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Original Research Article

Antimicrobial drug sensitivity pattern of *Pseudomonas aeruginosa* in respiratory infections

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ABSTRACT

Background: *Pseudomonas aeruginosa*, a gram-negative pathogen commonly associated with nosocomial infections is the most widespread multidrug-resistant pathogen causing pneumonia in hospitalized patients. Inadequate empirical therapy has been associated with high mortality and morbidity. Objective: To evaluate and analyze the antimicrobial susceptibility pattern of *P. aeruginosa* in respiratory infections in a tertiary care hospital.
Methods: The study was carried out at Kasturba Hospital, Manipal from Jan 2011 to Dec 2011. Specimens of 63 in-patients were analyzed who were culture positive for *P. aeruginosa.*
Results: Majority of patients were aged above 40yrs with a male preponderance. Specimens were taken from patients who were diagnosed with bronchiectasis, pneumonia, COPD, bronchial asthma etc. Overall the organism was most sensitive to carbapenems (87.3%) followed by cefoperazone-sulbactam combination (85.7%). Sensitivity to ceftazidime and cefepime was equal (82.5%) and was more when compared to piperacillin-tazobactam (81.5%). Overall resistance rate was highest for fluoroquinolones (23.8%) followed by aztreonam (22.2%).
Conclusions: Hence we would like to recommend cefoperazone-sulbactam as the preferred antipseudomonal agent and carbapenems as reserved drugs in treating pseudomonal lung infections. Use of fluoroquinolones and aztreonam as monotherapy in resistant P. aeruginosa infections should be restricted.

Keywords: Antimicrobial susceptibility, Antipseudomonal agents, Nosocomial infections, *P. aeruginosa*

INTRODUCTION

Pseudomonas aeruginosa, a gram-negative pathogen is commonly associated with nosocomial infections. It is involved in wide variety of human infections, ranging from superficial skin infections, acute and chronic lung infections to fulminant sepsis. It is distinguished as an opportunistic pathogen causing infection in patients with defective physical, phagocytic and immunological defense mechanisms.[1] Historically it was considered a major burn wound pathogen, an agent of bacteremia in neutropenics and the most common pathogen in cystic fibrosis patients. However, these interesting associations have undergone considerable changes. Now *P. aeruginosa* is the 2nd most common cause of nosocomial pneumonia (17%), 3rd important cause for urinary tract

infection (7%), 4th most common cause of surgical site infection, 5th most common isolate (9%) overall from all sites and 7th most frequently isolated pathogen from the bloodstream.[2]

Antimicrobial resistance (AMR) to broad spectrum antibiotics is an area of prime concern in pseudomonal lung infections.[1,3] It is the most widespread multidrug-resistant (MDR) gram-negative pathogen causing pneumonia in hospitalized patients. It not only limits therapeutic options but also affects clinical outcome by increasing morbidity and mortality.[4] Hence this study was conducted to determine the current antibiotic sensitivity and resistance rates which would help in laying down current recommendations for empirical antibiotic regimens for treating pseudomonal lung infections and also to minimize progression of MDR. The objective of the study was to analyze antimicrobial susceptibility patterns of *P. aeruginosa* in study population.

METHODS

The study was conducted in Kasturba Hospital, Manipal, Karnataka, India over a period of one year (January to December 2011). Study subjects included were patients aged above 18 years of either sex who got admitted to the hospital with respiratory tract infections during study period with positive culture for *P. aeruginosa*. Subjects were explained about the study and written informed consent was obtained.

A total of 63 patients with positive culture for *P. aeruginosa* were included in the study after considering inclusion and exclusion criteria. Pre-designed proforma was used to collect demographic details, laboratory data and treatment information of the patient. Microbiological data including specimen, presence of any associated organism, antibacterial sensitivity and resistance patterns of *P. aeruginosa* was noted.

Microbiology

Culture examination was carried out using blood agar, nutrient agar and MacConkey´s agar, followed by study of colony morphology, pigment production, positive oxidase reaction and oxidase in oxidation fermentation medium.[5] Antibiotic susceptibility was confirmed by disk diffusion technique on Muller-Hinton medium and was performed according to the Clinical Laboratory Standard Institute (CLSI) guidelines. Paper disks were impregnated with antibiotics. These were commercially procured from span diagnostics. Antibiotics which were tested for sensitivity are ceftazidime, cefoperazone-sulbactam, cefepime, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanic acid, aztreonam, carbapenem, gentamicin, tobramycin, amikacin, netilmicin and ciprofloxacin or levofloxacin.

Cultures were incubated overnight at 37°C. Diameter of the zone of inhibition was measured and compared to that

of standard strain and results were interpreted as sensitive and resistant, based on CLSI guidelines.[6]

Statistical analysis

Analysis was primarily descriptive. Data thus obtained was entered in excel sheet. Analysis was done using SPSS version 17.0 as percentages and proportions.

RESULTS

Out of 200 culture positive cases analysed 63 cases were due to respiratory infections, more commonly affecting the males (74.6%), and majority of them were aged 40 and above (Table 1). Majority of the patients which showed positive culture for P. aeruginosa were from bronchiectasis and pneumonia (Figure 1).
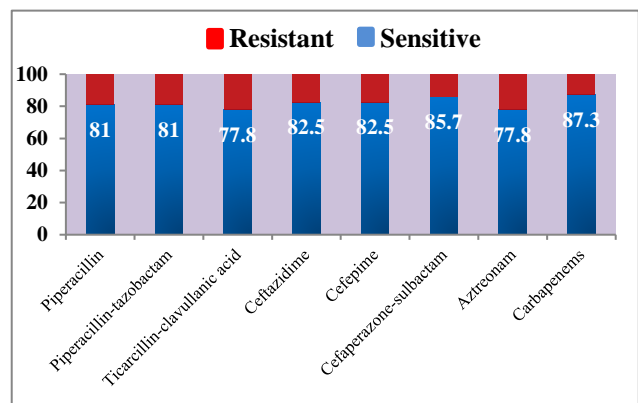
Table 1: Age and sex distribution of study subjects.

Age group (years)	Males	Females	Total (%)
18-40	6	2	8 (12.7)
41-60	20	7	27 (43)
>60	21	7	28 (44.3)
Total	47	16	63
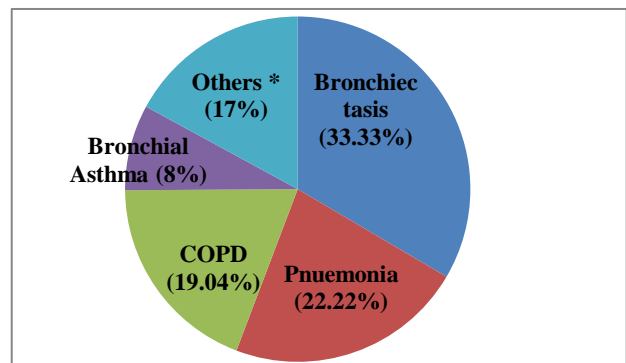
*Positive pseudomonal isolates from ear swab, tracheal swab, pleural fluid, endotracheal aspirate, bronchoalveolar lavage and intercostal drainage.

Figure 1: Disease distribution.

Figure 2: In vitro susceptibilities of *P. aeruginosa* to anti-pseudomonal β-lactam antibiotics.

Among the antipseudomonal penicillin tested piperacillin (81%) was the most sensitive drug and addition of tazobactam to piperacillin was not associated with increase in sensitivity rates. We observed highest resistance rates to ticarcillin-clavulanic acid (22.2%) combination and aztreonam (21.2%) among all β-lactam antibiotics tested. Overall the most sensitive drug was carbapenems (87.3%) which was followed by cefoperazone-sulbactam (85.7%) combination. There was no difference in sensitivity rates between 3rd generation cephalosporin ceftazidime and 4th generation cefepime (82.5%) (Figure 2).

Aminoglycosides were comparatively better than FQ's, especially amikacin which showed highest sensitivity (84.1%) in its group followed by netilmicin (82.5%). Overall the drugs showing highest resistance rates were FQ's (23.8%) followed by ticarcillin-clavulanic acid and aztreonam (Figure 3). The percentage of *P. aeruginosa* isolates that were pansusceptible to ceftazidime, carbapenems, tobramycin, and FQ's was 71.4%. The percentage of isolates that were single-drug resistant was 6.35% and MDR was 17.5% (Figure 4).
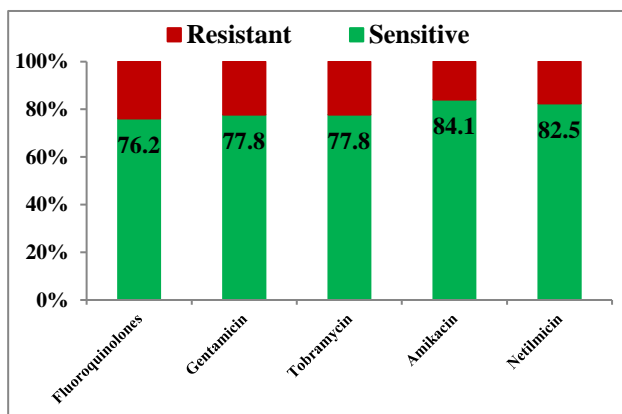
Figure 3: In vitro susceptibilities of *P. aeruginosa* to fluoroquinolones and aminoglycosides.
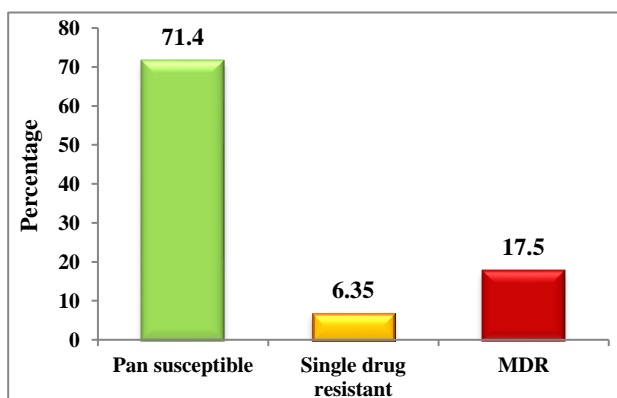
Figure 4: Pansusceptibility, single-drug resistance and Multidrug resistance (MDR).

Pansusceptible is defined as isolates sensitive to all the following agents: ceftazidime, imepenem/meropenem, tobramycin, and fluoroquinolone (i.e., ciprofloxacin or levofloxacin).

Single-drug resistance (SDR)

(SDR) is defined as resistance to only 1 of the following agents: ceftazidime, imipenem/meropenem, tobramycin, or a fluoroquinolone.

Multidrug resistance (MDR)

(MDR) is defined as resistance to ≥3 of the following agents: ceftazidime, imepenem/meropenem, tobramycin, or fluoroquinolone.

DISCUSSION

Out of 200 cases analyzed 32% of cases were respiratory pseudomonal infection. Patients with age above 40yrs (87%) where more commonly affected and there was a male preponderance (74.6%). Bronchiectasis, COPD and pneumonia accounted for 75% of cases making the organism the most common cause of respiratory tract infection amongst all hospital acquired infections (HAIs) (Figure 1). These findings were consistent with the similar studies done in India and worldwide.[7] It is amongst the most common causes of ventilator associated pneumonia and carries the highest mortality among hospital acquired infections. It is known to harbour in damaged bronchi of bronchiectasis patients leading to acute exacerbations.[4]

Among the β-lactam antibiotics tested carbapenems (87.3) showed highest sensitivity rates since this group has the widest spectrum of action among β-lactams and are very resistant to hydrolysis by most β-lactamases.[8] Interestingly the sensitivity rates of 3rd and 4th generation cephalosporins (84%) was superior to piperacillin-tazobactam (81%) combination the reason might be due to irrational prescription of piperacillin-tazobactam leading to resistance. Cefoperazone-sulbactam combination was superior among all cephalosporins and hence one of the preferred drugs used in treatment of respiratory pseudomonal infections. Ceftazidime and cefepime showed equal efficacy but slightly inferior to cefoperazone-sulbactam.[8,9]

Concurrent administration of β-lactamase inhibitor tazobactam did not enhance antipseudomonal sensitivity of piperacillin because resistance might probably due to either chromosomal β-lactamases or decreased permeability of piperacillin into the periplasmic space.[8] Aztreonam and ticarcillin-clavulanic acid (77.8%) showed highest resistance rates among the β-lactams, hence these are not good treatment options for treating pseudomonal infections.

Sensitivity pattern of aminoglycosides and FQ's was better when compared to other studies indicating the samples from respiratory tract infections were more

susceptible than the samples taken from overall pseudomonal infection which was done in others studies.[10,11] On comparing aminoglycosides with cephalosporins they demonstrated similar sensitivity pattern which was consistent with previous studies.[7] Amikacin (84.1%) demonstrated highest sensitivity rates followed by netilmicin (82.5%). FQ's demonstrated resistance rates similar to aztreonam and ticarcillin-clavulanic acid hence these are avoided in MDR infections.

Multidrug resistance phenotypes are slowly increasing in prevalence among *P. aeruginosa* isolates.[12-15] However, comparison between studies is often difficult, because definitions of multidrug resistance have not been uniform.[13,14,16] To analyze the MDR *P. aeruginosa* our study was compared with Karlowsky JA et al, frequency of MDR isolates were considerably high and SDR isolates were very low; indicating progression of MDR (Figure 4).[10] The most common MDR phenotype observed in our study was combination of resistance to ceftazidime, tobramycin and fluoroquinolones. The reasons for increasing nosocomial spread of MDR isolates may include lack of adherence to approved infection control policies in hospitals, increasing or cumulative antimicrobial use, and changes to the public health infrastructure.[16-20]

CONCLUSION

Susceptibility of antipseudomonal agents against respiratory isolates is comparatively better than overall isolates. Authors recommend cefoperazone-sulbactam, ceftazidime and cefepime as the 1st line drugs and carbapenems as reserve drugs in treating pseudomonal lung infections. Use of fluoroquinolones, aztreonam and ticarcillin-clavulanic acid as initial treatment for suspected *P. aeruginosa* infections should be restricted. Significant reduction in susceptibilities of *P. aeruginosa* isolates may compromise the ability to choose efficacious empirical regimens for treating this formidable pathogen especially in critically ill patients. The present study provides valuable information related to emerging trends in antimicrobial resistance to monotherapy, which is vital for clinicians in the selection of reliable empirical regimen for treating *P. aeruginosa* infections.

ACKNOWLEDGMENTS

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