PREVALENCE AND ANTIBIOTIC RESISTANCE PATTERN OF URINARY TRACT BACTERIAL INFECTIONS AMONG SYMPTOMATIC PATIENTS ATTENDING UNIVERSITY OF MAIDUGURI TEACHING HOSPITAL, NORTH EAST NIGERIA

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ABSTRACT

Urinary tract Infection (UTI) is one of the most common infections described among patients attending tertiary hospitals. In most cases empirical antimicrobial treatment was being initiated before the laboratory results are made available; thus the need for antibiotic resistance test for enhanced management of UTI with commonly used antibiotics. The study was designed to determine the prevalence of bacteria associated with UTI in symptomatic patients and antimicrobial susceptibility pattern of commonly sold antibiotics. It was a cross-sectional that involved 150 patients, aged 6 years and above, clinically suspected for UTI attending outpatient unit of the University of Maiduguri Teaching Hospital. A structured questionnaire was used to interview and obtain bio data from the patients after obtained consent. The overall prevalence of UTI was 62.0% (93/150). Escherichia coli (35.3%) and *Klebsiella spp*. (13.0%) were the most common organisms isolated. The recommended effective antibiotic for both the gram negative and positive within this region were Ciprofloxacin, Ofloxacin and Amoxicillin-clavulanic acid. This study provides useful laboratory data to monitor status of antimicrobial resistance of some uropathogens, to improve physicians prescribing habits, treatment recommendations and encourage the national regulatory agency in checkmating antibiotic abuse within the region.

Keywords: Prevalence, Bacteria, antibiotic, resistance, Urinary tract infection.

BACKGROUND

Urinary tract infection (UTI) is caused by the presence and growth of micro-organisms within the genito-urinary tract system. UTI are one of the most common bacterial infections in the human urinary system worldwide [1, 2]. UTI is the major cause of morbidity in both the hospital and community settings, and it occurs in all age groups [3, 4]. The infection can be detected among in and out patients [5]. Most of these infections involve the lower urinary tract and could be either symptomatic or asymptomatic. Patients are said to have Symptomatic urinary tract infections if the lower tract (acute cystitis) and upper tract (acute pyelonephritis have significant bacteriuria with associated bladder mucosal invasion or inflammation of the renal parenchyma, calices and pelvis respectively [6, 7]. Asymptomatic bacteriuria (ABU) is a condition characterized by presence of bacteria in two consecutive clear-voided urine

specimens both yielding positive cultures (≥105cfu/ml) of the same uropathogen in a patient without classical symptoms, or the presence of significant bacteriuria without the symptoms of an acute urinary tract infection [8]. The evidence of UTI is mostly confirmed by the presence of 10^5 microorganisms or of a single strain of bacterium per milliliter in two consecutive midstream samples of urine [9]. Infection of the lower or upper parts can generally spread to other parts, however, commonest among them is the ascending route through which organisms of the bowel flora contaminate the urethra, ascend to the bladder and migrate to the kidney or prostate Majority of the infections are caused by retrograde ascent of bacteria from fecal flora to bladder and kidney via urethra, especially in females whom the urethra is shorter, wider and more susceptible to trauma during sexual intercourse [7]. The bacteria also navigate its way through urethra up to the bladder especially during pregnancy and delivery [10]. Other studies have shown that despite the presence of some antibacterial factors in urine; pH, urea concentration, organic acids, salt concentration in the urine, inhibitors to bacterial adherence, low molecular weight oligosaccharide, bladder mucopolysaccharide, secretory IgA, lactoferrin, and the uro-pathogenic bacteria are able to adhere, grow and resist against host immune defense mechanism resulting to colonization and infection of the urogenital. Majority of pathogenic bacteria associated with UTIs are not life threatening and do not cause any irreversible damage except when there is involvement of kidneys with an increased risk of bacteremia [2, 11].

The emergence of antimicrobial resistance in the management of UTIs pose a serious challenge to public health in resource-limited countries due to lack infrastructural, circulation of fake and use of un-prescribed antibiotics. The antimicrobial resistance patterns of bacterial isolates from urinary tracts differ among bacterial and antibiotics, geographic regions and institutions [12, 13, 10]. The changing trend of antibiotic resistance have made it important to research into susceptibility profile of commonly used antibiotics at various intervals to guide in clinical management of the infections. The current growing concern regarding antimicrobial resistance worldwide involving gram negative bacteria such as *E.coli* , *Klebsiella spp* and *Proteus mirabilis,* are known to be the dominant causative agents of UTIs [14]. The aim of this study was to determine patterns of common etiologic agents associated with UTIs and antibiotic susceptibility among patients attending University Teaching Hospital Maiduguri, Nigeria.

MATERIALS AND METHODS

Study Area and Population.

The study was carried out in the Medical Microbiology Laboratory, of University of Maiduguri Teaching Hospital (UMTH). 150 urine samples were collected from these patients within the period of February and April 2012. The University of Maiduguri teaching hospital is a tertiary institution with 500 bed capacity with an outpatient attendance of over 80,000 patients per annum. Ethical clearance was sort from the UMTH Ethics Committee before the commencement of the study. Study questionnaire was prepared which include the following variables, age, sex, clinical details. Patients who visited UMTH for medical care and were referred to Medical Microbiology and Parasitology Laboratory for laboratory investigation for Urinary tract infection, and were recruited into this study. These patients did not include those who were on any antibiotic a week before the samples were collected. The urine Samples were collected into labeled 20 ml calibrated sterile universal containers from both inpatients and/or outpatients. The criteria for selection were based on patients seen either at the GOPD or those on admission with clinical conditions suggestive of urinary tract infection. The ages of the patients ranged from 6 and or ≥ 60 years. Informed consent of patients was

sought and verbally instructed on how to collect mid-stream urine and taken to the laboratory immediately for culturing.

Laboratory Procedures

The laboratory diagnosis of urinary tract infection is entirely dependent on the quality of the urine samples collected for examination and the conditions of their transportation to the laboratory. The Clean catch midstream urine samples (MSU) of about (10-15 ml) were collected in sterile disposable containers. The bottles were labeled with unique sample number, date and time of collection; then immediately delivered to bacteriology bench of the Microbiology laboratory. The samples were stored at 4^0C but not longer than 48 hours and were subjected to general examinations using direct microscopy for white blood cell (WBC) counting. These Urine samples were cultured on 5% blood agar, MacConkey, and Eosin-Methylene blue (EMB) agar (Oxoid Ltd, Bashingstore, Hampire, UK) using calibrated loops for semi-quantitative method and incubated in both aerobic and anaerobic conditions for 24 hours at 37°C. Cultures without any colony at the end of 24hrs incubation were further incubated for 48hrs. Samples with colony count equal or more than 10^5 Cfu/ml was considered positive. The isolates were identified and confirmed using standard microbiological methods including Gram staining, colonial morphology on media, growth on selective media, lactose and mannitol fermentation, H_2S production, catalase, oxidase, coagulase, indole, and citrate utilization, and urease tests were carried out on the isolates as previously described [15,16, 17].

Antimicrobial Susceptibility Testing

The antibiotic susceptibility testing was determined by disc diffusion method on Mueller-Hinton agar (Merck, Germany according to Clinical Standford Laboratory Institute (CSLI) [18] guideline. Both gram positive and gram negative discs were tested. Seven to eight discreet colonies of bacterial pathogens were inoculated in 5ml of sterile peptone water, to give fine bacterial suspension, equivalent to 0.5 in McFarland standard. A sterile swab was dipped into the bacterial suspension and was used to swab the surface on the labeled Mueller-Hinton agar plate to give a confluent growth. The concentrations of available drugs and antibiotic discs were; Clavulin (amoxicillin 20 µg: clavulanic acid10 µg: AMC, 30µg) Ciprofloxacin (CP, 5µg), Ofloxacin (OFX, 10µg), Gentamicin (GM, 10µg), Ampicillin (AM,10µg), Trimethoprim-sulfamethoxazole (SXT, 1.25/23.75µg),) and, Nalidixic acid (NA, 30µg) for Gram negative isolates, and Chloramphenicol (C, 30µg), Vancomycin (V, 30µg) and Tetracycline (TE, 30µg), The E. coli (ATCC 25922), Staphylococcus aureus (ATCC25923), and *Pseudomonas aeruginosa* (ATTC 27853) were used as quality control standard strains. Antibiotic discs were applied on the plate and incubated at 37^0C for 18-24 hours. The zone of growth inhibitions were measured with a standard calibrator to determine the isolate resistant or sensitive [18]

Table1. Prevalence of UTI and demographic characteristics attending University Teaching Hospital Maiduguri

Variables	No. Tested (%) N=150	No. Positive (%)	P-value
Age years			
≤15	36 (24.0)	9 (25.0)	
16-30	44 (29.3)	7 (16.0)	
31-45	39 (26.0)	11 (28.2)	0.678
46-60	17 (11.3)	4 (23.5)	
>61	14(9.3)	6(43.0)	
Mean	**38.55±20.05**	**38.55±20.05**	
Gender			
Male	58 (39.0)	29(50.0)	
Female	92 (61.0)	74(80.4)	0.072
Marital status			
Married	94 (62.6)	36 (38.3)	
Single	56(37.3)	12(25.5)	0.245
Educational level			
Illiterate (cannot read or write)	65(43.3)	8(12.3)	
≤Primary education	53(35.3)	11(21.0)	
>Secondary education	32(21.3)	6(18.7	0.06
Occupation			
Civil servant	29(19.0)	6(21.0)	
Trading	52(35.0)	9(17.3)	
Unemployed	41(27.0)	13(32.0)	0.871
Student	28(19.0)	5(18.0)	
History of catheterization			
Yes	13(9.0)	5(38.5)	
No	137(91.0)	19(14.0)	0.002
History of UTI			
Yes	24(16.3)	13(54.2)	
No	123(83.7)	26(21.1)	0.03

Table 2. Frequency of Uropathogens isolated from symptomatic Patients attending University of Maiduguri Teaching Hospital

Bacterial Isolates	Total: N=150 (%)
Gram Positive	
Staphylococcus aureus	12(8.0)
Gram negative	
Escherichia coli	53(35.3)
Klebsiella spp.	19(13.0)
Proteus spp.	6 (4.0)
Pseudomonas aeruginosa	3(2.0)
Total	93(62.0)

Table 3. Antimicrobial susceptibility pattern of bacteria isolated from urine culture of patients attending University of Maiduguri Teaching Hospital, Nigeria

Bacteria Isolated	Total No	S/R	Antimicrobial agents tested N0(%)							
			AMP	CIP	OFX	GM	AMC	SXT	NA	C
S. aureus	12 (8.0)	S R	4(33.3) 8(66.7)	11(91.7) 1(8.3)	9(75.0) 3(25.0)	11(91.7) 1(8.3)	10(83.3) 2(17.0)	3(25.0) 9(75.0)	2(16.7) 10(83.3)	3(25.0) 9(75.0)
E. coli	53(35.0)	S R	9(17.0) 44(83.0)	33(62.3) 20(37.7)	39(73.6) 14(26.4)	20(37.7) 33(62.3)	42(79.2) 11(20.8)	12(23.0) 41(77.0)	11(21.0 42(79.0	29(54.7) 24(45.3)
Klebsiella spp.	19(13.0)	S R	7(37.0) 12(63.0)	13(68.4) 6(31.6)	16(84.2) 3(15.8)	3(15.8) 16(84.2)	17(89.5) 2(10.5)	4(21.0) 15(79.0)	7(36.8) 12(63.2)	15(80.0) 4(20.0)
Proteus spp.	6 (4.0)	S R	2(33.3) 4(66.7)	5(83.3) 1(16.7)	4(66.7) 2(33.7)	4(66.7) 2(33.3)	6(100) -	1(16.7) 5(83.3)	- 6(100)	5(83.3) 1(16.7)
Pseudomons aeruginosa	3 (2.0)	S R	1(33.3) 2(66.7)	3(100) -	3(100) -	3(100) -	2(66.7) 1(33.3)	1(33.3) 2(66.7)	- 3(100)	2(66.7) 1(33.3)
Total	93(62.0)	S R	23(24.7) 70(75.3)	65(70.0) 28(30.)	71(76.0) 22(24.0)	38(41.0) 55(59.0)	77(83.0) 16(17.0)	22(24.0) 71(96.0)	22(23.7) 71(76.3)	36(39.0) 35(38.0)

Key: S=Sensitive, **R**=Resistance; AMP-Ampicillin, CIP-Ciprofloxacin, OFX-Ofloxacin, GM-Gentamicin, AMC-Amoxicillin-clavulanic acid, SXT- trimethoprim/sulfamethoxazole, NA- Nalidixic acid, C- Chloramphenicol,

Statistical Analysis

Descriptive statistical analysis was done using SPSS version 16.0, while the results was expressed using the Chi square to establish relationship between bacterial pathogens associated with Urinary tract infection in the demographic variables. Differences between proportions were assessed and statistical significant difference was considered at value of $P \leq 0.05$.

RESULTS

A total of 150 patients were enrolled in this study with mean age of 38.55±20.05 years (range 6-80). Among the study subjects, 58(39.0%) were male, 92(61.0%) were female, 94(63.0 %) were married, 56(37.0%) were single. Sixty five (43.3%) were illiterate, 53(35.3%) had primary education, 32(21.3%) had educational level of secondary and above, and 29(19.3%) were civil servants, 52(35.0 %) were petty traders, 41(27.0%) were unemployed, 28(19.0% were students. Thirteen (9.0%) patients had history of catheterization, 137(91.0%) had no history of catheterization. Twenty four (16.3%) had history of UTI, and 123(83.7%) had no history of UTI. However, bacteriuria was found to be high among these variables; the older age group >61 (43.0%), female (80.4%), married (38.3%), less or equal to primary education (21.0%), unemployed (32.0%), history of catheterization (38.5%) and previous history of UTI (54.2%) (Table1). A total of 93 (62.0%) bacterial uropathogens were isolated from 150 investigated symptomatic UTI patients for UTIs (Table 2). Out of the 124 bacterial isolates; *S. aureus* (8.0%), *E. coli* (35.3%), *Klebsiella spp*. (13.0%), Proteus spp. (4.0%) and *P . aeruginosa* (2.0%) (table2). The most common among the isolates were *E.coli* and *Klesiella spp*. Significant bacteriuria was observed in those with history of catheterization p=0.002, and previous history of UTI p=0.03 (table 1)

ANTIMICROBIAL SUSCEPTIBILITY RESULT

The antimicrobial susceptibility pattern of gram positive bacteria (n=12) is presented in Table 3. Gram-positive bacteria showed low level of resistance (<60%) to all antimicrobials tested except for Ampicillin (66.7), Trimethoprim/Sulfamethoxazole (75.0%), Nalidixic acid (83.3%) and Chloramphenicol (75.0%). The antimicrobial susceptibility pattern of gram-negative bacteria (n=81). All the isolates showed intermediate level of resistance (60-80%) against ampicillin, Trimethoprim/Sulfamethoxazole and Nalidixic acid. Low level of resistance (<60%) was observed against Ciprofloxacin, Ofloxacin, Gentamicin, Amoxicillin-clavulanic acid and Chloramphenicol. There were isolated cases of high resistance (>80%) of *E. coli* to Ampicillin (83.0), *Proteus spp* to trimethoprim/sulfamethoxazole (83.3%) and Nalidixic acid (100%), *Pseudomons aeruginosa* to Gentamicin (66.7%) , Trimethoprim/Sulfamethoxazole (66.7%) and Nalidixic acid (100%) (table 3).

DISCUSSION

Urinary tract infection (UTI) is one of the most common infections encountered and treated worldwide. The trend of uropathogens and their antibiotic susceptibility pattern continued to change [19].This study examined the distribution and antimicrobial resistance pattern of bacterial pathogens associated with UTI isolated from patients attending university of Maiduguri Teaching Hospital. The overall prevalence among symptomatic patients was 62.0% which corroborates earlier reported findings in; Nigeria [14, 12, 10], Ethiopia [20, 21]. The majority of the age group tested was 31-45 years with frequency of 28.2% and this may be due to high sexual activity. The highest positivity was among the older age group >61 (43.0%). This factor may be due to history of catheterization and associated recurrent infections. Majority of the study population were females (61.0%) with frequency of 80.4% (p=0.07), this finding correlate with other reports which showed that females are more prone to UTIs than males [22, 23, 20]. Likewise, UTIs was more common among the women of reproductive age groups (16-30 years) which agreed with earlier studies in Nigeria [24] and other countries [25, 26]. The prevalence of isolated bacteria was higher in this study compared with similar studies in the country [27, 10]. This prevalence differs with other reported studies [28, 21]. This might be due to referred suspected cases from other health facilities to the tertiary institution for better management purposes and data sampling procedures, perhaps small sample size. The significant bacteriuria among those with history of Catheterization (p=0.002) and previous history of UTI (p=0.03) was expected and this has been corroborated that the use of an indwelling urethral catheter is strongly associated with high frequency of symptomatic urinary tract bacteremia and even co-morbidities resulting from other complications [29, 30, 31, 32].

In this study, E. coli remain the most prevalent uropathogens which was isolated in 35.3% of the isolated bacteria. This again was consistent with other studies in Nigeria and abroad even with slightly observed differences [12, 20, 21]. Other commonly isolated bacterial uropathogens were; *S. aureus* (8.0%), *Klebsiella spp. (13.0*%), *Proteus spp.* (4.0%) and *Pseudomonas aeruginosa* (2.0%). This was similar when compared with other studies in Nigeria and other countries [4, 17, 33].

The other common gram negative isolates were *Klebsiella spp*, and this corroborated earlier reported the findings in Nigeria and Ethiopia [34, 35, 20]. The study observed mixed isolates in 5 samples which suggest that suspected UTI could be due to multiple infections in symptomatic patients that could complicate diagnosis and management. Some reported

studies have eluded this to under lying factors associated with indwelling catheters (complications [29, 31]. However, our study confirmed that there was no major deviation from known frequency pattern of bacteria isolates among symptomatic UTI patients investigated in tertiary institutions. This study observed significant association of some risk factors such as previous history of UTI and catheterization amongst the symptomatic patients. Previous UTI as a risk factor suggest that bacteriuria can be present with or without symptoms of UTI. It can be inferred that colonization of uropathogens in urinary tract of after incidents UTI and catheterization could stimulate immunologic and physiologic reactions that may have increased bacterial adherence to uroepithelial cells. This in effect can obstruct urinary tract resulting in unknown complications [36].

The Staphylococcus species are normal body flora and commonly found in the environment with consistent human infection, therefore the resistant profile of *S. aureus* (not susceptible) to some available antibiotics (Ampicillin, Trimetoprim-sulphamethoxazole ,Nalidixic acid and Chloramphenicol may not be surprising but sensitive to the third generation cephalosporins, and this was consistent with earlier reported studies in Nigeria [37, 38]. The observed decreased susceptibility to some of these drugs may be due to self-medication and indiscriminate use of the antibiotics in the study area.

This study observed that *E. coli* isolates had 66.7% resistant to Ampicillin, 75.0% to Trimetoprim-sulphamethoxazole and 83.3% to Nalidixic acid, but relatively sensitive to chloramphenicol. *E.coli* was found to be very sensitive to Ciprofloxacin, Ofloxacin, Gentamicin, and Amoxicillin-clavulanic acid. This was consistent with other studies in some parts of Nigeria [33, 24], Cameroon [39], Ethiopia [35, 20]. In the present study most of the gram negatives isolates (59.6%) were susceptible to amoxicillin-clavulanic acid. It was also observed that apart from *E.coli* sensitivity, other gram negative isolates such as *Klebsiella*, *Proteus* and *Pseudomonas* were also highly sensitive to Ofloxacin, Gentamicin, and Amoxicillin-clavulanic acid and chloramphenicol, but weakly sensitive to Ciprofloxacin, and slightly resistance to Ampicillin, Trimetoprim-sulphamethoxazole and Nalidixic acid. *Proteus spp* was highly sensitive to all the study antibiotics but resistant to nalidixic acid and ampicillin. Pseudomonas was found to very sensitive to Ciprofloxacin, Ofloxacin, Gentamicin, and Amoxicillin-clavulanic acid and slightly sensitive to chloramphenicol, but highly resistant to Nalidixic acid and weakly resistant to ampicillin andTrimetoprim-sulphamethoxazole. In general, there was a slight difference in antibiotic susceptibility pattern with weak resistance to Ampicillin and strong resistance to Nalidixic acid. This pattern might be attributed to indiscriminate use of un-prescribed antibiotics and highly prescribing habits of antibiotics by clinicians within the region [36]. Further reasons could be due to the role of patent medicine stores, private pharmacies, hospitals and clinics, self-medication and uncontrolled purchase of drugs across the counter resulting in drug resistance as earlier reported [40, 41], it was however, indicated in various researches the reasons for differences might be due to factors related to lack policy commitment, poverty and infrastructural challenges [42, 43, 44].

The study observed that the isolated gram positive bacteria and few gram negative isolates were resistant to two or more drugs. This indicates increase in multi-drug resistance which poses a concern in the management of uropathogens in Nigeria. This suggests the need for proper enforcement of the recommended nationwide antimicrobial surveillance and in-vitro susceptibility testing policy to avoid the spread of resistant bacterial strains in the country. It's also suggestive that more studies be carried using molecular methods with specific primers to know the exact gene responsible for each resistance in a strain of bacteria for

effective treatment and prevention strategies. The limitation of this this study was the use of referred patients to the tertiary hospital which may not be true representation of the general population. There was also selection bias of antibiotics tested since it was restricted to available commercial antibiotic discs.

CONCLUSION

The findings of this study have revealed common uropathogens and the antibiotic resistance pattern associated with UTI. we observed multidrug resistances of isolates to antibiotics which is consistent with the information in literature, and test results with broad spectrum antibiotics showed that Gram-positive isolates showed more resistant than Gram negative isolates, therefore it is recommended antibiotic susceptibility testing be used to guide choice of antibiotics for management of urinary tract infections. It is believed that information generated from the study would provide a baseline for continuous surveillance of uropathogens spectrum and their resistance pattern to ensure appropriate treatment and prevent further development of drug resistance. Presently, the most appropriate therapeutic agents for the empirical management of community associated UTI are the fluoroquinolones like the ciprofloxacin which could serve as a guide in clinical management of patients with UTIs. The study could also add to the existing baseline data for further epidemiological studies on bacteria associated with UTI, and to improve treatment recommendations in the region, help policy makers and enforcement agents in establishing effective mechanism to checkmate antibiotic abuse.

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CONFLICT OF INTEREST

All authors declare that they have no conflict of interest

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