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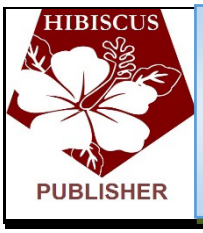

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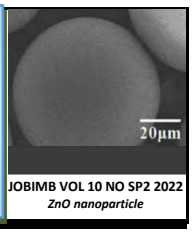

Antimicrobial Resistance Pattern of Clinical Isolates of *Pseudomonas aeruginosa* from Urinary Tract Infections in Wukari, Taraba state, Nigeria

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ABSTRACT

Pseudomonas aeruginosa is a potent nosocomial pathogen of immunocompromised individuals, causing several infections while also resisting chemotherapy with conventional antimicrobial agents. Hence, this study was carried out to determine the antimicrobial resistance pattern of *P. aeruginosa* associated with urinary tract infections (UTIs) in Wukari, Taraba State. Thirty (30) voided midstream urine were collected from clinically diagnosed UTI patients attending Wukari general hospital and cultured aerobically on MacConkey agar and cysteine-lactose-electrolyte-deficient (CLED) agar. Bacterial isolates were identified by Gram staining and conventional biochemical tests. Antimicrobial sensitivity testing was done using the modified Kirby-Bauer method of the disc diffusion test. A total of 46 uropathogens were isolated of which 8 (17.39%) were identified as *P. aeruginosa*. Of these 8 isolates, 6 (75%) were isolated from male patients while 2 (25%) were isolated from female patients. All isolates of *P. aeruginosa* were susceptible to imipenem, ofloxacin, gentamicin, and levofloxacin. The resistances included resistance to amoxicillin-clavulanate (100%), cefepime (87.5%), cefotaxime (87.5%), ampiclox (75%), ceftriaxone (62.5%), cefuroxime (62.5%), and nalidixic acid (37.5%). High resistance rates against penicillins and cephalosporins are an indication of intrinsic resistance in *P. aeruginosa*. Hence, chemotherapy with imipenem, ofloxacin, gentamicin, and levofloxacin should be regularly monitored to prevent the development of resistant strains.

INTRODUCTION

Urinary tract infections (UTIs) are one of the most common infections in clinical settings, culminating in the hospital visitation and hospitalisation of large numbers of patients globally [1]. Urinary tract infection is a condition of severe inflammation of any part of the urinary tract system due to microorganisms and their products. Urinary tract infections can include infections of the kidney, ureter, urinary bladder, and urethra [2-3]. UTIs occur both in males and females; however, it is more prevalent in females due to the short anatomy of their urinary tract system, and a urethra that lies close to the genital tract [4]. *Pseudomonas aeruginosa* is one of the different aetiologies of urinary tract infections.

Pseudomonas aeruginosa is a Gram-negative bacillus, catalase-positive, and oxidase-positive aerobe. It is an opportunistic pathogen that is most associated with nosocomial and life-threatening infections, especially among immunocompromised and critically ill patients [5]. The organism causes respiratory tract infections, urinary tract infections, wound infections, and otitis media; readily forming biofilms that enable it to cause infections [6-7]. Despite its associated morbidities and mortalities, the public health significance of *P. aeruginosa* is exacerbated by the widespread distribution of antibiotic-resistant and multidrug-resistant strains of the organism in both clinical and community settings [8-9].

Antimicrobial resistance (AMR) has become a stagnated public health challenge globally. The challenge of AMR strains is not delimited to increasing morbidity and mortality rates in patients, but also includes the accruing of huge extra costs to healthcare systems [10]. According to Garcia-Fernandez *et al.*, mortality rates due to antimicrobial-resistant microbial infections are estimated to surpass cancer-associated mortalities by 2050

[11]. The widespread dissemination of antimicrobial resistance has been associated with several factors, including indiscriminate prescription and usage of antibiotics, over-the-counter sale of antibiotics without a proper prescription, and indiscriminate agricultural use of antimicrobial agents as stimulants for improved yield and treatment against infections and diseases. These, and myriad of other factors ultimately contribute to bacterial adaptation to selective pressure against antimicrobial agents, which then culminates in the development of antimicrobial-resistant and multidrug-resistant strains [12-14].

Antimicrobial resistance in *P. aeruginosa* is mediated by both chromosomal and plasmid mechanisms [15]. Chromosomal resistance includes mutational derepression of the AmpC beta-lactamase (penicillins and cephalosporins), mutational modification of drug targets (fluoroquinolones), mutation of outer membrane proteins that prevent drug uptake (carbapenems), and overexpression of efflux systems (beta-lactams, fluoroquinolones, and aminoglycosides) while the plasmid-mediated acquisition of resistance genes for beta-lactamases and aminoglycoside-modifying enzymes have been reported [16-17]. The public health significance of antimicrobial-resistant strains calls for the need to regularly monitor the antimicrobial resistance pattern of bacterial pathogens as this will help in the appropriate selection of antibiotics to prevent the evolution of resistant strains [4]. Hence, this study was carried out to determine the antibiotic resistance pattern of uropathogenic *Pseudomonas aeruginosa* in a secondary healthcare center in Wukari, Taraba State, Nigeria.

MATERIALS AND METHODS

Study area

Wukari is one of the local government areas of Taraba State, Nigeria. It is located between longitude $7^0$57'E and latitude $9^0$42'. Wukari is bounded by Ibi local government to the north, Donga local government to the east, Gassol local government to the northeast, and Ukum local government area of Benue State to the south [18]. Wukari is cosmopolitan, dominated by people from different cultures and tribes including, but not limited to, Jukun, Kutep, Tiv. The majority of residents of the local government area are farmers, herdsmen, fishermen, and traders. Wukari is endowed with several educational institutions, including primary schools, secondary schools, and two tertiary institutions- Federal University Wukari and Kwararafa University [18].

Sample collection and ethical approval

Thirty (30) voided mid-stream urine specimens were collected from clinically diagnosed patients with urinary tract infections at different primary and secondary health care centres within Wukari metropolis, Wukari, Taraba State. Ethical approval was obtained from the ethical review committee of General Hospital Wukari. Individual patients were properly informed about the aim, objectives, and benefits of the study prior to them giving consent to be included in the study.

Sample culture and bacterial identification

Urine samples were cultured primarily on cysteine lactose electrolyte deficient (CLED) agar (Oxoid, UK) and MacConkey agar (Oxoid, UK) and incubated aerobically at 37 °C for 18 – 24 hours. Individual and morphologically dissimilar bacterial colonies from the primary culture plates were subcultured on freshly prepared MacConkey agar and incubated aerobically at 37 °C for 18 – 24 hours. Individual bacterial isolates were identified by Gram's differential staining and conventional biochemical tests including catalase, oxidase, citrate, indole, and triple sugar iron agar tests [19-20]. *Pseudomonas aeruginosa* isolates were identified as catalase-positive, oxidase-positive, citrate-positive, indole-negative, H_2S-negative Gram-negative bacilli with alkaline slant and alkaline base with triple sugar iron agar test.

Antibiotic sensitivity testing

Overnight cultures of the bacterial isolates were standardized to 0.5 McFarland standard using normal saline. Standardized bacterial inocula were then used to inoculate the surface of freshly prepared Mueller-Hinton agar plates using sterile swabs. Using the modified Kirby-Bauer method of disc diffusion test, antibiotic multidiscs (Optu Disc) were aseptically placed on inoculated agar plates. *Pseudomonas aeruginosa* isolates were tested against ceftriaxone (30 µg), cefuroxime (30 µg), ampiclox (30 µg), cefotaxime (30 µg), imipenem (10 µg), ofloxacin (5 µg), gentamicin (10 µg), nalidixic acid (30 µg), levofloxacin (5 µg), cefixime (30 µg), and amoxicillin/clavulanate (30 µg).

Prediffusion of antibiotics was allowed for 10 minutes before incubating aerobically at 37 °C for 16 – 18 hours. After incubation, zones of inhibition (ZIDs) on individual sensitivity plates were observed and measured in millimetres. Measured ZIDs were then compared with standards reported by Clinical laboratory standards institute and used to classify bacterial isolates as susceptible, intermediate, and resistant to individual antibiotics [21].

RESULTS

A total of forty-six (46) bacterial isolates were recovered from the collected thirty (30) urine samples. Of the 46 isolates, 8 (17.39%) were *P. aeruginosa*. **Table 1** shows the prevalence of *P. aeruginosa* in patients with UTIs in Wukari. Of the 30 patients included in the study, 8 (26.67%) were positive for *P. aeruginosa*-associated UTI. Of the 8 UTI-associated *P. aeruginosa*, 6 (75.0%) were recovered from male patients while 2 (25.0%) were recovered from female patients. However, there is no significant difference in the prevalence of *P. aeruginosa* with the age (p= 0.987986) and sex (p= 0.151446) of patients. **Table 2** shows the antibiotic sensitivity pattern of uropathogenic *P. aeruginosa*. All isolates were susceptible to imipenem, ofloxacin, gentamicin, and levofloxacin and resistant to amoxicillin/clavulanate. The organism was most resistant to cefixime (87.5%), cefotaxime (87.5%), ampiclox (75%), cefuroxime (62.5%), ceftriaxone (62.5%), and nalidixic acid (37.5%).

Table 1. Prevalence of *P. aeruginosa* by age and sex of patients with urinary tract infections.

	Sex (%)			
Age	Male (n= 16)	Female (n= 14)	Total (n=46)	p-value
0 – 9	0 (0.0)	0 (0.0)	0 (0.0)	0.987986
10 – 19	0 (0.0)	0 (0.0)	0 (0.0)	
20 – 29	3 (50.0)	1 (50.0)	4 (40.0)	
30 – 39	2 (33.33)	1 (50.0)	3 (50.0)	
40 – 49	1 (16.67)	0 (0.0)	1 (50.0)	
Total	6 (75.0)	2 (25.0)	8 (17.39)	0.151446

Table 2. Antibiotic sensitivity pattern of *P. aeruginosa* causing urinary tract infections.

Antibiotic	Sensitivity	
	Susceptible (%)	Resistant (%)
Ceftriaxone (30 µg)	3 (37.5)	5 (62.5)
Cefuroxime (30 µg)	3 (37.5)	5 (62.5)
Ampiclox (30 µg)	2 (25)	6 (75)
Cefotaxime (30 µg)	1 (12.5)	7 (87.5)
Imipenem (10 µg)	8 (100.0)	0 (0.0)
Ofloxacin (5 µg)	8 (100.0)	0 (0.0)
Gentamicin (10 µg)	8 (100.0)	0 (0.0)
Nalidixic acid (30 µg)	5 (62.5)	3 (37.5)
Levofloxacin (5 µg)	8 (100.0)	0 (0.0)
Cefepime (30 µg)	1 (12.5)	7 (87.5)
Amoxicillin/Clavulanate (30 µg)	0 (0.0)	8 (100.0)

DISCUSSION

Pseudomonas aeruginosa is a potent nosocomial pathogen of critically ill and immunocompromised patients. The organism possesses a vast array of pathogenic factors that allows it to cause a vast array of infections and diseases, while also resisting conventional antimicrobial agents. One such disease associated with *P. aeruginosa* is urinary tract infections, a common condition that commands numerous hospital visitations and hospitalizations annually. In this study, a 17.39% prevalence of *P. aeruginosa* was reported among uropathogenic bacteria which is significantly higher than the 4% reported by Brown *et al.* in asymptomatic UTIs in Wukari [22]. Similar studies have also reported lower prevalence rates of *Pseudomonas aeruginosa* in UTIs than that reported in this study [1, 23-31]. However, the reported prevalence is lower than the 18.70% reported in Egypt [32].

P. aeruginosa isolates in this study were highly resistant to ceftriaxone, cefuroxime, ampiclox, cefotaxime, cefepime, and amoxicillin-clavulanate. Conversely, the isolates were sensitive to imipenem, ofloxacin, gentamicin, levofloxacin, and nalidixic acid. *P. aeruginosa* has been reported to possess intrinsic resistance to most beta-lactam antibiotics such as cephalosporins and penicillins due to its outer lipopolysaccharide membrane which decreases antibiotic permeability and uptake into the cell [7, 33-34]. *Pseudomonas aeruginosa* strains have also been reported that encode the gene for *AmpC* beta-lactamases that confers intrinsic resistance to most beta-lactam antibiotics [16,35]. High resistance patterns in *P. aeruginosa* against beta-lactam antibiotics have also been reported in related studies. In Ethiopia, Tuem *et al.* [1] reported 81.8% and 100% resistance to ampicillin and ceftriaxone respectively, Addis *et al*. [23] reported 100% resistance to ceftriaxone, and Motbainor *et al.* [28] reported 100% resistance to ampicillin, amoxicillin-clavulanate, ceftriaxone, and cefotaxime.
Mohamed *et al*. [27] reported high resistance rates in uropathogenic *P. aeruginosa* against beta-lactam antibiotics and fluoroquinolones, while Abbas *et al.* [32] reported high resistance against beta-lactams but minimal resistance against fluoroquinolones, carbapenems, and aminoglycosides. Minimal resistance against fluoroquinolones, aminoglycosides, and carbapenems reported in this study is supported by reports in similar studies [1, 23-27].

Several studies have also positively correlated antibiotic resistance in *P. aeruginosa* with the production of biofilms [34, 36-37]. Low resistance in uropathogenic *P. aeruginosa* against imipenem, ofloxacin, levofloxacin, and gentamicin shows that the antibiotics can be employed in the treatment of *P. aeruginosa* infections in the area. However, care should be taken to prevent inappropriate therapy that can cause the evolution of resistant strains that yields poor clinical outcomes [38]. However, in a bid to reduce the risk associated with the evolution of antibiotic-resistant strains, several researchers have suggested combination therapy in the treatment of *P. aeruginosa* infections [39-40].

CONCLUSION

This study was carried out as surveillance of antibiotic resistance patterns in uropathogenic *P. aeruginosa* in Wukari, Taraba State. From the study, isolates of *P. aeruginosa* were resistant to ampiclox, amoxicillin-clavulanate, ceftriaxone, cefepime, cefuroxime, and cefotaxime but sensitive to imipenem, levofloxacin, ofloxacin, and gentamicin. Hence, imipenem, levofloxacin, and gentamicin can be employed in the treatment of *P. aeruginosa* infections in this area.

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