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Prevalence and Bacteriological Profile of Carbapenem Resistant Gram-Negative Bacteria at a Tertiary Care Hospital, Navi Mumbai

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Abstract **Original Research Article**

Antimicrobial resistance has emerged as a challenging threat in the healthcare sector with the micro organisms developing newer mechanisms for resistance against the first line and also the newer antibiotics available. The number of infections particularly caused by the gram negative bacteria have been ever increasing. It is known that most of the clinically relevant bacteria are capable of acquiring and expressing resistance to antimicrobial agents commonly used to treat infections. Clinicians generally use the Carbapenem antibiotics as a last resort in patients who do not respond to the beta lactams, including the extended spectrum penicillins and the cepahalosporins. The present study was undertaken, to determine the prevalence and bacteriological profile of Carbapenem resistant Gram negative bacteria in the clinical isolates of admitted patients at a tertiary care hospital Navi Mumbai. This was a prospective observational study conducted at Dr D Y Patil Hospital Nerul Navi Mumbai, from January 2019-June2019. The clinical specimens received in the microbiology laboratory were processed as per the standard microbiological methods. The bacteria were identified using manual culture techniques and were tested for antibiotic susceptibility by the Kirby Bauer Disc Diffusion method as per the CLSI guidelines 2019. A total of 4040 samples were received in the microbiology laboratory from the in patient department. Out of which 1560 samples showed growth and 1114 samples were gram negative bacteria. Most commonly isolated organism was Klebsiella pneumonia (*n*=147, 56%) followed by Escherichia coli (*n*=74, 28%). Overall the most frequent source of bacterial isolation was Urinary tract infection (36%). Out of these 29% were Carbapenem Resistant. This concludes, a prevalence of 29% is considerably high and alarming. We have to restrict use of Carbapenems to prevent further increase in the resistance pattern. Early detection, isolation and contact precaution plays an important role in rapid dissemination of Carbapenem Resistant infections.

Keywords: Carbapenem Resistant Gram-Negative Bacilli, Enterobacteriacae, Urine, ICU.

INTRODUCTION

It is known that most of the clinically relevant bacteria are capable of acquiring and expressing resistance to antimicrobial agents commonly used to treat infections [1].

Antimicrobial resistance has emerged as a challenging threat in the healthcare sector with the micro-organisms developing newer mechanisms for resistance against the routinely used and the newer antibiotics available. The number of infections particularly those caused by the gram negative bacteria have been ever increasing with a large number of epidemics encountered [1].

Amongst the gram negative organisms, the Enterobacteriacae inhabit a wide variety of niches, including the human gastro-intestinal tract and various environmental sites. They are currently the major cause of both, the community-acquired, healthcare-associated infections, including urinary tract infections, blood stream infections, respiratory tract infections etc [2].

Every clinically relevant species is capable of acquiring and using one or more mechanisms into developing antimicrobial resistance [3].

Clinicians generally use the Carbapenem group of antibiotics as a last resort in patients who do not respond to the beta-lactams, including the extended spectrum penicillins and the cepahalosporins. Carbapenems generally have an exceptionally broad spectrum of activity [4].

In the past decade, along with the production of Extended Spectrum Beta Lactamases (ESBL) and AmpC production, gram-negative bacilli including Pseudomonas, Acinetobacter and Enterobacteriaciae are now capable of developing Carbapenemase enzymes that confer resistance to the bacteria. Besides, the carbapenemases, the bacteria develop resistance by overexpression of efflux pumps, lack of porin channels present in bacterial cell membrane and inability to appropriately bind to the Penicillin Binding Proteins [5].

Due to the rapid increase in the prevalence and high mortality rates encountered with these Carbapenem Resistant *Enterobacteriaciae* (CR-GNB), their early detection and restricted use is of utmost importance.

Hence, the present study was carried to determine the prevalence and the bacteriological profile of Carbapenem Resistant Gram-Negative bacteria in clinical isolates in our hospital.

MATERIAL AND METHODS

A prospective study was conducted at a tertiary care hospital in Navi Mumbai, India over a period of 6 months from January 2019 till June 2019.

A total number of 4040 specimens were collected from IPD patients for further investigations. The various clinical specimens included were urine, pus & wound swabs, sputum, endotracheal secretions, blood and other sterile body fluids.

All the Carbapenam resistant gram-negative bacteria were included in the study.

The samples were processed as per the standard protocol for isolation and identification of aerobic bacteria [6].

The antibiotic susceptibility testing was carried out for Ampicillin (10 µg), Amoxicillin-Clavulanic acid (20/10µg), Piperacillin-Tazobactam (100/10µg), Ceftriaxone (30µg), Cefuroxime (30µg), Ceftazidime-Clavulanic acid (30/10µg), Cefipime (30µg), Imipenem (10µg), Amikacin (30µg), Gentamicin (10µg), Ciprofloxacin (5µg), Norfloxacin(U) (10µg), Trimethoprim-Sulfamethoxazole (1.25/23.75µg), Nitrofurantoin(U)(300 µg).

Colistin susceptibility testing is outsourced to an external laboratory.

For quality control, ATCC Strain of Escherichia *coli* 25922, *Staphylococcus aureus* 29213 *and Pseudomonas aeruginosa* 27853 were used.

Zone diameter of <19 mm for Imipenem disc was considered as resistant to carbapenem antimicrobials. (CLSI-2019).

RESULTS

A total number of 4040 samples were processed in the present study.

A total of 1560 samples showed growth and out of which 1114 strains of gram-negative bacteria were isolated (71.41%). From these specimens, various strains of *Enterobactericae* family, *Pseudomonas aeruginosa*, *Acinetobacter* spp., & other non-fermenter gram-negative bacilli were isolated.Out of 1114 isolates of gram-negative bacilli, 323 were CRE. The overall CRE prevalence in our study was 28.99%. The most commonly isolated organism was Klebsiella pneumoniae (38%) followed by Escherichia coli (21%) (Fig-1).

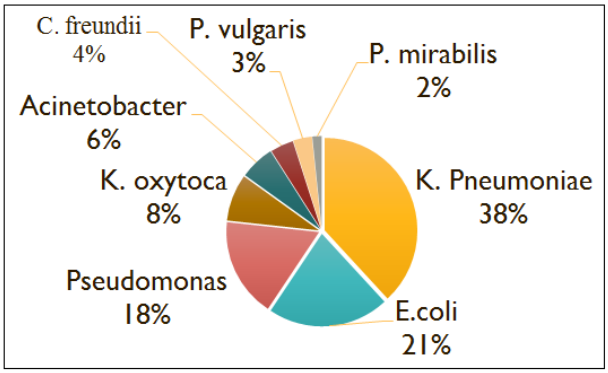

Fig-1: Distribution of bacterial species among CR GNB

116 samples were from urine, 61 samples were from pus & wound swabs, 58 samples were from sputum, 26 samples were from blood, 17 samples were from E.T. secretions and 7 samples were from other body fluids (Fig-2).

Overall, the most frequent source of bacterial isolation was urine (36%) followed by pus & wound swab specimens (19%).

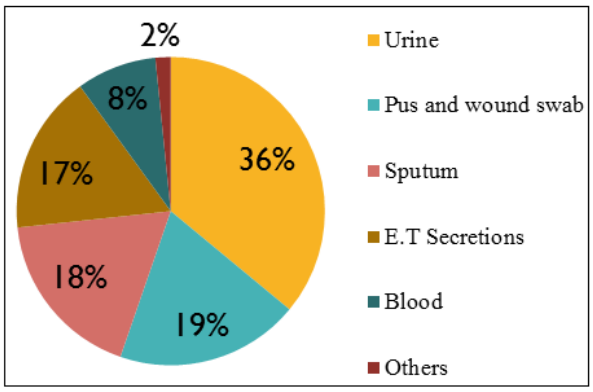

Fig-2: Distribution of CR-GNB among various clinical specimens

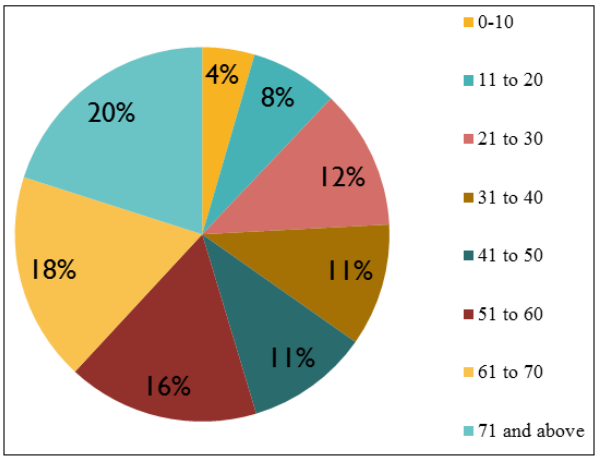

Fig-3: Age wise distribution of the CR GNB isolates

Maximum CRE strains were isolated from ICU (43.46%) followed by 19.51% from Medicine ward (Table-1).

Table-1: CR-GNB Distribution in different wards

CR-GNB Distribution	
Intensive Care Unit	43.56 %
Medicine ward	19.51 %
Surgery Ward	15.04 %
OBGY Ward	9.75 %
Orthopaedics ward	8.94 %
Paediatrics ward	7.31 %

Table-2: Shows Sex Wise Distribution of CR-GNB isolate

Males	62%
Females	38%

DISCUSSION

Increase in the rate of resistance to carbapenem antibiotics among gram-negative isolates is a worldwide concern, especially in developing countries [2].

In this study, high rates of CRE (29%) were observed. Rapid increase of CR-GBN has been reported in India as well as globally [2].

Similarly, a high prevalence of CRE (36.4%) was observed by Taneja *et al*., [7]. Navaneeth *et al*., [20] reported 12% prevalence of CRE in their study P. Gladstone et.al reported a prevalence of 12.2% CRE in their study in Vellore [8].

In the year 2010, resistance to carbapenems was reported in 10%–66% of gram-negative isolates in Saudi Arabia [9].

In this study, Urine was the leading specimen showing highest CRE isolates. Similarly, in studies by Satyajeet Pawar *et al*., [2] from Karad (31.76%), Nair *et al*., [10] from Mumbai (42%) and Singh *et al*., (39.4%) [11], urine was found to be the major contributor of CRE infections.

In the critical care patients, various invasive procedures and the duration of hospital stay contribute to be the high risk factors for the CRE infections.

The most commonly isolated organism in this study was *Klebsiella pneumoniae* (38%) followed by *E.coli* (21%) from the CR-GNB isolates. Similarly, in a study by Shio Shin et al in Taiwan, K. *pneumonia* was most commonly isolated organism. (29.4 %) [12].

Ejaz *et al*., also reported *K. pneumonia* as the most commonly isolated organism in their study (13.03 %) [13]. Jin Suk Kang *et al*., have reported *K. pneumonia* to be the most common isolate (72.7%) [14]

Similar findings were observed in studies by Satyajeet Pawar *et al*., *K. pneumonia* (68%) was the leading isolated followed by *E. coli* (19%) (2). Lorenzoni *et al*., found 95.7% of strains of CRE to be *Klebsiellapneumonia* [15].

Similarly, in a study by Chatterjee et al in north India, *K. pneumonia* was the most commonly isolated followed by *E.coli*. (66 %) [16].

Amongst the Gram Negative Bacilli, the *Enterobacteriaciae* form a major part of the normal gut flora and the increase in the incidence of CR-GNB is being observed due to the increase in the horizontal transmission of plasmid borne genes that are responsible for carbapenemase production [1].

CONCLUSION

This study showed a significantly high rate of Carbapenem Resistance among *Gram Negative Bacteria* isolated from the hospitalized patients which is in accordance with other studies conducted in different parts of India and globally. This alarms us towards a restricted use of Carbapenems to prevent further increase in the Carbapenem resistance.

Early detection, isolation and contact prevention of CR-GNB patients play an important role in preventing and rapid dissemination of such Infections.

Also, the detection of CR-GNB as colonizers of the hospitalized patients will play an important role in prevention of CRE infections.

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