A 5-years Retrospective Analysis of Urinary Bacterial Pathogens and their Antimicrobial Sensitivity Pattern in a Tertiary Hospital in Maiduguri, Nigeria.

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Abstract: Urinary tract infection is a common clinical episode seen within the hospital and community setting but the prevalence level varies with aetiological agents and their resistant pattern. The retrospective study determined the prevalence of bacterial pathogens isolated from urinary tract infection and their antimicrobial sensitivity pattern**.** Bacteriological data of mid-stream urine samples collected from patients with suspected cases of urinary tract infection presented at the hospital were analyzed by standard bacterial methods. Of the 21,840 urine specimens analysed over the study period, 6314(28.9%) showed significant bacteruria and yielded positive bacteria growth. Gender distribution of 3552(56.3%) females and 2762(43.7%) males giving female to male ratio of 1.3:1.Gram-negative bacteria accounted for 4949(78.4%) of bacterial pathogens isolated compared to 1365(21.6%) gram-positive bacteria. *Escherichia coli* was the predominate pathogens, 2170(34.4%), followed by *Staphylococcus aureus*, 1230(19.5%), *Klebsiella spp*, 1179(18.7%). High frequency of occurrence of bacterial isolated was recorded within age-group 16-30(34.2%) and 31-50years(31.9%). A descending trend in the frequency of isolates was observed with bacterial isolates and patients age-group(*E.coli, S.aureus* and *Klebsiella spp*) with patients within age-group 0-5years to 16-30years, and ascending trend with *Proteus spp* and *Pseudomonas spp* within age-group 16-30 years to >50years. The antimicrobial sensitivity pattern of bacterial pathogens demonstrated similar pattern as reported studies of high sensitivity to quinolones, aminoglycosides, and macrolides and resistant to commonly prescribed and administered agents in the hospital and community setting. The study findings revealed the uropathogens and their sensitivity pattern, that could serve as a guide in empirical therapy of urinary tract infection in our hospital.

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1. Introduction

Urinary tract infection is a common clinical episode that affects patients within all ages, sexes, associated with variety of clinical conditions and it is ranked second to respiratory tract infection, in cases seen in developing countries(Maskel 1982, Stamm et al, 1989, Johnson and Stamm 1989, Rabasa and Shatima, 2001). In hospital setting, morbidity and mortality rate due to UTI is considered to be relatively high, but mis-diagnosis is the common due to asymptomatic presentations observed in some clinical conditions like renal failure, hypertension and cardiac failure(Stamm et al 1989, Johnson and Stamm 1989). The prevalence of asymptomatic UTI varies with age and gender, but ranged between 6-7% among pregnant women, 10-15% among hospitalized elderly patients with clinical conditions like diabetes mellitus among women and urine outlet obstruction among men (De Louvois 1979, Stamm et al, 1980, Lipsky 1989, Pozill et al, 1994). In childhood UTI, association with bacteremia and severe malnutrition have been reported(Wijeshinsha 1982, Jenna et al, 1996, Rabasa and Shatima 2001).Colonization of vaginal introitus by rectal coliforms, multiplication of microorganism due to incomplete emptying of the bladder and partial urethral obstruction in cases of prostatic hypertrophy are some of the predisposing risk factors of UTI pathogenesis (Sobel, 1987). Bacterial pathogens implicated in UTI are diverse, and the prevalence varies with geographical location, sex, age, studied population and underlying clinical conditions, but the gram-negative bacteria, particularly of the family

Enterobacteriaceae predominate in most studies (Farrell et al,2003, Erben et al, 2009)

In most documented studies, the high resistance pattern observed with uropathogens is primarily a reflection of societal self-medication practices, a common norm in the treatment and management of UTI. The approach to curbing the clinical complications associated with UTI will depends on better understanding of the prevalent uropathogens and their antimicrobial susceptibility pattern. Therefore, the retrospective study was designed to determine the urinary bacterial pathogens and their antimicrobial sensitivity pattern of UTI seen in the hospital over the 5 years study period.

2. Materials and Methods

The retrospective study was conducted in the department of Medical Microbiology, University of Maiduguri Teaching Hospital between January 2007 to December 2011. Bacteriological data of urine analysis over the study period were extracted from laboratory records and entered into the study database. Diagnostic criteria of inclusion, urine specimens with significant bacteruria($X10^5$CFU), bacterial pathogens isolated and single urine bacteriological data per patient. Repeat analysis of the same patient, and catheter urine results were excluded. Demographic variables of the patients collected includes, age, sex, bacterial pathogens isolated and antimicrobial sensitivity pattern.

Mid-stream urine specimens analyzed were from patients presented at the hospital with suspected cases of urinary tract infections. The urine specimens were cultured on CLED(Cystine –Lactose-Electrolyte-Deficient) agar plates, using standard wire loop and incubated at 37^0C for 24 hours. Urine specimens with significant bacteruria (10^5CFU/organism) were recorded positive. Positive urinary bacterial pathogens were furthered identified by standard bacteriological procedures (Lennette et al, 1979).

Antimicrobial susceptibility pattern was determined by disc diffusion method, using Mueller-Hinton agar plates(Bauer et al, 1966).The following antimicrobial discs were tested, ofloxacin(Ofx), ceftazidime (Caz), cefuroxime (Cxm), gentamicin(Gen), co-trimoxazole (Sxt), tetracycline (Tet), ciprofloxacin(Cip), nalidixic acid(Nal), Penicillin (Pen), ampicillin (Amp), nitrofuratoin (Nit), and azithromycin(Azm). The zone of inhibition diameter was measured using a calibrated ruler to classify the bacterial isolates into either sensitive, intermediate or resistant.

Data analysis; The demographic variables of positive urinary tract infections and bacterial pathogens isolated were collated and analyzed using SPSS version 16.0. The values were expressed in means, standard deviation and percentages. Comparison of demographic variables was determined by chi-square test. The level of significance of $p<0.05$ was employed.

3. Results

Of the 21840 urine specimens analyzed, 6314(28.9%) showed significant bacteruria and yielded bacterial growth. The mean age of the patient was 25.48± 10.50years, gender distribution of 3552(56.3%) females and 2762(43.7%) males, giving female to male ratio of 1.3:1. Gram-negative bacteria accounted for 4949(78.4%) of the urinary bacterial pathogens isolated and 1365(21.6%) gram-positive bacteria. *E.coli* predominate among the isolates, 2170(34.4%), followed by *S.aureus* 1230(19.5%), *Klebsiella spp* 1179(18.7%),Proteus spp 710(11.2%), *Pseudomonas spp* 590(9.3%), Coliforms 300(4.7%) and streptococcus spp 135(2.1%). The distribution of urinary bacterial pathogens and patients gender as presented in figure 1, *E.coli, S.aureus* and *Klebsiella spp* predominate among the female patients, while Proteus spp and Pseudomonas spp among males patients. Statistical significance difference was observed between bacterial isolates and the gender(<0.05).

Table 1 depict the distribution of urinary bacterial pathogens according to age-group of the patients, the peak of UTI was observed within the age-group 16-30years (43.2%) and 31-50years(31.9%) respectively. Distinctive pattern was observed with the frequency of occurrence of the pathogens isolated. A descending trend in the frequency of occurrence of *E.coli, S.aureus* and *Klebsiella spp* was observed with the age-group 0-5 years and 16-30years. In contrast, an ascending trend with *Proteus spp* and *Pseudomonas spp* in age-group 16-30 years and >50yers.

The antimicrobial sensitivity pattern of urinary bacterial pathogens(figure 2), majority of the bacterial pathogens isolated exhibited high sensitivity level(>60%) to ofloxacin, ciprofloxacin, gentamicin, azithromycin and nitrofuratoin, and low sensitivity level (<30%) was observed with co-trimoxazole, tetracycline, penicillin, and ampicillin. *Pseudomonas spp*, *Proteus spp* and Coliforms exhibited low sensitivity to nalidixic acid, nitrofuratoin, azithromycin, cefuroxime and ceftazidime.

4. Discussion

Bacteriological result outcome of urine analysis in suspected cases of urinary tract infection are known to be influenced by several factors like age, sex, geographical location, studied population, underlying clinical conditions, and methodology employed (Bronsema et al, 1993, Farrell et al 2003, Erben et al 2009, Okesola and Oni 2009). Therefore, the need for locally generated epidemiological information becomes imperative for better understanding and clinical approach in treatment and management strategy.

In this study, the uropathogens prevalence level of 28.4% was reported, this level was lower when compared to 67.2% reported in a similar hospital-based study conducted in Yola, that is within the same geographical region (El-Mohammed 2009). However, varied prevalence levels had been reported in other studies conducted in Nigeria, 22% in Ibadan (Okesola and Oni 2009),60% in Lafia(Kolawole et al 2009) while outside Nigeria, 8.7% was reported Iran(Amin et al 2009). In catheter-associated UTI study conducted in Abeokuta, a prevalence level of 41.1% was reported (Abaeze and Abasiama, 2011). In community based studies, prevalence level of 52% was reported in Abeokuta (Ojo et al 2007),39.69% in Benin(Oladeinde et al 2011), and 77.9% reported among prison inmates in Enugu(Mbata 2007), while 53.3% was reported in India (Prakash and Saxena 2013). Apart from the abovementioned factors responsible for the variation in the prevalence level of UTI, urinary catheterization procedures and prolonged hospitalization are also known predisposing risk factors of UTI(Farrell et al, 2003).

The effect of gender on uropathogens prevalence is common phenomenon in most UTI studies(El-Mohammed 2009, Oladeinde et al 2011, Pranfar et al, 2014), similar trend was observed in this study, in which female accounted for 56.3% compared to male,43.7%. The reasons advanced for such pattern includes the anatomical structure of female genitourinary tract and its close proximity of vaginal to anus that tends to predispose it to possible fecal coliforms contamination due poor hygienic conditions and sexual activity, same uropathogens harbor in male urethra have been isolated in the female sexual partner vagina(Stamm et al, 1989, Johnson and Stamm 1989). Among the male patients, *Proteus spp* and Pseudomonas spp predominate Proteus spp is common inhabitant of preputial sac and its active mobility and swarming ability might enables the pathogen to readily transverse the long urethra of males(Sobel, 1987). The breakdown of the UTI prevalence level within the age-group showed that high frequency of uropathogens occurred within 16-30years(44.3%) and 31-50years(21.7%). Such pattern exhibited might not be surprising, as these patients belongs to the reproductive group involved in high sexual activity, one of the predisposing factor of UTI, while the level of 15.9% reported within patient >50years might be due catheter-associated UTI, a common clinical episode associated with urethral structure conditions(Sobel, 1996, Farell et al, 2003, Erben et al, 2009)

As reported in most studies, Gram-negative bacteria accounts for the majority of uropathogens isolated, which consistent with our findings, 78.3% uropathogens were due to gram-negative and 21.6% gram-positive bacteria isolates(El-Mohammed 2009, Okesola and Oni, 2009, Oladenide et al, 2011, Prakash and Saxena 2013,Piranfar et al 2014) *E.coli* isolates predominate followed by *S.aureus* and *Klebsiella spp.* This pattern is consistent with the findings of some studies, although difference was observed in the degree of isolation rate and number of other pathogens isolated. Reasons for such pattern might not be farfetched, as the effect of self-medication practice is capable of suppressing the chances of bacterial isolation even in the cases of significant bacteruria, the laboratory diagnosis technique employed and the interpretation of result also influences the isolation rate and antimicrobial susceptibility pattern. In addition, the use of quantitative culture and specific identification of bacterial pathogens helps differentiate true uropathogens from contaminant(Sobel 1987).

In UTI studies-either hospital/or community-based, the common observation is the varied the prevalence of uropathogens resistance pattern which is attributable to factors like geographical location, societies and the predisposing risk factors abovementioned. In sub-saharan African countries, relatively high resistance pattern, particularly to commonly affordable and available agents have been reported in most documented studies, which is a reflection of the irrational and excessive use of these agents in the community in the treatment of UTI(Erben et al, 2009). This similar observation is reflected in this study with uropathogens high sensitivity level to ofloxacin, gentamicin, azithromycin, ciprofloxacin and nitrofurantoin. In contrast, to highly reduced sensitivity pattern with ampicillin, penicillin, tetracycline, co-trimoxazole and cefuroxime. These agents are really affordable and available, and can easily be purchased in the patent medicine in the community. Although, different antimicrobial susceptibility pattern have been reported in different other documented studies, but comparison of such data might be rather difficult because of several factors are capable of influencing the results outcome. Such factors includes, antibiotic consumption pattern of the patients and the geographical locations, clinical conditions (untreated/recurrent or complicated UTI) or the laboratory methodology employed.

In conclusion, This retrospective study had revealed the prevalent uropathogens and their antimicrobial sensitivity pattern of the UTI cases seen at the hospital over the study period. We are of opinion that while the study findings provides insight into the antimicrobial agent of choice for the treatment and management of UTI, periodic surveillance studies should be encouraged for early detection of changes in the prevalent pathogens and their resistant pattern.

Figure 1. Distribution of urinary bacterial Pathogens according to patients gender.
(Not shown)

Table 1. The distribution of urinary bacterial pathogens according to age-group of the patients(%).

Bacterial Pathogens	0-5years	6-15	16-30	31-50	>50	Total
E.coli	345(5.5)	150(2.4)	950(15.0)	440(7.0)	285(4.5)	2170(34.4)
S.aureus	65(1.0)	90(1.4)	710(11.2)	300(4.8)	65(1.0)	1230(19.5)
Klebsiella spp	220(3.5)	44(0.7)	505(8.0)	250(4.0)	160(2.5)	1179(18.4)
Proteus spp	80(1.3)	15(0.3)	235(3.7)	175(2.8)	205(3.2)	710(11.2)
Pseudomonas spp	25(0.4)	40(0.6)	160(2.5)	115(1.8)	250(4.0)	590(9.3)
Coliforms	25(0.4)	20(0.3)	150(2.4)	65(1.0)	8(0.1)	300(4.8
Streptococcus spp	15(0.3)	5(0.07)	90(1.4)	25(0.4)		135(2.1)
Total	**775(12.3)**	**364(5.8)**	**2800(44.3)**	**1370(21.7)**	**1005(15.9)**	**6314(100)**

Figure 2. Antimicrobial sensitivity pattern of urinary bacterial pathogens isolated
(Note shown)

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