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PREVALENCE OF CARBAPENEM RESISTANCE AND ANTIBIOTIC RESISTANCE PROFILES OF GRAM NEGATIVE BACTERIAL ISOLATES FROM ICU IN AKOLA, INDIA

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ABSTRACT

Aim: Infections due to gram negative bacteria (GNB) mostly affect debilitated patients in intensive care units (ICUs). They are difficult to be controlled and treated due to its prolonged environmental survival and its ability to produce resistance to multiple antimicrobial agents. The present study was carried out to ascertain the prevalence of carbapenem resistance and antibiotic resistance profiles of GNB isolates from ICU.

Methodology: A total of 270 samples from patients of ICU & NICU (Blood-194, CSF-21, Vitreous/ Aqueous fluid-20, Pleural/ Peritoneal fluid-35) were included in the study. BACTEC bottles and BACTEC™ 9050 automated culture system was used. Positive GNB cultures were processed for identification and AST with Vitek-2.

Results: Common isolates were *Escherichia coli, Klebsiella pneumoniae, Pseudomomas aeruginosa, Acinetobacter baumannii and Enterobacter cloacae* and others were *Sphingomonas paucimobilis, Salmonella paratyphi A* and *Serratia spp.* Carbapenem resistance was 41% overall. Resistance to other broad spectrum antibiotics like amikacin, cefepime and colistin was also high. Tigecycline was the only available option with least amount of resistance except, *Pseudomonas spp.* which is a worrying fact.

Conclusions: Direct identification and AST with Vitek-2 gave rapid and reliable results which leads to a significant reduction of patient's morbidity, mortality and medical care cost. Carbapenem resistance was significantly high which was also seen with other broad spectrum antibiotics like amikacin, cefepime and colistin. Tigecycline was the only available option which is a worrying fact. Considerable efforts will be required to maintain the effectiveness of higher antibiotics by rational use & antibiotic stewardship.

Key Words: Vitek-2, GNB, ICU, AST

INTRODUCTION

Infections due to gram negative bacteria (GNB) especially, family Enterobacteriaceae and non-fermenter mostly affect debilitated patients in intensive care units (ICUs). They are difficult to be controlled and treated due to its prolonged environmental survival and its ability to produce resistance to multiple antimicrobial agents.[1]

Beta-lactam antibiotics are among the most widely prescribed antibiotics worldwide.[2] They are important components of empirical therapy in ICUs and high risk wards. The emergence of resistance to these agents in the past two decades has resulted in a major clinical crisis.[3] Antibiotic resistance among Gram-negative bacilli (GNB) is a rapidly expanding problem due to the organisms' ability to mutate, and to acquire and transmit plasmids and other mobile genetic elements encoding resistance genes.[4] There are indications that poor outcome occurred when patients with serious infections caused by Extended spectrum beta-lactamases (ESBLs) and Metallo beta-lactamases (MBLs) producing organisms were treated with antibiotics to which the organisms were resistant.[5]

The detection of organisms in the blood and other specimens is one of the most important tasks performed by the clinical microbiology laboratory. However, standard microbiology diagnosis of infections is slow because most of the GNB

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require an incubation period of 6-24 hours in an automated incubation system. An additional incubation time of 24-48 hours is needed for the biochemical or immunological identification tests and determination of antimicrobial susceptibility testing (AST).[6]

We aimed to give the clinician with early information about the results of culture using Vitek-2 allowing a better prognosis and a reduced mortality rate of the ICU patients.

The present study was carried out to ascertain the prevalence of carbapenem resistance and antibiotic resistance profiles of GNB isolates from ICU.

MATERIAL AND METHODS

The present study was conducted in Micro Point Hitech Microbiology Laboratory extending over a period of 15 months from April 2013 to June 2014. A total of 270 samples from patients of ICU & NICU (Blood-194, CSF-21, Vitreous / Aqueous fluid-20, Pleural / Peritoneal fluid-35) were included in the study. Special blood/fluid culture BACTEC bottles were used and processed in the BACTEC™ 9050 automated culture system (Becton Dickinson, Sparks, Maryland). Positive GNB cultures (Graph.1) were processed for identification and AST with Vitek-2 com (bioMérieux, France) using the ID-GN and the AST-N280 and AST-N281 cards. *E.coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 strains were used for quality control.

RESULTS

Common isolates - *Escherichia coli* (55), *Klebsiella pneumonia* (23), *Pseudomomas aeruginosa* (9), *Acinetobacter baumannii* (4), *Enterobacter cloacae* (7).

Others- *Sphingomonas paucimobilis* (2), *Salmonella paratyphi A* (2), *Serratia spp.* (2).

Resistance rates of some higher antibiotics are given in Table.1. and significant figures are made bold.

DISCUSSION

Carbapenem resistance was extremely slow to appear in *Enterobacteriaceae*, with rates of under 1% even after 20 years of imipenem use.[7] However, in the last decade, carbapenemase-producing pathogens cause infections that are difficult to treat and have high mortality rates, due to their appearance in multidrug-resistant (MDR) pathogens such as *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter spp*.[8]

In our study, *E.coli* followed by *Klebsiella spp*. and *Pseudomonas spp*. were the prevalent organisms (Graph 2) which was also found in many other studies.[9-15]

Carbapenem resistance was significantly high (41% overall) (Graph.3) in our study which was similar to other studies.[16-18] Resistance to other broad spectrum antibiotics like amikacin, cefepime and colistin was also high (Table.1) in the present study which was also found in few other studies.[19-21] Tigecycline was the only available option with least amount of resistance except, *Pseudomonas spp.* which is a worrying fact. But excessive reliability on this option can cause increase in resistance and thus an end of antibiotic era because we will be left with no other options in such MDR infections.

This shows the importance of hospital environment as source of MDR producing organisms. The environment in the ICUs is more vicious due to their co-morbid conditions along with more invasive procedures super added with irrational and extensive use of antibiotics.

The Vitek-2 system which uses a new fluorescence-based technology, was used for the identification and AST of GN clinical isolates. This system monitors the bacterial growth and calculates MICs (Minimal Inhibitory Concentrations) using a unique algorithm. In addition, the Vitek-2 system incorporates several technical improvements which automate many procedures that were performed manually with the previous Vitek system.[22] The direct-identification reporting time of Vitek-2 was about three hrs. Direct testing of susceptibility to 19 antibiotics, i.e., amikacin, ampicillin, ampicillin/sulbactam, aztreonam, cefazolin, ceftriaxone, ciprofloxacin, Extended-Spectrum Beta-Lactamase (ESBL) (include: Cefepime, cefotaxime, ceftazidime, clavulanic acid), colistin, gentamicin, imipenem, meropenem, nitrofurantoin, tigecycline, tobramycin and trimethoprim-sulfamethoxazole was about. Vitek-2 system gave rapid and reliable results with shortening the turnaround time of microbiological laboratory by 24 hrs.

CONCLUSIONS

Direct identification and AST with Vitek-2 gave rapid and reliable results which leads to a significant reduction of patient's morbidity, mortality and medical care cost. The most frequently isolated organism were *E.coli, Klebsiella spp.* and *Pseudomonas spp.* Carbapenem resistance was significantly high which was also seen with other broad spectrum antibiotics like amikacin, cefepime and colistin. Tigecycline was the only available option which is a worrying fact. But excessive reliability on this option can cause increase in its resistance. In the face of continuing development of resistance, considerable efforts will be required to maintain the effectiveness of higher antibiotics by rational use and antibiotic stewardship.

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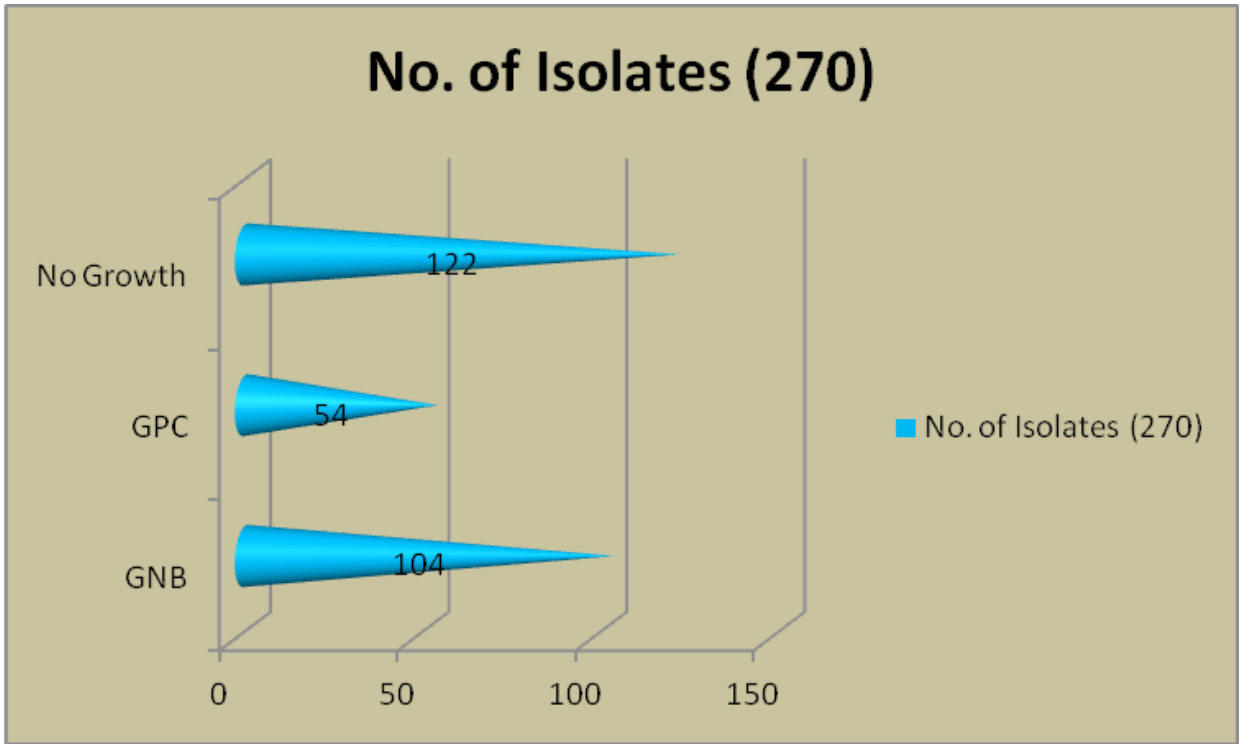
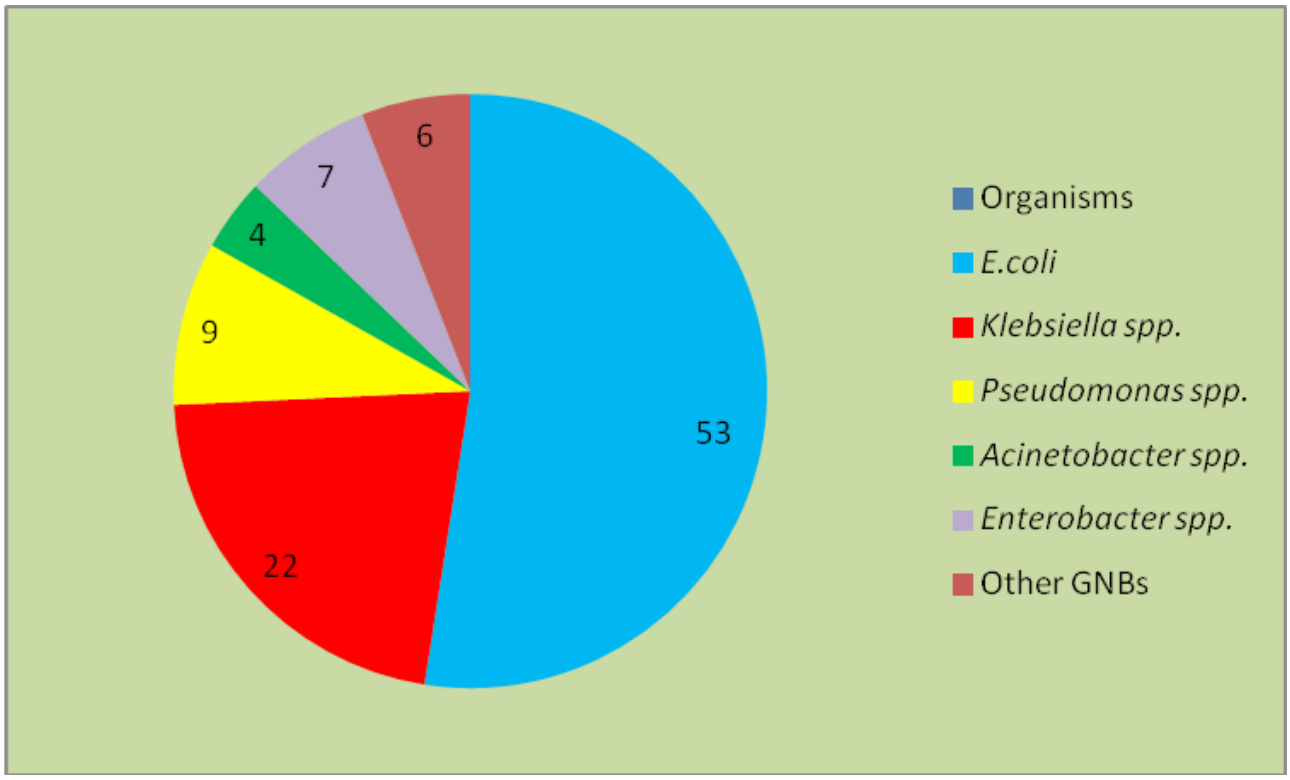
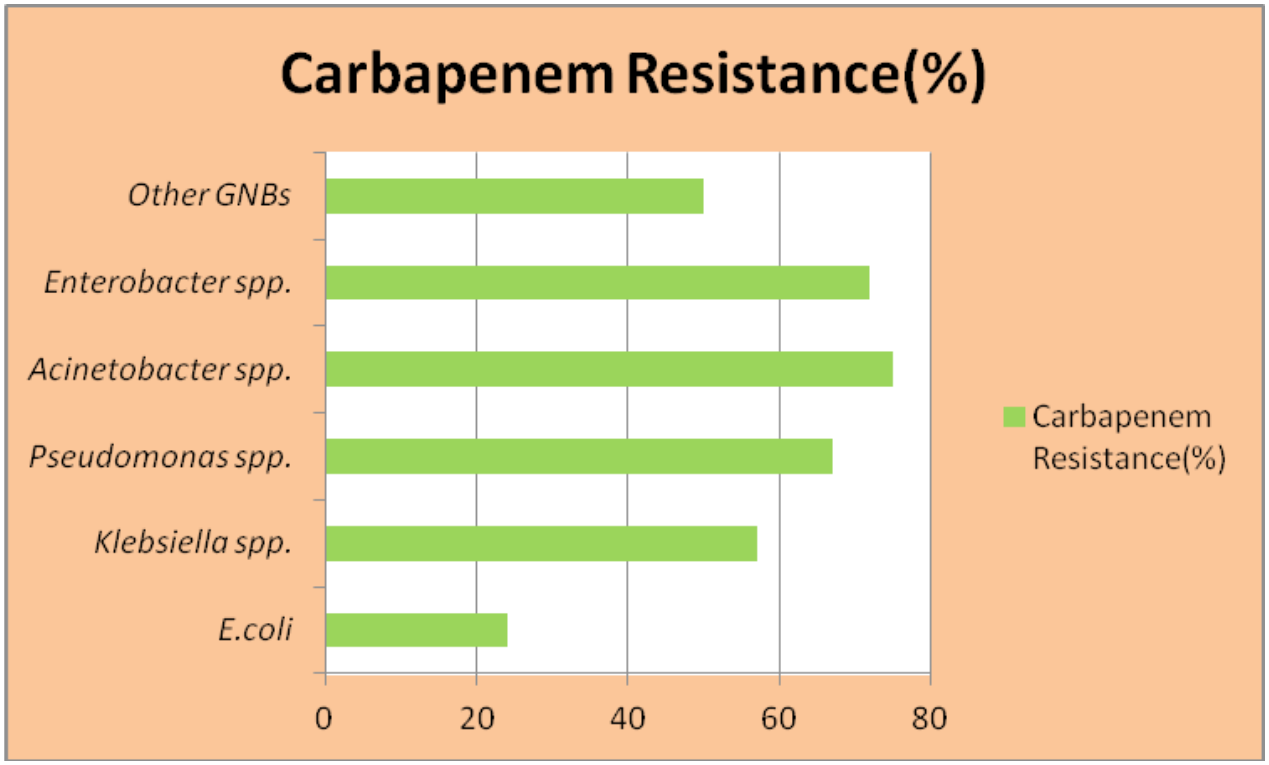


Graph 1: Distribution of isolates (n=270)



Graph 2: Distribution of GNB (%) (n=104)



Graph 3: Carbapenem resistance (%) among GNBs

Table 1: Resistance rates (%) of some higher antibiotics to GNBs

Antibiotics Organisms	Amikacin	Cefepime	Carbapenem	Colistin	Tigecycline
E.coli	22	46	25	13	6
K.pneumoniae	22	**65**	40	17	22
P.aeruginosa	**56**	46	**67**	22	**99**
A.baumanii	75	0	75	25	0
E.cloacae	29	57	72	0	0
Other GNBs	40	**60**	**60**	40	20

Abbreviations
GNB-Gram negative bacteria
ICU-Intensive care unit
NICU- Neonatal intensive care unit
AST-Antibiotic susceptibility testing
MDR-Multidrug-resistant
MICs-Minimal Inhibitory Concentrations
ESBLs-Extended spectrum beta-lactamases
MBLs-Metallo beta-lactamases