Evaluation of Empirical Antibiotic Prescription and Urinalysis in Patients with Symptoms Suggestive of Uncomplicated Urinary Tract Infection in Abakaliki, Nigeria

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Citation

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Abstract

Objective: To investigate the pattern of antibiotic prescriptions to patients with symptoms suggestive of uncomplicated urinary tract infection (UTI), the appropriateness of such prescriptions based on outcomes of subsequent urine culture and susceptibility test and the role of routine urinalysis in the diagnosis of UTI.Methods: Urine samples from 500 patients provisionally diagnosed of UTI and given empirical antibiotic prescription were subjected to dipstick analysis, microscopy and quantitative culture using standard methods. Antimicrobial susceptibility of isolates from cultures that yielded significant bacteriuria ($\geq 10^5$ cfu/ml) was carried out using the Kirby-Bauer disc diffusion technique.Results: Significant bacteriuria was recorded in 213 (42.6 %) of the urine specimens while 182 (36.4 %) showed insignificant bacteriuria and 105 (21.0 %) were sterile. Amoxycillin plus clavulanic acid was the most frequently prescribed antibiotic (23.6 %) and Clarithromycin was the least (1.4 %). Only 99 (46.5 %) of the isolates from the 213 positive cultures were found to be sensitive to the antibiotics empirically prescribed, with ciprofloxacin exhibiting the broadest spectrum of in vitro activity against the isolates. Urinalysis results for nitrite, protein and pyuria were comparable to that of culture. Conclusion: UTI is likely over-diagnosed in the study area and urinalysis result if well interpreted could be a guide to empirical prescriptions prior to results of culture and sensitivity tests. However, ciprofloxacin should be considered as the choice antibiotic when empirical prescriptions are inevitable.

INTRODUCTION

Antibiotic prescriptions without proper indication has been noted as a major contributory factor to the growing rate of bacteria resistance to antimicrobial agents.[1-3] Urinary tract infection (UTI) is one of the most common causes of morbidity in the general population, accounting for the majority of hospital visits.[4] However, majority of patients do not eventually demonstrate significant bacteriuria.[2] Urinalysis has been argued as cost effective adjunct to culture in the diagnosis and management of UTI[5]. The aims of this study therefore were to evaluate pattern of antibiotic prescriptions, the appropriateness of such prescriptions and the role of routine urinalysis in the diagnosis of UTI.

MATERIALS AND METHODS

STUDY SITE

This study was conducted at Ebonyi State University Teaching Hospital (EBSUTH), Abakaliki. The hospital is a state owned tertiary health facility serving a population of about 255,000 within Abakaliki, the state capital. It also serves as a referral centre to other hospitals in the state and its environs. The study spanned from November 2008 to October 2009.

STUDY POPULATION

These comprised individuals who were attending the Out Patient Clinic of the hospital with symptoms suggestive of urinary tract infection and were provisionally diagnosed as such and were prescribed antibiotics prior to urine culture and sensitivity test. Patients with symptoms but did not receive empirical antibiotic prescription were excluded from the study. The protocol for this study was approved by the Ethics and Research Committee of Ebonyi State University Teaching Hospital, Abakaliki. The approval was on the agreement that patient anonymity must be maintained, good laboratory practice/quality control ensured, and that every finding would be treated with utmost confidentiality and for the purpose of this research only. All work was performed according to the international guidelines for human

experimentation in clinical research. [6]

SAMPLE COLLECTION

Midstream "clean catch" urine samples were collected from 500 adult patients who gave their consent to participate in the study, into sterile plastic universal containers. Information on prescribed antibiotics was retrieved from Out-patient drug sales register at the Pharmacy Department as most out-patients of the hospital procure their drugs at the hospital Pharmacy.

SAMPLE ANALYSIS

Standard laboratory methods and techniques were used in the analysis of the urine specimens. Briefly, aliquot (5.0 ml) of the unspunned sample was tested with dipstick (Macromed, Johannesburg, S.A.). The results of leucocyte esterase (Le), Blood (Bld), protein (Prot) and Nitrite (Nit) were recorded after appropriate reaction times. Leucocyte esterase was considered positive in the presence of any shade of colour change after 2 minutes. Nitrite was recorded positive if there was any colour change at one minute. Blood and protein were recorded positive at any shade of colour change after one minute. Thereafter the urine samples were centrifuged and examined microscopically for pus cells and casts, and subsequently the urine samples were aseptically inoculated into blood agar and MacConkey agar by standard loop technique. Plates were incubated aerobically at 37C for 24 hours and then observed for bacterial growth. [7] A growth of $\geq 10^5$ colony forming units per millilitre was considered as significant.[8] The organisms isolated from the samples showing significant bacteriuria were identified using colonial characteristics, Grams reaction, motility test and biochemical reaction . [9]

PREPARATION OF ANTIBIOTIC DISC/SUSCEPTIBILITY TEST

The antibiotic discs used for this study were prepared according to the method described by Ochei and Kolhatkar.[10] The antibiotics were amoxicillin + clavulanic acid, ampiclox, erythromycin, clarithromycin, ofloxacin, ciprofloxacin, pefloxacin, cotrimoxazole, and cefuroxime. The antibiotics had official registration of the National Agency for Food and Drug Administration and Control (NAFDAC), Nigeria with their expiration dates ranging from December 2010-July 2011. The discs were impregnated with the antibiotic solutions to obtain the following concentrations per disc: Amoxycillin plus Clavulanic acid (30 µg), Ampiclox (30 µg), Erythromycin (30 µg), Clarithromycin (30 µg), Ciprofloxacin (10 µg), Ofloxacin (10 µg), Pefloxacin (10 µg), Cotrimoxazole (30 µg), and Cefuroxime (30 µg).

ANTIBIOTIC SENSITIVITY TESTING

Few colonies of the respective isolates purified on Nutrient Agar® were suspended in sterile peptone water to obtain a turbidity corresponding to MacFarland 0.5 [9] were used as inoculums. The Kirby-Bauer modified disc diffusion technique [9] was used for the sensitivity testing. The discs were evenly distributed on the sensitivity agar in such a way that they were 15 mm from the edge of the plate and 25 mm from one another. Each disc was gently pressed to ensure its sufficient contact with the sensitivity agar media. The plates were then incubated at 37 ^{o}C for 24 hours[10]. Corresponding discs from ABTEC Biologicals Ltd, UK were used as controls. Guidelines of the National Committee for Clinical Laboratory Standards were followed for the interpretation of the sensitivity results.

STATISTICAL ANALYSIS

Data were analysed for mean and standard deviation, percentage/proportions and comparison of parameters were done using one way analysis of variance (One-Way ANOVA) with level of statistical significance set at less than 0.05 ($p < 0.05$).

RESULTS

The age range of our patients was 18-52 years (mean = 42 ± 4.3 years). Two hundred and fifty one (50.2 %) of the samples were from males and 249 (49.8 %) were from females. From table 1, although more abnormalities were detected in urine samples from female patients in comparison to that found in the male samples, these were not statistically significant ($p > 0.05$). However, it was observed that urinalysis results for nitrite, protein and pyuria were comparable ($p > 0.05$) to that of culture result while that of leucocyte esterase and blood were significantly ($p < 0.05$) higher and lower respectively than that of culture results.

Figure 1

Table 1: Distributions of abnormal urinary findings according to sex (percentages in parenthesis)

	Age(yrs)	LE	Nitrite	Blood	Protein	Pyuria	Significant bacteriuria
Male (n = 251)	43 ± 3.2	197 (78.5)	77 (30.7)	37 (14.7)	107 (42.6)	111 (44.2)	81 (38.0)
Female (249)	41± 4.1	209 (83.9)	93 (37.3)	47 (18.9)	129 (51.8)	147 (59.0)	132 (62.0)
Total	42 ±4.3	404 (81.2)	170 (34.0)	84 (16.8)	236 (47.2)	258 (51.6)	213 (42.6)

LE: Leucocyte esterase.

Significant bacteriuria was recorded in 213 (42.6 %) of the urine specimens while 182 (36.4 %) showed insignificant bacteriuria and 105 (21 %) were sterile.

From table 2, Amoxycillin plus Clavulanic acid was the most frequently prescribed antibiotic (23.6 %), followed in decreasing order by Ampiclox (21.4 %), Cotrimoxazole (17.8 %), Ciprofloxacin (16.6 %), Ofloxacin (7.6 %), Cefuroxime (5 %), Erythromycin (4.2), Pefloxacin (2.4 %), Clarithromycin (1.4 %).

The organisms grown on the culture of all the 213 specimens with significant bacteriuria were as follows (table 3): Escherichia coli 79 (37.1 %), Staphylococcus species 59 (27.7 %), Klebsiella species 23 (10.8 %), Enterococcus species 23 (10.8 %), Proteus species 14 (6.6 %), Pseudomonas aeruginosa 8 (3.7) and Streptococcus species 7 (3.3).

Figure 2

Table 2: Frequency of prescription of each antibiotic and the number of specimens that yielded significant bacteriuria (percentages in parenthesis)

Antibiotics	Frequency	Number of significant culture
Amoxycilli+ Clavulanic acid	118 (23.6)	62 (52.5)
Ampiclox	107 (21.4)	40 (37.4)
Cotrimoxazole	89 (17.8)	26 (29.2)
Ciprofloxacin	83 (16.6)	39 (47.0)
Ofloxacin	38 (7.6)	17 (44.7)
Pefloxacin	12 (2.4)	4 (33.3)
Cefuroxime	25 (5.0)	12 (48.0)
Erythromycin	21 (4.2)	9 (42.9)
Clarithromycin	7 (1.4)	4 9 (57.1)
Total	500 (100)	213 (42.6)

Out of 62 isolates obtained from patients that received Amoxycillin + clavulanic acid as empirical prescription whose specimens also yielded significant bacteriuria, only 25 (40.3 %) were sensitive to the drug (table 3). Other observations on the rest of the antibiotics studied were as follows: Ampiclox (n = 40): 15 (37.5 %) sensitive, 25 (62.5 %) resistant; Cotrimoxazole (n = 26): 8 (30.8 %) sensitive, 18 (69.2 %) resistant; Ciprofloxacin (n = 39): 28 (71.8 %) sensitive, 11 (28.2 %) resistant; Ofloxacin (n = 17): 10 (58.8 %) sensitive, 7 (41.2 %) resistant; Pefloxacin (n = 4): 2 (50 %) sensitive, 2 (50 %) resistant; Cefuroxime (n = 12): 4 (33.3 %) sensitive, 8 (66.7 %) resistant; Erythromycin (n = 9): 5 (55.6 %) sensitive, 4 (44.4 %) resistant; Clarithromycin (n = 4): 2 (50 %) sensitive, 2 (50 %) resistant.

Figure 3

Table 3: Ratios of susceptible to resistant organisms with respect to prescribed antibiotics

Antibiotics	Organisms isolated from significant bacteriuria (% prevalence)							Total
	E. coli (37.1)	Kleb.sp (10.8)	Proteus sp (6.6)	Pseudo.sp (3.7)	Staph. sp (27.7)	Srept. sp (3.3)	Entero. sp (10.8)	
Amoxy.+Clavul acid (n = 62)	**9**: 17	**0**: 5	**1**: 2	**0**: 3	**10**: 7	-	**5**: 3	**25**: 37
Ampiclox (n = 40)	**3**: 12	**0**: 2	**0**: 1	-	**11**: 8	**1**: 2	-	**15**: 25
Cotrimoxazole (n = 26)	**4**: 5	**1**: 1	**2**: 4	**0**: 2	**1**: 2	-	**0**: 4	**8**: 18
Ciprofloxacin (n = 39)	**10**: 3	**4**: 4	**2**: 0	**1**: 0	**6**: 3	-	**5**: 1	**28**: 11
Ofloxacin (n = 17)	**5**: 2	**3**: 1	-	-	**2**: 3	-	**0**: 1	**10**: 7
Pefloxacin (n = 4)	**0**: 1	-	-	-	**1**: 0	-	**1**: 1	**2**: 2
Cefuroxime (n = 12)	**1**: 4	**0**: 1	**0**: 1	**0**: 1	**1**: 1	**2**: 0	-	**4**: 8
Erythromycin (n = 9)	**0**: 3	-	**0**: 1	-	**3**: 0	-	**2**: 0	**5**: 4
Clarithromycin (n = 4)	-	**0**: 1	-	**0**: 1	-	**2**: 1	-	**2**: 2
Total	**23**: 47	**8**:15	**5**: 9	**1**: 7	**35**: 24	**5**: 2	**13**: 10	**99**:114

n = Number of patients

Bolded figures represent number of patients whose isolates were susceptible to the antibiotics prescribed.

Normal figures represent number of patients whose isolates were resistant to the antibiotics prescribed.

DISCUSSION

This study recorded significant bacteriuria in 42.6 % of the study populations with the percentage of urine samples with positive nitrite (34.0 %), protein (47.2 %) and pyuria (51.6 %) comparable to urine samples that yielded significant bacteriuria (42.6 %). Urinary tract infection (UTI) prevalence of 42.6 % recorded in this study was higher than 22 % and 34 % reported by Jombo et al. [11] and Obi et al. [12] respectively. It is also higher than 21.6 % reported by Ugwuja and Ugwu [13] among young adults. The reason for this higher prevalence may be due to subject selection. While the present study concentrated on individuals with symptoms suggestive of UTI, others were done on apparently healthy asymptomatic subjects. The comparable percentages of abnormal urinary findings (presence of nitrite, proteinuria and pyuria) and significant bacteriuria suggests that these abnormal urinary findings may be early signs for UTI. Studies have shown that in addition to microscopic examination of uncentrifuged gram-stain urine drops for the detection of significant bacteriuria,[14] nitrite dipstick and leucocyte esterase test compared with bacteriological culture as gold standard for the diagnosis of UTI.[15]

The uropathogens isolated from the present study were

similar to those in other studies.[16, 17] The most frequently isolated organism (Escherichia coli) in this study agrees with the findings in earlier works.[13, 18, 19] However it contrasted the findings of Ehinmadu [20] where Pseudomonas aeruginosa was the most common isolated pathogen. Although the reason for the disparities in the types of micro-organism is not obvious, it could be that environment plays a significant role in determining the types and frequency of micro-organisms isolated from urine.

Excessive prescription of antibiotics, especially in non-bacterial infections has been identified as one of the causes of emergence of resistant strains.[21] In the present study, no correlation was made between frequency of antibiotic prescriptions and resistance pattern observed. However, amoxycillin-clavulanic acid which was most frequently prescribed had a sum resistance of 59.7 % in comparison to Ampiclox and cotrimoxazole that were less frequently prescribed with sum resistance of 62.6 % and 69.2 % respectively. The percentage resistance of microorganisms to antibiotics had earlier been used as a criterion to include or exclude such antibiotic from the list of choice agents for the treatment of UTI.[15] If this is extrapolated to this study, it can be argued that those antibiotics that were relatively most resisted, especially the cotrimoxazole, Cefuroxime, Clarithromycin, Ampiclox and amoxycillin-clavulanic acid should be excluded from empirical treatment of uncomplicated urinary tract infections in this environment. The antibiotic susceptibility of E. coli, being the most frequently isolated pathogen from UTI has been used as an index to determine potential agents for the treatment of the infections.[15] Again, in the present study, the highest percentage susceptibility of E coli was recorded in favour of ciprofloxacine. Ehinmadu [20] and Kadiri et al. [22] had earlier reported quinolones, including ciprofloxacine to be highly active against common urinary pathogens and that they can be readily employed in the treatment of UTI in Nigeria, when culture results are unavailable. From the present study 80.2 % of the empirical antibiotic prescriptions might have been inappropriate or unnecessary. These comprised prescriptions received by 187 patients whose urine samples did not yield significant bacteriuria and the ones received by patients (114) from whom the organisms isolated were resistant to the antibiotics prescribed. Published rates of unnecessary antibiotics use ranged from 41 % to 91 %.[23]

The higher rate observed in this study could be a reflection of over-diagnosis of UTI. We therefore conclude that although urinalysis may guides empirical antibiotic prescriptions, culture and sensitivity test prior to such prescriptions remain the best approach in avoiding the problems of rising antimicrobial resistance. However, Ciprofloxacin, a fluoroquinolone may be considered the first choice in empirical prescription.

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