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# ANTIBIOTIC RESISTANCE TREND OF *PSEUDOMONAS AERUGINOSA* IN PORT HARCOURT

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## ABSTRACT

**A study was carried out in a tertiary government teaching hospital in Nigeria to assess the resistance trend of *Pseudomonas aeruginosa* over a four year period, 1997-2002 and to compare the percentage resistance of isolates in in-patients and out-patients. The resistance pattern of five hundred and eighteen (518) non duplicate *P. aeruginosa* strains against gentamycin, ampicillin, augmentin, ciprofloxacin, pefloxacin, tetracycline, ceftazidime, cefuroxime, ceftriaxone, cefotaxime were investigated using the disc diffusion method. The results indicated that the resistance rates were higher among the beta-lactam antibiotics; ampicillin (96-98%), cefotaxime (90-95%) and cefuroxime (80-84%). Over the years, the clinical isolates were significantly more sensitive to fluoroquinolones (80-96%) with higher rates of resistance observed for isolates from in-patients (14.4-25.6%) compared to the out-patients (4.2-15.6%). A decreasing resistance trend was observed for some antibiotics such as ciprofloxacin with decreasing resistance from 19% in year 1997-1998 to 4% in 1999-2000. Establishing an antibiotic resistance surveillance system and continual review of antibiotic policies is an important factor in containing the resistance trend of *P. aeruginosa*.**

## INTRODUCTION

The emergence of multi-drug resistant *P. aeruginosa* remains a global public health burden and a current concern (1, 2). The increasing morbidity, mortality and higher health cost associated with multi-drug resistant Pseudomonas infection (1, 3) necessitate this concern.

Globally, multi-drug resistant *P. aeruginosa* are increasingly implicated in both community acquired and nosocomial infections affecting predominantly patients in intensive care units (ICU's) (1-9).

National surveillance data by National Nosocomial Infections Surveillance System (NNIS) for 1992-2003 reports from U.S. hospital has reported a 32% increase in imipenem, 37% to quinolones and 22% increase in resistance to 3rd generation cephalosporins (10). Furthermore, countries in Europe, Asia and some developing countries have reported similar trends (3, 6, 11). However, in the UK, resistance rates have been reported as stable and low (12).

Various clinical studies in Nigeria reports that *P. aeruginosa* is the major gram negative pathogen involved in both nosocomial (5, 13) and community acquired infection (7). Furthermore, Kehinde *et al* (14) reported 80% resistance of Pseudomonas isolated from burn wounds.

*P. aeruginosa* is inherently resistant to many antimicrobial agents (15, 16,17). Thus, the pattern of antibiotic use and prevalence of resistant strains differ widely in different settings (8, 18), impacting directly on the selection of antibiotic resistance. The above fact necessitates the need to establish the antibiotic resistant pattern of *P. aeruginosa* to commonly used antibiotics in Nigeria. This is with a view to obtaining baseline information on the drug resistant trend of *P. aeruginosa* for appropriate antibiotic therapy in the face of changing resistance trend.

The aim of this study is to describe the resistance pattern of *P. aeruginosa* in the University of Port Harcourt Teaching Hospital, Port Harcourt over a four-year period from 1997 to 2000 in order to contribute in the development of antibiotic policy for the hospital.

## MATERIALS AND METHODS

Five hundred and eighteen (518) non duplicate *P. aeruginosa* isolates were collected over a four year period from various clinical specimens from patients presenting at the University of Port Harcourt Teaching Hospital, in Port Harcourt metropolis, Nigeria. Repeat isolates and samples from same patients were excluded. Bacterial isolates were identified as *P. aeruginosa* using standard techniques (19). Minimum inhibitory concentration (MIC) was determined by disc diffusion method according to modified Kirby-Bauer NCCLS modified technique (20). Commercially available antibiotics tested were; Ceftriaxone (CRO), Ciprofloxacin (CIP), Pefloxacin (PEF), Gentamycin (GEN), Cefuroxime (CXM), Augmentin (AUG), Ceftazidime (CAZ), Tetracycline (TET), Ampicillin (AMP). After overnight incubation at 35°C, zone sizes were measured and interpreted using NCCLS interpretive guidelines. The reference strain *P. aeruginosa* ATCC 27853 was used. Data obtained was analyzed using epi-info soft ware, version 6.04.

## RESULT

Table 1 summarizes the overall resistant pattern of *P. aeruginosa* isolated from both in-patient and out patient. *P. aeruginosa* strains resistant to most antibiotics were from in-patients. However, strains from out-patients were significantly more sensitive to gentamycin (68.5%), ciprofloxacin (95.8%).

Frequency of resistance was highest among the β-lactam antibiotics; ampicillin (97%-98%), augmentin (80%-95%), cefotaxime (83.9%-90.2%) and ceftriaxone (58.9-70.4%). Resistance level for aminoglycosides, gentamycin were 53.3% and 31.5% for isolates from in-patients and out-patients respectively.

Resistance levels for the fluoroquinolones were 4.2%-14.4% for ciprofloxacin and 5.6% -25.6% for pefloxacin showing a decreasing trend over the four years.

Resistance trend for the other antibiotics did not differ remarkably over the period (Fig 1) except for ceftriaxone with resistance decreasing from 63% in 1997-1998 to 48% in 1999-2000.

76% (79) and 78% (118) of ceftazidime and ceftriaxone resistant strains respectively were sensitive to the ciprofloxacin resistant isolates. However, only 20% (70) of the cefuroxime resistant isolates were sensitive to ciprofloxacin. Furthermore of the cefuroxime resistant isolate 68% and 62.4% were susceptible to cefotaxime and ceftazidime respectively.

**Table 1: Comparison of percentage resistance of P. aeruginosa isolates from in-patients and out-patients to various antibiotics**

% Of Resistance

| Antibiotics | In-patient Isolates % (n) | Out-Patient Isolates % (n) | P value |
|---|---|---|---|
| Gentamycin | 53.5 (150) | 31.5(127) | <0.001 |
| Ciprofloxacin | 14.4 (90) | 4.2(95) | <0.05 |
| Cefotaxime | 90.2 (41) | 83.9 (31) | NS |
| Pefloxacin | 25.6 (78) | 15.6 (90) | NS |
| Tetracycline | 97.5 (122) | 89.6 (106) | <0.05 |
| Ceftazidime | 26.3 (80) | 24.2 (62) | NS |
| Augmentin | 95.0 (46) | 80.0 (20) | NS |
| Ampicillin | 98.0 (113) | 97.0 (88) | NS |
| Ceftriaxone | 70.4 (71) | 58.9 (56) | NS |
| Cefuroxime | 80.0 (46) | 83.0 (49) | NS |

## DISCUSSION

*P. aeruginosa* presents a particular challenge due to its inherent resistance to many antimicrobial agents. In Nigeria, many studies have described P. aeruginosa as a major gram-negative pathogen associated with both nosocomial and community acquired infection (5, 7, 14).

In our study, highest resistance was observed in general among isolates from in-patients especially shown to be resistant in particular to the β-lactam antibiotics. However, resistance was statistically significant ($p<0.05$) for isolates resistant to a group of antibiotics; gentamycin, ciprofloxacin, and tetracycline. Most studies have reported similar trend (4, 10, 12) especially in the intensive care units (21). This trend is attributable to the pattern of antibiotic usage, which in most cases is higher in this setting (8). Over the years, various extended spectrum β-lactamases has been found in *P. aeruginosa* (15, 17, 22). Carmeli *et al.* (1) and Gencer *et al.* (6) reported that Increasing resistance to the β-lactam by *P. aeruginosa* during treatment occurs more frequently in imipenem than in ceftazidime and ciprofloxacin. Furthermore, Higgins *et al.* (20), in their own study reported that imipenem resistance does not necessarily mean blanket resistance to all available drugs. Overall, our study indicated lower resistance to ceftazidime and ciprofloxacin 26.3% and 14.2% for isolates from out-patients and 24.2% and 4.2% from in-patients respectively.

Resistance among the Beta-lactam antibiotics especially to ampicillin, augmentin, cefuroxime and cefotaxime was more frequent all year round. Furthermore, compared with earlier studies in Nigeria (14) and elsewhere (6,22), there is a clear tendency towards decreasing resistance for all groups of antibiotics over the years with significant decrease ($p< 0.05$) for ciprofloxacin (19% to 4%), gentamycin (48% to 30%), ceftriaxone (63% to 48%) and tetracycline (97% to 90%). The significant decrease in resistance for gentamycin may indicate the controlled use as the drug of choice for gram negative bacteremia in the hospital. It is generally cited that anti-pseudomonal drugs available for the clinicians include the aminoglycosides, ureidopenicillin, ceftazidime, carbapenem and ciprofloxacin (19, 23). In the local setting, ceftazidime is considered as one reserve drug for multi drug resistant organism including Pseudomonas species. From our study, ceftazidime resistant strains tend to be sensitive to the fluoroquinolones such as ciprofloxacin (77.7%) and pefloxacin (73.0%). Again, ciprofloxacin resistance decreased from 19% in (1997-1998) to 4% in (1999-2000) suggesting that ciprofloxacin may be of therapeutic value with ceftazidime resistant strains.

In summary, resistance of *P.aeruginosa* to β – lactams remains common in our environment. The fact that the high resistance of the organism to most antibiotic remains stable over the years is of grave concern. It adds to the global concern about the rising incidence in resistance (24) especially by *P. aeruginosa* (particularly in intensive care settings) which compromises therapy. The study suggests that a significant percentage of these multi-resistant organisms are hospital acquired. Nipping this problem in the bud requires a review of the hospital antibiotic and hygiene policies and establishing a robust antimicrobial surveillance system. Also, allocation of resources to infection control and raising awareness among health workers and patients on the rising threat of multi drug resistant *P.aeruginosa may* be useful particularly in the face of re-emerging and emerging infectious diseases. Further work to type these *P. aeruginosa* resistant phenotypes is ongoing.

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