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Nosocomial and community acquired uropathogenic isolates of *Proteus mirabilis* and antimicrobial susceptibility profiles at a university hospital in Sub-Saharan Africa

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ABSTRACT

Objective: To ascertain antimicrobial susceptibility profile of *Proteus mirabilis* (*P. mirabilis*) from clinical urine specimens at a university hospital in the spate of its recorded increasing resistance patterns.**Methods:** The study was retrospective in nature. Data generated from urine cultures of patients at University of Calabar Teaching Hospital for a period of five years (2004-2009) were compiled. Relevant information obtained were age and gender of patients, organisms recovered and their antibiotic susceptibility patterns. *P. mirabilis* was identified using standard laboratory procedures. **Results:** *P. mirabilis* showed the highest resistance against ampicillin, cloxacillin, amoxicillin, tetracycline, co-trimoxazole, erythromycin and chloramphenicol (100%-37.2%) while colistin, ofloxacin, ciprofloxacin, ceftriaxone, nalidixic acid and nitrofurantoin recorded the highest activity (59.1%-96.9%) with no drug recording 100% activity. The resistance of the nosocomial isolates of the organism were significantly higher than the community acquired isolates against that of the common antibiotics in use ($P<0.05$). **Conclusions:** Extreme caution should be exercised in antibiotic administration in hospital setting and the potential benefits adequately assessed while control of nosocomial infections be given a priority so as to limit the spread of resistant bacteria.

1. Introduction

Proteus mirabilis (*P. mirabilis*), a member of the Enterobacteriaceae is often considered to be implicated in contaminations and colonizations[1,2]. The organism is also often linked with several pyogenic infections and has been strongly associated with urinary tract infections (UTIs) among humans[3-5]. The different types of fimbriae expressed by the organisms such as PmfA, PmfC, PmfD, PmfE and PmfF play cardinal roles in colonization of urinary bladder and urethra and are believed to contribute to the pathogenesis of UTI among humans[6-8]. The rapid mutation of the virulent genes of *Proteus* species generally has also been attributed to its immunological evasion and pathogenicity in the urinary pathway as well as its ability to withstand the acidic microenvironment of the genitourinary tract[9,10].

Over the last decade, treatment of infections caused by *P. mirabilis* have often been accompanied by varied and mixed outcomes[11,12]. In USA isolates of *P. mirabilis* from infections lesions were all found to be beta-lactamase producing and were also resistant to ampicillin, gentamicin, ceftazidime, cefotaxime, cefuroxime, cefalothin, cefepime, piperacillin, trimethoprim/sulphamethoxazole and ciprofloxacin[13]. Also in Italy, a prolonged form of bacteremia difficult to treat with majority of the commonly available antibiotics as found to be caused by VIM-1 metallo-beta-lactamase-producing *P. mirabilis*[14]. Furthermore, in Poland, 10.4%-18.7% ESPL *P. mirabilis* strains principally from urine were isolated at a university hospital over a three year period showing high multiple resistance to over four antimicrobials in common use[15]. *P. mirabilis* from UTIs was similarly found to show high multiple resistance against all the common antimicrobials in Greece, Nigeria and Portugal[16-18].

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In view of the relevance of UTIs in clinical practice occasioned by the reversible and irreversible genitourinary complications and distant tissue damages, prompt and timely treatment of UTIs becomes necessary[19-21]. In Calabar city and environs as is the case in several parts of rural Sub-Saharan Africa, treatment of UTIs is often accompanied by lack of appropriate laboratory facilities to carry out comprehensive antimicrobial sensitivity patterns, this leads to wrong empirical drug selections with attendant treatment failures and propagation of resistant bacteria[22-24]. It is in this regard that this study was set up to ascertain the antibiotic susceptibility patterns of uropathogenic *P. mirabilis* isolates from a Nigerian university hospital so as to offer a guide to clinicians who may be constrained by inadequate facilities or time.

2. Materials and methods

2.1. Setting

The study was carried out at University of Calabar Teaching Hospital (UCTH), which is situated in Calabar city, the capital of Cross Rivers State, south-south Nigeria.

2.2. Procedure

The study was retrospective in nature; data generated from cultured urine specimens and the antibiotic susceptibility pattern of bacteria recovered from them by the microbiology laboratory of UCTH were compiled for a period of five years (1st February, 2004 - 31st January, 2009). The urine specimens were collected, transported, stored and processed using standard laboratory procedures while modified Kirby-Bauer's diffusion method was used to carry out susceptibility testing[25,26]. *P. mirabilis* recovered from urine specimens was identified based on its cultural and biochemical properties. Microorganisms recovered were grouped into nosocomial or community acquired based on the epidemiological circumstance of the urine specimens.

2.3. Nosocomial infection

Micro-organisms recovered from urine specimens of patients who have been on admission for more than 24 h for which features of bacterial colonization were not present at the time of initial presentation to the hospital.

2.4. Community acquired infection

Micro-organisms recovered from urine of patients who were not on admission in the hospital, and from patients within 24 h of admission or patients originally admitted for probable blood related infections. Other relevant information such as: age, sex were obtained from patients records.

2.5. Analysis of results

The results were analyzed using Epi Info-6, statistical software, P values $\leqslant 0.05$ were considered significant.

3. Results

A total of 7 348 urine specimens were processed by the microbiology laboratory during the study period with 565 (7.7%) infections. Infections of community acquired (CA) origin were 391 (69.2%) while 174 (30.8%) were nosocomial (NC) in nature. *P. mirabilis* was recovered from 73 of the 565 infected urine specimens (12.9%) comprising 29 (29.7%) CA and 44 (60.3%) NC isolates respectively from 31 (42.5%) males and 42 (57.5%) females with no significant gender difference ($P>0.05$) (Table 1). Other microbial isolates recovered from the urine samples were *Escherichia coli* 18.6% (109), *Klebsiella pneumoniae* 14.8% (87), *Enterococcus faecalis* 12.4% (73), *Staphylococcus aureus* 10.7% (63), *Pseudomonas aeruginosa* 8.5% (56), Coagulase negative *Staphylococci* (CONS) 8.0% (47), *Enterobacter* species 5.6% (33), *Citrobacter* species 4.3% (25) and other *Proteus* species 0.7% (4). The age intervals with the highest number of *P. mirabilis* isolates were (in years) 40-49 (17, 23.3%), 50-59 (14, 19.2%) and 10-19 (11, 15.1%) while ages with the lowest number of *P. mirabilis* isolates were those $\geqslant$80 (0, 0.0%), 0-9 (3, 4.1%) and 60-69 (5, 6.3%) with no significant age difference ($P>0.05$) (Table 1).

Table 1
Age and gender distribution of *P. mirabilis* associated UTI at a university hospital in southern Nigeria.

Age (years)	Male		Female		Total (%)
	CA (%)	NC (%)	CA (%)	NC (%)	
0-9	0 (0.0)	3 (100)	0 (0)	0 (0)	3 (4.1)
10-19	2 (18.1)	1 (9.1)	4 (36.4)	4 (36.4)	11 (15.1)
20-29	1 (11.1)	5 (55.6)	1 (11.1)	2 (22.2)	9 (12.3)
30-39	3 (50.0)	3 (50.0)	0 (0.0)	0 (0.0)	6 (8.2)
40-49	0 (0.0)	4 (23.5)	7 (41.2)	6 (35.3)	17 (23.3)
50-59	0 (0.0)	1 (7.1)	5 (35.7)	8 (47.2)	14 (19.2)
60-69	1 (20.0)	4 (80.0)	0 (0.0)	0 (0.0)	5 (6.3)
70-79	2 (28.6)	1 (14.2)	2 (28.6)	2 (28.6)	7 (9.6)
$\geqslant$80	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unclassified	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	1 (1.3)
Total	9	22	20	22	73 (100)

An analysis of the pattern of multiple resistance of *P. mirabilis* isolates showed that none (0%) was susceptible to all the antibiotics tested or resistant to only 1–2 antibiotics; 17 (23.3%) were resistant to 3–4 antibiotics; 49 (67.1%) were resistant to 5–6 antibiotics and 7 (9.6%) isolates resistant to 7 antibiotics and above. More than 93% (27/29) of the NC isolates were resistant to 6 drugs and above compared to 47.7% (21) of the CA isolates ($P<0.05$) (Figure 1).

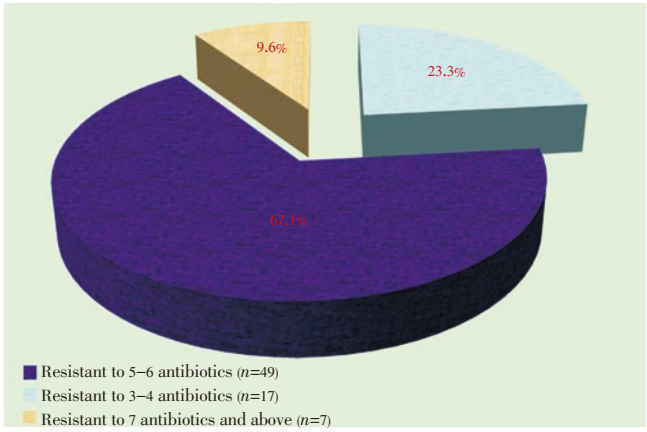

Figure 1. Pattern of antimicrobial resistance of *P. mirabilis* isolates from clinical urinary specimens at a university hospital in southern Nigeria.

A review of the antimicrobial susceptibility profile of *P. mirabilis* from the clinical urine specimens showed that ciprofloxacin, ceftazidime, ceftriaxone, nalidixic acid, nitrofurantoin, colistin and amikacin were the most active antibiotics (activities 59.1%–96.6%). Antibiotics with the lowest activities were ampicillin, cloxacillin, amoxicillin, tetracycline, co–trimoxazole, chloramphenicol and erythromycin (0%–17.2%). The susceptibility of the NC isolates of *P. mirabilis* against ampicillin, cloxacillin, amoxicillin, augmentin, streptomycin, gentamicin, chloramphenicol and erythromycin was significantly lower than their community acquired (CA) counterparts ($P<0.05$), (Figure 2).

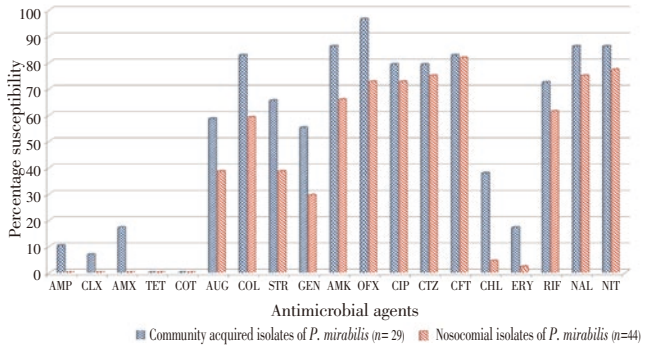

Figure 2. Antimicrobial susceptibility patterns of *P. mirabilis* from clinical urine specimens at a university hospital in southern Nigeria. AMP– Ampicillin; CLX– Cloxacillin; AMX– Amoxicillin; TET– Tetracycline; COT– Co–trimoxazole; AUG– Augmentin (clavulanic acid + amoxicillin); COL– Colistin; STR– Streptomycin; GEN– Gentamicin; AMK– Amikacin; OFX– Ofloxacin; CIP– Ciprofloxacin; CTZ– Ceftazidime; CFT– Ceftriaxone; CHL– Chloramphenicol; ERY– Erythromycin; RIF– Rifampicin; NAL– Nalidixic acid; NIT– Nitrofurantoin.

4. Discussion

P. mirabilis was isolated in 73 (12.9%) of the 565 infected urine specimens from the entire 7 348 urine specimens processed. Activity of ampicillin, cloxacillin, tetracycline, co–trimoxazole, erythromycin and chloramphenicol on both the CA and nosocomial NC isolates of *P. mirabilis* was generally less than 40% (range 0%– 37.0%). The most active drugs were colistin, Ofloxacin, ciprofloxacin, ceftriaxone, nalidixic acid and nitrofurantoin (activities 59.1%–96.6%) with no antibiotic recording 100% activity against the organism.

The findings from this present study compares favourably with that from Croatia[27], Italy[28], Argentina[29], Israel[30] and Japan[31] where activities of ampicillin, cloxacillin, tetracycline, erythromycin, chloramphenicol and co–trimoxazole against *P. mirabilis* ranged 0%–28.7%. This makes empirical treatment of *P. mirabilis* UTIs with these antimicrobial agents exceedingly a great challenge with the propensities of high treatment failures. This may be more pronounced in communities where facilities may be lacking to ascertain their exact activity profile against the organism[32–34]. The advantage of comparatively simpler features of laboratory identification of *P. mirabilis* due to its unique cultural characteristics on solid agar media could largely be compromised by its high multiple resistance in the course of managing its infections including UTIs[35,36].

The generally high rates of multiple resistance of the NC isolates of *P. mirabilis* as compared to the CA species observed in the present study is also another clinical challenge. Similar significantly higher resistance of the organism among the NC isolates compared to their CA counterpart has well been documented in Brazil[37], Bosnia[38,39], Taiwan[40] and Poland[41]. The acquisition of beta–lactamases and carbapenemases by the bacterium has largely been attributed to this high pattern of resistance[42,43]. The benefits of antibiotics prescriptions and intake among hospitalized patients should be seriously weighed against the undesired side effect of contributing to the spread of antibiotic resistance. Also dosages should be adequately gauged in terms of drug quantity as well as treatment duration in order to limit the spread of resistant bacteria in the hospital setting[44,45].

The findings from the present study are however different from the outcome of similar studies in: Italy where resistance of *P. mirabilis* to third generation cephalosporins was generally up to 75%[46]; Taiwan where a 100% susceptibility of *P. mirabilis* to tigecycline was documented[47]; China where resistance of *P. mirabilis* against quinolones was up to 80%[48]; and in Greece where third generation cephalosporins were found to have little usefulness in the treatment of children with UTIs caused by ESBL–producing *P. mirabilis* species[49]. This global but varying antimicrobial resistance pattern of *P. mirabilis* should be closely monitored by carrying out local antimicrobial susceptibility patterns and this should be reviewed periodically[50].

Generally control of nosocomial infections in hospitals should be taken seriously with the composition of a vibrant

infection control committees and infection control teams with appropriate surveillance mechanisms put in place. This would limit the spread of the highly multiply resistant bacterial strains in the hospital settings and also limit their probable spill-over effect on the wider community[34,51]. These committees may also draw guidelines for prevention of infections in hospitals for other smaller health settings in their vicinity especially in the developing nations of the world where such services may not be readily available.

In conclusion, the present study has shown that *P. mirabilis* isolates from urinary tract infections are highly resistant to most of the antibiotics in common use. Prudent and judicious use of antibiotics among physicians should be emphasised while control and spread of nosocomial infections seriously checked to limit the spread of resistant bacteria. Furthermore, ciprofloxacin, colistin, ofloxacin, ceftriaxone, cefuroxime, nitrofurantoin and nalidixic acid may be considered for empirical treatment of *P. mirabilis* UTIs in the community where susceptibility reports may no be readily available.

Conflict of interest statement

We declare that we have no conflict of interest.

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