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Prevalence of Carbapenem Resistant Gram Negative Bacteria in Rural Hospital Mahabubnagar, Telangana and Systemic Review

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A B S T R A C T

Antimicrobial resistance is serious threat to global health. WHO has declared that antibiotic resistance is one of the top 10 threats to global public health. One of the most useful drugs which possesses broadest spectrum of activity against Gram negative bacterial pathogens are Carbapenems. But with emergence of super bugs several recent studies have shown that the resistance to carbapenems is increasing throughout the world. WHO has identified carbapenem resistant gram negative bacterial infections as priority pathogen list to treat.in my present study 38% of carbapenem resistance is seen and the predominant organism is *Klebsiella pneumoniae* with 56% .most of the CRGNB are isolated from NICU and Paediatric ward. Conclusion Carbapenem resistant gram negative clinical isolates are increasing in rapid rate because of gene transfer throughout the world. In a country like India with huge population, in order to control the spread of these microorganisms, serious steps need to be taken which include contact precautions, hand hygiene , proper medical waste disposal, restricted use of invasive devises and adherent to antibiotic stewardship.

Introduction

Antimicrobial resistance is serious threat to global health. WHO has declared that antibiotic resistance is one of the top 10 threats to global public health. With increase in antibiotic resistance, it threatens the ability of doctors to treat even normal infections (1) throughout the world. Various antimicrobials are used to fight against these drug resistant pathogens. One of the most useful drugs which possesses broadest spectrum of activity against Gram negative bacterial pathogens are Carbapenems. These are used as last line of defence and are defined as 4:5 fused ring lactam of penicillin with a double bond between C-2 and C-3 but with the substitution of carbon with sulphur at C-1 (2). But with emergence of super bugs several recent studies have shown that the resistance to

carbapenems is increasing throughout the world. WHO has identified carbapenem resistant gram negative bacterial infections as priority pathogen list to treat (1).

Several studies have shown that resistance to carbapenems is prevalent throughout India. In lower middle income countries like India with a population of 1.25 billion, the total expenditure on Indian health percapita is 109$ which is far less when compared to the other countries (3) the emergence of antimicrobial resistance in India poses a serious threat to public health which increases mortality, morbidity and economic loss. The specific risk factors for development of antibiotic resistance are substandard living and hygienic conditions, misuse of antibiotics, over the counter and parallel market access,counterfeit or poor quality drugs. As there is ignorance in the risk factor, there were emergence of resistant bacteria, as the microorganisms are capable of transferring genes from one species to another through gene transfer. These microorganisms evolved by various resistance mechanisms against antibiotics which includes loss of porins, beta lactamases in periplasmic space, overexpression of transmembrane efflux pump, the presence of antibiotic modifying enzymes, target site mutation, ribosomal mutations or modifications, metabolic bypass mechanisms, mutations in the lipopolysaccharides and these resistance mechanisms are mostly found in gram negative bacteria (4).

The distribution of multi drug resistant gram negative bacteria varies in different regions in India and the magnitude is directly related to the use of particular antibiotic at that particular area. Carbapenems are the class of beta –lactam antibiotics which mainly act on penicillin binding proteins and leads to cell lysis and they are used to treat MDRGNB infections but with emergence of carbapenem resistant organisms and now there are challenging the antimicrobial therapy The most commonly used carbapenems are imipenem, meropenem, ertapenems and doripenems. There are many mechanisms which cause resistance but the important and most predominant one is carbapenemase production (5). so the primary objective of the present study is to know the prevalence of CRGNB which is important for good infectious control practice and for management of treatment and preventing the spread and decrease the mortality and morbidity.

Materials and Methods

Before start of the present study institutional ethical clearance was taken SVSMC/IEC Approval/no.05/2018-623.

Study design- The study was a prospective study done in the Department of Microbiology, SVS Medical College and hospitals

Study period: was from March 2018-December-2020

Samples – various clinical samples such as; pus blood, sputum, stool, urine, endotracheal aspirates and other body fluids collected from Patients who are hospitalized for greater than 2 days or more in preceding 90 days, residing in nursing home and long term care facilities, Home infusion therapy including antibiotics, Chronic dialysis within 30 days, home wound care, Family members with multi drug resistant and all gram negative bacilli isolated from patients admitted in the hospital.

All the IP samples, received in the Department of Microbiology svs medical college for a period of year are taken and they are identified upto species level by a battery of biochemical reaction and its antimicrobial sensitivity testing was done by VITEK 2 compact system as well as by Kirby baur disc diffusion method The carbapenem resistant

organisms included are *Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, E. coli, and Enterobacter species, Proteus mirabilis, Citrobacter sps, Burkolderia* sps, *Spingomonas* sps

Antibiotic sensitivity testing

Antibiotic susceptibility testing of Gram negative bacilli was performed by both disc diffusion (Kirby-baur) methods as well as by automated VITEK 2 compact (BIOMERIEUX) and interpreted according to Clinical and Laboratory Standards Institute (CLSI 2016) recommendations(7).

The drugs which are used by Kirby-baur disc diffusion method were Gentamicin (10mcg), Ampicillin (10mcg), Cefuroxime 30mcg), Cefotaxime (30mcg), Ceftazidime (30mcg), Amikacin (30mcg), Ciprofloxacin (5mcg), Imipenem (10mcg), Meropenem (10mcg)(Hi Media Laboratories Pvt.Ltd., Mumbai, India). The isolates which show resistant for imipenem and Meropenem (zone diameter of 16-21mm, MIC value of ≥4 µg/ml) are considered as carbapenem resistance.

Statistical analysis

Excel format is used for data entry and tabulated, statistical analysis was performed using spss version 20 and graph pad prism software version 6.0

Results and Discussion

Out of 1032 gram negative isolates 396(38%) organisms are carbapenem resistant strains.

The most predominant strains isolated were of *Klebsiella pneumoniae* with 56% of strains being carbapenem resistant followed by *pseudomonas aeruginosa* 24%, *Escherichia coli* 6.5%, *Acinetobacter* sp 4.2%, *Enterobacter* sp 2.7%, *Citrobacter sps, Proteus sps, Burkholderia sps,* and *Splengomonas* (Table 1).

Distribution of resistant strains in different age group

Most of the resistant organisms were seen in age group of 0- 21 years with 61% followed by 21-40 years with 14% and the least is in 81-100 years in my study (Fig. 1).

Most of the patients were from paediatric and neonatal care (46%) unit followed by general ward (27%) and ICU with 19% (Table 2).

Among the clinical samples Endotracheal secreations 99(25%) were the predominant specimen followed by blood with 89(22%) and pus 80(20%). The prevalence of carbapenem resistance strain in the present study was (n=396) 38%. The predominant organisms was *Klebsiella pneumoniae* (56%) which was isolated predominantly from Endotracheal secretions (30%) followed by blood stream infection (28%). The second predominant isolated organism is *pseudomonas sps* (24%) which was isolated predominantly from pus samples (60%). In *Escherichia coli* 27% are isolated from stool samples indicates excessive use of broad spectrum of antibiotics and if the hygienic conditions are not proper it leads to the dissemination of these organisms with in the hospital. The percentage of carbapenem resistant in enterobacteriaceae CRE was 68% (n=272) and 38.3% (n=124) was nonfermenting CRGNB (Table 3).

The prevalence of CRGNB in present study was 38.3% which was conducted in south India Telangana state. The prevalence of Carbapenem resistant gram negative bacteria varies from 5.5% to 59% in south India. It is difficult to estimate the true burden of antibiotic resistance with in India because of

the lack of mandatory national surveillance system, differing methodology of antibiotic susceptibility testing laboratories and non-uniform samples selection strategies. The antibiotic resistance patterns vary in different places which are probably attributed to the varying antibiogram of different hospitals.

In the present study more number of CRGNB strains were among *Klebsiella pneumoniae* 56% followed by *pseudomonas aeruginosa* with 24% and *Escherichia coli* with 6.5% and remaining species of CRGNB were in between 4.2%to 0.25%. In northern India Punjab 57% of isolates were *Escherichia coli* followed by *Klebsiella* and *Acinetobacter* which constituted 17%. In Western India Maharashtra the predominant isolates were *Klebsiella pneumoniae* 63% followed by *Escherichia coli* 19% (8) (9).

Table.1 The resistant organism are shown in the table

Organisms	Number of isolates (396)	Percentage
Klebsiella pneumoniae	223	56%
Pseudomonas aeruginosa	98	24%
Escherichia coli	26	6.5%
***Acinetobacter* sp**	17	4.2%
***Enterobacter* sp**	11	2.7%
Citrobactersps	7	1.7%
***Proteus* sps**	5	1.2%
***Burkholderia* sps**	8	2%
Splengomonas	1	0.25%

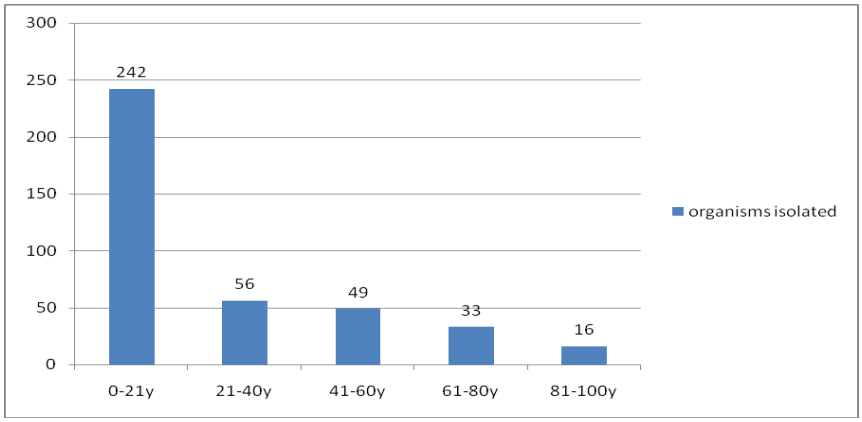
Table.2 Ward wise distribution

ICU	RICU	WARD	NICU/PICU	Total
78	26	109	183	396
19%	6.5%	27.5%	46.2%	

Table.3 Prevalence of CRGNB in different samples

ORGANISMS	BLOOD	CSF	ET	PUS	URINE	SPUTUM	STOOL	OTHERS	TOTAL
Klebsiellasps	64	5	67	30	9	36	4	8	223
Pseudomonas	12	-	4	48	3	28		3	98
E coli	3	2	3		10	1	7		26
Enterobacter	2	1	4		4				11
Acinetobacter	3		12		1	1			17
Burkoladeria	1		7						8
Proteus sps	2		1		1			1	5
Citrobactersps	2		1	2	2				7
Sphingomonas	-							1	1
Total	89	8	99	80	30	66	11	13	396

Fig.1 Age wise distribution



The prevalence of carbapenem resistant enterobacteriace in our study was 68% which is higher than that of Wattal *et al.,* (10) and Gupta *et al.,* (11) with 12% and 51% respectively. In the present study most of the resistant isolates were found in endotracheal tube, blood and were isolated from paediatric intensive care which are on par with Shekhar *et al.*, study (12). The carbapenem resistant gram negative bacteria were completely resistant to ceftazidime, ceftriaxone, cefepine, cefoxitin and piperacillin and tazobactam. Colistin and tigicycline are used to treat carbapenem resistant strain infection but it is quite shocking as some of these organisms are showing resistance to colistin (4%) as well as tigecycline 16%. The increase in resistance was observed mostly because of improper usage of antibiotics, issuing of antimicrobials without prescription (6).

In conclusion carbapenem resistant gram negative clinical isolates are increasing in rapid rate because of gene transfer throughout the world. In a country like India with huge population, in order to control the spread of these microorganisms, serious steps need to be taken which include contact precautions, hand hygiene, proper medical waste disposal, restricted use of invasive devises and adherent to antibiotic stewardship.

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