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PREVALENCE OF CARBAPENEMASE PRODUCING PSEUDOMONAS AERUGINOSA IN ICU PATIENTS.

Medical Science

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ABSTRACT

BACKGROUND: In recent decades, the global emergence development of multidrug resistance and pan drug resistance in *Pseudomonas aeruginosa* has been observed. This opportunistic pathogen is responsible for causing various infections especially in the intensive care units, resulting almost 10% of hospital acquired infections. So, the aim of the study is to investigate the prevalence of infections due to CRPA among ICU admitted patients.

METHODS. Two hundred consecutive ICU patients in which *Pseudomonas aeruginosa* infection was isolated from different clinical specimens were enrolled in this retrospective multicenter case-control study from January 2018 to January 2019. The prevalence of carbapenemase resistance was analyzed by using Modified Kirby-Bauer disc diffusion technique for antimicrobial susceptibility testing. MBL production was detected by E-Test.

RESULTS. Out of 200 Pseudomonas aeruginosa isolates, a total of 62 isolates were screening test positive on the basis of their reduced susceptibility to meropenem or imipenem. 21/62 was confirmed MBL positive by E-Test.

CONCLUSION: The rate of Carbapenem resistance was significantly higher in ICU with a stay for over a week. Increasing antimicrobial resistance and limited therapeutic options to treat carbapenem-resistant bacteria prompted us to evaluate the clinical outcomes associated with health related infections.

KEYWORDS

Carbapenemase, Intensive care unit, Carbapenem resistant Pseudomonas aeruginosa (CRPA), multidrug-resistant bacteremia.

INTRODUCTION:

The discovery of Carbapenems in the 1980s was the beginning of a new treatment option for serious bacterial infections, resistance towards these drugs especially towards Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter baumanii have been the alarming matter of concern these days. The presence of carbapenem resistant organisms has been limited the choice of appropriate antibiotic therapy. There are three mechanism of ß-lactam antibiotic resistance, including carbapenems. These mechanisms are the production of ß-lactamase which cleave the amide bond of the ß-lactam ring, the possession of an altered or acquired penicillin binding protein with low affinity for ß-lactams and over expression of efflux pump mechanism.[1]. Development of antibiotic resistance in Intensive Care Units (ICUs) is a worldwide problem.

Serious infections caused by bacteria that have become resistant to commonly used antibiotics have become a major global healthcare problem in the 21st century [2]. They not only are more severe and require longer and more complex treatments, but they are also significantly more expensive to treat [2-6].

Pseudomonas spp. are one of the most common isolated organism associated with infections in ICU patients including bacteremia, urinary tract infections, and surgical site infections, but they predominate as agents of lower respiratory tract infections.[5]

Considering the critical risk to public health, the Centers for Disease Control and Prevention has identified carbapenem-resistant Enterobacteriaceae (CRE) as an urgent threat [7], and the World Health Organization has initiated the development of antibiotics against CRE and carbapenem-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* [8].

This study was performed to investigate the prevalence and risk factors of CRPA infection in ICU admission patients and to elucidate a reliable therapeutic options for CRPA infection.

MATERIALS & METHODS

The study was conducted in the Department of Microbiology, Ayaan Institute of Medical Sciences, Teaching Hospital & Research Centre, Hyderabad. During this period, total 200 clinical isolates of *P.aeruginosa* were collected from ICU patients, out of them 62 were carbapenem resistant. These were isolated from clinical specimens such as pus (22), urine (18), blood (1), sputum(3), endotracheal tube(12), folley's catheter tip (2), ascitic fluid (1) and throat swab (3). The organisms were identified by their colony characteristics, staining procedures, pigment production, motility and other relevant biochemical reactions as per standard laboratory methods for identification of bacteria (CLSI guidelines 2018).[9]

SCREENING TEST FOR MBL DETECTION

Susceptibility to various classes of antimicrobial agents was determined by disc diffusion method according to Clinical Laboratory Standard Institute (CLSI) guidelines,2018. [9] The antibiotics tested were amikacin (30 µg), ciprofloxacin (5 µg), ceftazidime (30 µg), aztreonam (30 µg), piperacillin-tazobactam (100/10 µg), imipenem (10 µg), meropenem (10 µg), colistin (10 µg) and polymyxin B (300 units) (Hi-media Laboratories, Mumbai, India). Isolates resistant to imipenem and meropenem were considered as screening positive.

PHENOTYPIC CONFIRMATORY TEST

MBL E-test

The E-test MBL Strip contains a double sided seven-dilution range of IP(Imipenem) (4 to 256 µg/ml) and Imipenem (1 to 64µg/ml) in combination with a fixed concentration of EDTA is considered as the most sensitive method for MBL detection]. The E-test was done according to manufacturer's instructions. MIC ratio of IP/ IPI (Imipenem+ EDTA) of >8 or >3 log dilutions indicates MBL production. [Walsh T etal., 2002][10]

RESULT AND DISCUSSION

During the study period, out of 200 Pseudomonas aeruginosa isolates, a total of 62 isolates were screening test positive on the basis of their reduced susceptibility to meropenem or imipenem. Out of these 62 isolates, 22 were from pus, 10 were urine, 3 were sputum, 12 endotracheal tube, 1 blood, 2 were folley's catheter tip, 1 ascitic fluid and 3 throat swab. Screening positive 62 isolates were confirmed by MBL E-test 21/62 showed metallo beta lactamase test positive by phenotypic methods.

In India the studies done on metallo beta lactamase producing non fermenters are numerous. The prevalence of metallo beta lactamase producers among Carbapenem resistant isolates (Resistant to either or both Imipenem and Meropenem) in the present study was found to be 21/200. The results vary all over the country. The rate of metallo beta lactamase production in our study is much lower compared to most of the other studies done in India It has been reported as low as 7.5%(Gupta et al, 2006) to as high as 100%(Navaneeth et al, 2002).[11,12]

In the present study, pus comprised for the majority of specimen followed by urine, sputum endotracheal aspirations, blood, and other sample. This study is similar to the study by Ranjan et al, 2014 where the majority of specimen included was pus (48.28%).This study is different from the study done by Wankhede etal. where the majority of specimen was wound swab (44.11%). The criteria for choosing the isolates for MBL screening are varied. Some studies have chosen Ceftazidime resistant strains for screening MBL(Hemalatha et al,2005). Most of the studies have chosen Imipenem resistant strains for screening of MBL. In the present study strains resistant towards either or both Imipenem and Meropenem were included. However all the isolates included in the study was resistant to Ceftazidime. 62/200(31%) Pseudomonas *aeruginosa*showed screening test positive. The similar finding were seen by Buchunde et al,2012.[13,14]

Seriously ill-patients in ICUs during treatment mostly requires central lines, dialysis catheters, broad spectrum antibiotics, and mechanical ventilation for prolonged period, which make them to acquire resistant hospital-acquired infections. In our study only 40% of our patients had received carbapenems, but virtually all had antibiotic exposure, this suggests that healthcare exposure and overall prior antibiotic exposure may be more important risk factors for developing carbapenem resistant infections rather than prior receipt of carbapenems.

For early detection and implementation of infection control CDC has implemented guidelines [15] It includes 8 basic measures which have been included in the prevention strategies and include laboratory detection; rigorous implementation and monitoring of infection control measures such as hand hygiene, contact precautions, isolation, setting up of infection control committee, proper medical waste disposal, and maintenance of environmental hygiene; education and training of health care personnel on proper use and rationale of infection control measures along with appreciation/reward of units/staff for best infection control; minimal use of invasive devices; antibiotic stewardship; effective and rational dosing of antibiotics integrating pharmacokinetic and pharmacodynamic profiles of the antibiotic with the microbiological data (minimal inhibitory concentration); screening of epidemiologically linked contacts of colonized or infected patients, active surveillance; and coordinated efforts among health care facilities and encouragement of antimicrobial research and development.

Hospital antibiotic policy should be formulated using the antimicrobial sensitivity data of ICU and referral intrahospital units. Empiric therapy should be based on local antibiograms and antimicrobial susceptibility patterns. Carbapenems are time-dependent bactericidal agents and optimizing carbapenem therapy includes correct dosing and extending time above MIC.[16,17] In addition, the use of carbapenem should be restricted, and they should be used as "reserve drugs," to decrease the selection pressure from antibiotic exposure.

CONCLUSION

This study confirmed that the prevalence of carbapenem-resistant pseudomonas aeruginosa in ICU is high. The present study had several limitations. It was a single centre study with small sample size and the details of previous antibiotic treatment were not available in all patients. Further studies must be done to explain the resistance mechanisms occurring in these isolates.

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