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MULTIDRUG RESISTANT *PSEUDOMONAS AERUGINOSA* IN CONTEMPORARY MEDICAL PRACTICE: FINDINGS FROM URINARY ISOLATES AT A NIGERIAN UNIVERSITY TEACHING HOSPITAL

G. T. A. JOMBO, P. JONAH[1] AND J. A. AYENI[1]

Department of Medical Microbiology & Parasitology, College Medical Sciences, University of Calabar, Calabar, Nigeria. E-mail: jombogodwin@yahoo.com Tel +234 8039726398

[1]Department of Medical Microbiology, Jos University Teaching Hospital, P MB 2076, Jos Nigeria.

Summary: Pseudomonas aeruginosa is a bacterium that is often encountered in urinary tract infection (UTI) worldwide and has shown varied antibiotic susceptibility patterns. This study was therefore designed to ascertain the antibiotic susceptibility patterns of the organism in Jos. Data on antimicrobial susceptibility of P. aeruginosa generated from urine samples by the Microbiology laboratory of Jos University Teaching Hospital (JUTH) was compiled for a period of three years (July 2001- June 2004). Additional information was obtained from the records department of the hospital. Samples were collected, stored and processed using standard laboratory procedures. The rate of isolation of P. aeruginosa from urine samples was found to be 4.6% (n=127) from 12,458 samples. From male population 34% (n=43) were isolated and 66% (n=84) were recovered from females population with a significant ($P < 0.05$) gender difference. All the 100% isolates of P. aeruginosa were resistant to penicillin, cloxacillin, tetracycline, nitrofurantoin and nalidixic acid. While 67% were sensitive to augmentin, sensitivity to ofloxacin was 92%, ciprofloxacin 92% and cefuroxime (86%). The resistance pattern of P. aeruginosa from urine against antibiotics was extremely high. Prophylactic antibiotic medication against UTI should be carefully weighed against this undesirable possible outcome (resistance). Susceptibility testing should be adopted as a basic routine laboratory procedure in hospitals and clinics in order to guide appropriately on the right choice of antibiotics. Finally, ofloxacin, ciprofloxacin, and cefuroxime should be considered on isolation of P. aeruginosa from UTI, especially in the absence of a sensitivity report as well as for prophylactic options.

Key Words: *Antimicrobial Susceptibility; Pseudomonas aeruginosa; UTI*

Introduction

Pseudomonas aeruginosa, a gram negative aerobic bacillus is a common environmental organism that causes a wide variety of infections in humans (Woods, *et al,* 1986; Owlia, *et al,* 2000) and opportunistic infections. These infections among others include: bacteriaemia, endocarditis, meningitis, otitis media, osteomyelitis, diarrhoea and enterocolitis, green nail syndrome of skin and urinary tract infection which is usually hospital acquired (Govon, 1989; Ogiwara, *et al,* 1999).

P. aeruginosa possesses several virulence factors which aid in its pathogenicity and resistance to antimicrobial agents (Cane & Walsh, 1999; Lee, *et al,* 2003). These include: possession of mucus- an alginate capsule (Hodges, & Gordon, 1991; Owlia, *et al,* 2001; Ahangarzadeh-Rezaee, *et al,* 2002), presence of exoenzymes S, elastase and phospholipase C (Slack, & Nichols, 1981; Livermore, 1987; Behzadiyan-Nejad*, et al*, 1989); and an active Chaperone Usher pathway (Ichimiya, *et al,* 1994; Vallet, *et al,* 2001).

P. aeruginosa has been shown to be resistant to several antibiotics. In a study carried out in Tunis, Tunisia (Bousseimi, *et al,* 2005), 60.9% of the *P. aeruginosa* isolates were resistant to piperacillin, 53.4% to ceftazidime, 37.6% to imipenem, 70.6% to cefsulodime, 59.3% to tobramycin, 80% to gentamycin, 62.4% to amikacin, and 53.4% to ciprofloxacin. In a similar study carried out in Turkey (Goniugur, *et al,* 2003), resistance of *P.aeruginosa* to gentamicin and tobramycin was found to be 70%, while studies carried out in Spain (Bouza, *et al,* 1999) and Italy (Bonfiglio, *et al,* 1998) showed similar figures. Findings from America (Ronald, & Jones, 2001) showed that, 16.3% of *P. aeruginosa* isolates were resistant to fluoroquinolones and over 80% of the isolates were resistant to Co-trimoxazole, erythromycin, and ampicillin in several studies (Jones, *et al,* 1998; Jones, 1999; Bradford, 2001).

Studies carried out in Nigeria and other African countries on urine and other body secretions have shown closely related but varying findings: Findings

from Nsukka, Nigeria (Chah, *et al,* 2003) on 96 humans showed that, over 80% of *P. aeruginosa* isolates were resistant to cephalexin, co-trimoxazole (80%), ampicillin (73%), gentamicin (70%) and nalidixic acid (70%). In another related study in Enugu (Onyemelukwe, *et al,* 2003), 98.9% of the isolates of *P. aeruginosa* were sensitive to cephalexin and 93.8% to nitrofurantoin. In Gombe (Ahmad, & Kudi, 2003), *P. aeruginosa* was found to be 88.5%, 63.7%, and 61.7% sensitive to gentamicin, cefuroxime, and cephalexin respectively while other antimicrobials tested showed no activity. Also in Ibadan (Oni, *et al*, 2002), *P. aeruginosa* was found to be resistant to co-trimoxazole, ampicillin, and tetracycline but susceptible (over 90%) to Ceftazidime, azithromycin, ceftriaxone, cefuroxime and gentamicin. In Ethiopia (Ferede, *et al,* 2001), *Pseudomonas* species isolated from a study were found to be sensitive to kanamycin (72%), augmentin (84%), and gentamicin (88%), but resistant to all the commonly used antibiotics.

Effective management of *P. aeruginosa* resistance in urinary tract infection (UTI) by health personnel would require a good back ground knowledge of the prevailing antimicrobial susceptibility patterns of the organism. Such information would be even more valuable in the rural health centres of the country where antimicrobial susceptibility reports more often than not, are, understandably, unavailable. These indeed formed the basis for the present study.

Materials and Methods

Setting: The study was carried out at the Medical Microbiology Laboratory of Jos University Teaching Hospital (JUTH), Jos Plateau state in north central Nigeria.

Procedure: The study was retrospectively undertaken; data generated from the antibiotic susceptibility pattern of *Pseudomonas aeruginosa* from urinary isolates against the antibiotics tested was compiled for a period of 36 months (July 2001-June 2004). Samples were collected, stored and processed using standard laboratory procedures while antimicrobial susceptibility test were based on Kirby-Bauer's diffusion method (Duguid, 1989; Scott, 1989; Govon, 1989). Other relevant information such as age and sex were obtained from the patients records.

Analysis of Results: The results were analysed using Epi Info-6 statistical software, p values ≤ 0.05 were considered significant.

Results

One hundred and twenty seven (4.6%) isolates of *P. aeruginosa* were recovered from the 12,458 urine samples processed during the study period; comprising 43 (34.0%) from males and 84 (66.0%) from females, ($P< 0.05$).

Figure 1 shows the antimicrobial susceptibility pattern of *P. aeruginosa* from urine under study. All the isolates (100%) of *P. aeruginosa* from the urine samples were resistant to: ampicillin, penicillin, tetracycline, nitrofurantoin, nalidixic acid, and cloxacillin. The isolates were however: 22% (n=28), 16% (n=20), and 47% (n=59) susceptible to chloramphenicol, co-trimoxazole and gentamicin respectively; while 67% (n=85), 65% (n=82), 92% (n=117), 92% (n=117), and 86% (n=109) were susceptible to: augmentin, ceftriaxone, ciprofloxacin, ofloxacin, and cefuroxime respectively.

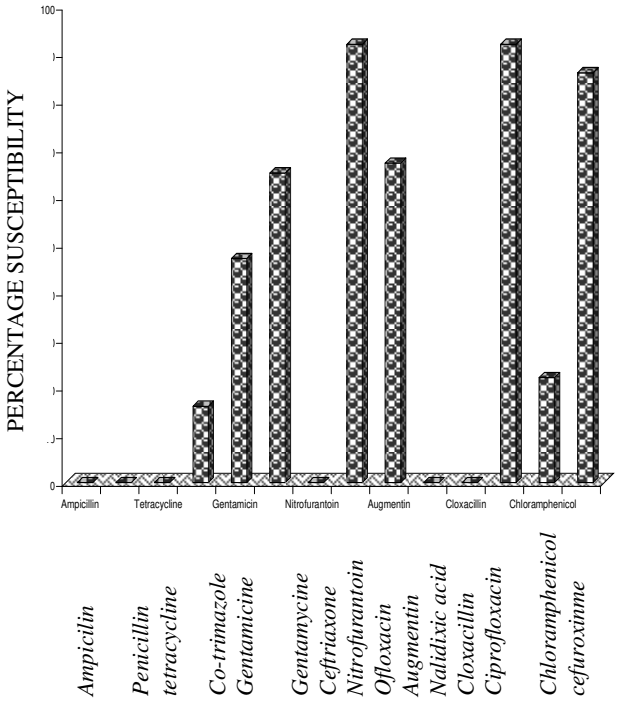

Fig. 1: Antimicrobial susceptibility pattern of urinary isolates of Pseudomonas aeruginosa from Jos

Discussion

The study was designed to ascertain the antibiotic susceptibility patterns of *P. aeruginosa* from urine specimens in Jos. A total of 127 isolates of *P. aeruginosa* were recovered from urine during the study period comprising 66% from females and 34% from males with a significant gender difference ($p<0.05$). This difference could be attributed to the general trend of higher incidence of UTI among females compared to their male counterpart as has earlier been documented (Barnett, & Stephens, 1997; Noskin, *et al,* 2001).

All the isolates of *P. aeruginosa* (100%) in the present study were resistant to penicillin, ampicillin, cloxacillin, tetracycline, nalidixic acid and nitrofurantoin, while the highest sensitivity rate of 92% was recorded with ofloxacin and ciprofloxacin. These findings compare favorably with that of: Goniugur *et al* (2003) in Turkey on 249 isolates of *P. aeruginosa* in a teaching hospital where 100% resistance to ampicillin and penicillin was recorded; Sule *et al,* (2002) in Sagamu, Nigeria who reported a sensitivity of *P. aeruginosa* to aminoglycosides in the range of 61.8%- 75%, fluoroquinolones, 82.8%- 89.2% and co-trimoxazole, ampicillin, and tetracycline, 1.7%- 46.8%; Taiwo *et al,* (2002) in Ilorin who reported *P. aeruginosa* to be sensitive in the range 70%- 94% to ofloxacin and ciprofloxacin, and 55%- 90% to gentamicin, ceftriaxone, azithromycin, and ampicillin; and Olayinka, *et al,* (2004), in Zaria who reported a 27.8% of the 92 isolates of *P. aeruginosa* to be of Ceftazidime + gentamicin + pefloxacin + ofloxacin resistance pattern. Also in Pakistan (Ogundipeju, & Nwobu, 2004), *P. aeruginosa* was similarly reported to be 75%, 30%, and 10% susceptible to gentamicin, streptomycin and tetracycline respectively; while in Japan, Ogiwara, *et al* (1999) as well reported a high resistance (over 90%) of the organisms to tetracycline, nalidixic acid, nitrofurantoin, co-trimoxazole and ampicillin.

Similar susceptibility patterns of *P. aeruginosa* were also reported in Saudi Arabia and Kuwait (Rotimi, *et al,* 1998), Canada and Brazil (Pfaller, *et al,* 1998), and South Korea (Cane, & Walsh, 1999). Findings from this study also compares well with that from Egypt which showed a resistance of about 95% *P. aeruginosa* isolates against ampicillin (Elkholy, *et al*, 2003). This high resistance of *P. aeruginosa* is believed to be as a result of the ability of the organism to undergo mutation and acquire resistant genes at a faster rate compared to *Enterobacteriaceae* (Woods*, et al,* 1986).

Administration of antibiotics as a prophylactic measure against UTI should always be analysed critically and the benefits seen to be well above the side effects of which resistance is one of them, before choosing such a management option (Struelens, 1998). Prolonged or permanent urethral catheterizations are notable scenarios often encountered and their benefits need be periodically reviewed. Also, health personnel should be aware of the prevailing antimicrobial activity pattern of, at least, the locally available antibiotics against *P. aeruginosa* so as to make correct or near correct prescriptions in the absence of a comprehensive antimicrobial susceptibility report (Swedish-Norwegian Consensus Group, 1998). This would help reduce the external stimuli from inappropriate drug prescriptions towards the development and acquisition of resistance genes by bacteria (Ayliffe, 1996).

In view of the current rate of antimicrobial resistance of *Pseudomonas* as found in the present study, antimicrobial susceptibility testing by Microbiology laboratories of hospitals and clinics should be made a routine practice in such health centres. Also the procurement of reagents and materials for susceptibility testing along with the requisite personnel should be considered a basic laboratory requirement in order to boost this conventional practice.

Regional referral health centres (Teaching hospitals, Government specialist hospitals and other major General hospitals) should assist in compiling periodic or at least monthly antimicrobial susceptibility patterns of bacterial isolates for probable consultation by health personnel in the respective health institutions. Such data could be made available to the neighboring smaller clinics and health centres incapable of carrying out sensitivity tests so as to help guide the relevant health personnel on the most suitable antibiotic to prescribe.

The findings from this study are however different from that of Bouza, *et al,* (1999) in Spain (Bouza, *et al,* 1999) who recorded much lower resistance figures of antibiotics tested against *P. aeruginosa* as follows- imipenem, 8%; tobramycin-piperacillin, 10%; aztreonam, 23%; cefepime, 17%; imipenem, 14%; amikacin, 9%; ticarcillin, 13%; ceftazidime, 15%; ofloxacin, 30%, and gentamicin, 31% in a study on 136 hospitals. The carbapenems, meropenems and quinolones which constitute the bulk of the antibiotics used in the Spanish study under review are relatively newer drugs against which bacteria are yet to develop widespread resistance genes. This also further buttresses the fact that, prolonged contact of antibiotics with bacteria stimulates them to develop resistance, an occurrence which can be controlled if the duration of contact is adequately and considerably shortened through prudent and more justifiable reasons for antibiotics prescriptions and intake.

In conclusion, this study has shown that, the rate of antibiotics resistance against *P. aeruginosa* is extremely high in Jos. Prudent and more justifiable reasons for antibiotics consumption both for prophylactic and therapeutic use against UTI should be critically weighed against the side effect of resistance development. Furthermore, antimicrobial susceptibility testing should be performed as a basic laboratory procedure among hospitals and clinics so as to aid in the choice of antibiotics prescriptions. Also sensitivity data should be generated by referral

health centres and periodically sent to neighboring smaller, often less equipped clinics for regular reference. Finally, cefuroxime, ofloxacin, and ciprofloxacin should be recommended on isolation of *P. aeruginosa* in the absence of a viable susceptibility report.

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