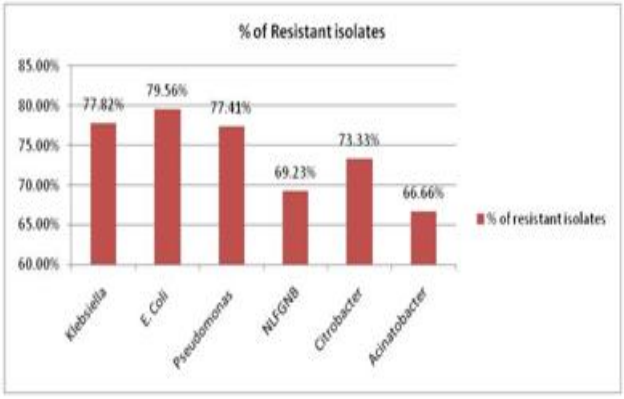

Figure 2: Pattern of resistance to imipenem among GNB

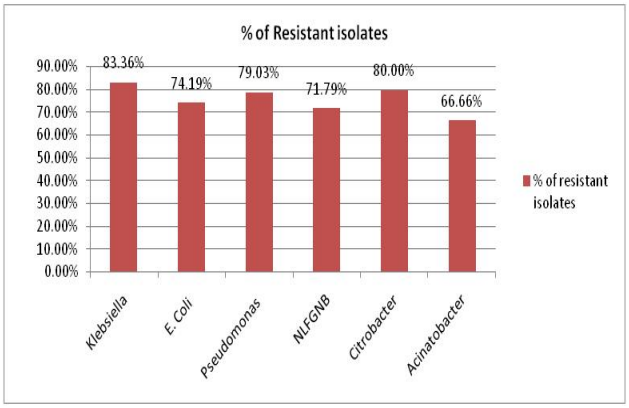

Figure 3: Pattern of resistance to meropenem among GNB

DISCUSSION

As per the study done by Plüss-Suard et al 2013, it was observed that the resistance rate of P. aeruginosa to carbapenems was 19% (weighted mean) (range, 4% to 31%) for all hospitals. The lowest rate was observed in the hospitals of central Switzerland (10%) (Range, 6% to 11%), followed by the ones of southern-western (20%) (Range, 4% to 31%) and eastern Switzerland (26%) (Range, 8% to 30%) (P = 0.27).[7]

Around 23% of the isolates were non-susceptible to imipenem, 21.5% were non-susceptible to meropenem, and 21% were resistant to both carbapenems. Our data shows that carbapenem resistance was associated with significantly increased 30-day mortality rates but that the relationship depended on the degree of severity of the underlying disease.[8] A survey conducted in Korea found that the resistant proportion reportedly grew from 13% in 2003 to 51% in 2008-2009.[9] In present study, it was found that resistance to carbapenem was 78.35% in gram negative isolates. Imipenem was found to be resistant in around 76.97% while meropenem was resistant in 79.74% of isolates. The level of resistance to carbapenem in present study is found to be high as compared to other studies.

The possible explanation for the high level of resistance among the gram negative bacteria in our study region could be indiscriminate and irrational use of antibiotics, poor hygienic practices, lack of hand washing practices, absence of barrier nursing, and no provision of isolation wards or the patients having infection with multidrug resistant strains. Once the multidrug resistant strains gets entered in the hospital, it easily gets prevalent widely as there is no method and practices to check its transmission. Multi- drug resistant strains grows through natural selection because antibiotic commonly used is ineffective against them. Bacteria have tendency for development of resistance, but we promote the spread of resistant strains. Health care worker have major role in transmission of these resistant strains in hospital and in the community. However, the development of carbapenem resistance among these pathogens is attributed to extensive use of carbapenem.[10]

There are some limitations in our study. It is a single centric hospital based observational cross sectional study. There is gape in information regarding Demographic characteristics of patient. Culture and sensitivity analysis was done on the blood specimen routinely received in the microbiology department.

CONCLUSION

We have found high level of resistance to carbapenem among the gram negative bacteria in our study. Carbapenem is a novel class of antimicrobial agents having broad clinical spectrum of activity against gram negative as well as high potency. Carbapenem resistant bacteria represent a major challenge to clinicians, since carbapenem are considered as the reserve drug for the management of life threatening infection and multidrug resistant strains. Terrific high level of resistance to carbepenem is threat to the society and community. Multi-centric study is required to find out more comprehensive information regarding carbepenem resistance. We urgently need planning and strategies to prevent spread of carbepenem resistant strains.

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