



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

Study of Nitrofurantoin Susceptibility in Urinary Isolates of E.coli – A Need to Revert Back to Older Drugs

Raminder Sandhu^{1*}, Kanwardeep Singh², Gaurav Sharma³

1. Department of Microbiology, BPS Govt. Medical College for Women, Sonapat (Haryana), India.

2. Department of Microbiology, Govt. Medical College, Amritsar (Punjab), India

3. Department of Forensic Medicine, BPS Govt. Medical College for Women, Sonapat(Haryana), India.

ABSTRACT

Urinary tract infections have a high incidence in general population, with potential complications and constantly shifting trends in drug resistance that emphasizes the importance of selecting appropriate antimicrobial therapy. The present study shall focus on nitrofurantoin susceptibility in urinary E.coli isolates which heralds shifting trends in drug resistance among uropathogens and emphasizes on the need to revert back to older urinary antimicrobial agents. The study shall serve as an update on the susceptibility of E.coli to various commonly used antibiotics. A retrospective study was conducted by analyzing culture results and antimicrobial susceptibility pattern of E.coli isolated from 4533 urine samples collected from both inpatients and outpatients in Microbiology Department of tertiary care institute from January 2013 to December 2013. E.coli isolates depicted maximum sensitivity to Nitrofurantoin (87.12%) followed by Amikacin (86.53%) and Gentamicin (68.19%) whereas resistance remained high to Cefazolin (86.82%), Norfloxacin (84.53%), Cotrimoxazole (82.23%), Amoxyclav (82.23%) and Ciprofloxacin (76.22%). Nitrofurantoin susceptibility of E.coli isolates remained high in females (90.61%) as compared to males (83.09%). Among inpatients maximum sensitivity to nitrofurantoin was exhibited by isolates recovered from Gynae/obstetrics ward (94.59%) followed by pediatrics ward (82.35%). The study depicts promising use of Nitrofurantoin as narrow spectrum antibiotic to de-escalate the selection pressure and as fluoroquinolones sparing drug in areas where Cotrimoxazole resistance remains high in the uncomplicated cystitis. Clinicians should use local surveillance data to formulate empiric selection of antibiotic therapy in urinary tract infections.

Keywords: Nitrofurantoin, UTI, antimicrobialsusceptibility

*Corresponding Author Email: sandhuraminder19@yahoo.com

Received 05July 2014, Accepted15July2014

Please cite this article as: Sandhu R *et al.*, Study of Nitrofurantoin Susceptibility in Urinary Isolates of E.coli – A Need to Revert Back to Older Drugs. American Journal of PharmTech Research 2014.

INTRODUCTION

Urinary tract infections (UTI) are the most common bacterial infections affecting humans throughout their lifetime. They are the frequent cause of morbidity in outpatients as well as most frequently involved in the cause of nosocomial infection in many hospitals ¹. The majority of these infections are uncomplicated UTIs such as acute uncomplicated cystitis. Lower UTI (LUTI) constitutes the real burden of UTIs in the primary care setting and is usually treated empirically ². Compounded by a diminishing number of new agents entering clinical practice, resistance is widely recognized as a major threat to public health sectors. UTI is a serious ailment in human due to increasing frequency, recurrence and difficulty in eradication; it poses stiff challenge to the medical professionals. It is much more common in women than in men, due to anatomical and physiological reasons; by virtue of its position urinogenital tract is more vulnerable to bacterial infections caused by both internal and external flora ³. *Escherichia coli* are the most common pathogen in LUTIs. Extended-spectrum -lactamase (ESBL)-producing *E. coli*-related UTI is an emerging problem in many parts of the world. In serious cases the major treatment choices are carbapenems, which usually require hospitalization and are associated with higher antibiotic costs ⁴. Unfortunately, there are not too many treatment alternatives to carbapenems. Nitrofurantoin (NFT) is indicated in the treatment of uncomplicated LUTI. NFT is effective in vitro against *E. coli* strains, including ESBL-producers^{5,6} Knowledge of the local bacterial etiology and susceptibility patterns is required to trace any change that might have occurred in time so that updated recommendation for optimal empirical therapy of UTI can be made ⁷.

The aim of the present study was to determine the changing trend of antimicrobial resistance pattern of *E.coli*, isolated from suspected cases of urinary tract infections among both inpatients and outpatients.

MATERIALS AND METHODS

Study design

A descriptive analysis of culture results of urine samples was performed at Microbiology department of BPS, GMC for Women, KhanpurKalan. The sex and age of patients, the organism isolated and the antimicrobial susceptibility profiles were collected from the registration records using a standard data collection form.

Culture and Identification

As the standard operation procedures show clean-catch midstream morning urine specimens were collected using sterile wide mouth disposable plastic container. Urine samples were plated on

MacConkey agar and Blood agar (Hi-Media labs Ltd.) using calibrated wire loops and then incubated aerobically at 37 °C for 24 h. From positive cultures, uropathogens were identified according to the standard operational procedures as per the standard microbiological methods⁸. A significant bacterium was considered if urine culture yielded $\geq 10^5$ cfu /mL.

Antimicrobial susceptibility testing

According to the standard operational procedures, in vitro antimicrobial susceptibility testing was done on Mueller-Hinton agar (Hi-Media Lab Ltd, India) using Kirby-Bauer disk diffusion method. A suspension of test organism was made in sterile normal saline and turbidity adjusted to 0.5 McFarland standards. The test organism was uniformly seeded over the surface of Mueller Hinton agar plates. The plates were allowed to dry for 10 minutes before application of antibiotic impregnated discs. The plates were incubated at 37°C for 16-18 hours. After incubation clear zones around the antibiotic discs were measured with a ruler and recorded in millimeters⁹. The antimicrobial agents tested were: Cefazolin (30µg), Nitrofurantoin (300µg), Amoxycylav (30µg), Gentamicin (10µg), Amikacin (30µg), Ciprofloxacin (5µg), Norfloxacin (10µg), Cefuroxime (30µg), Cefotaxime (30µg), and Cotrimoxazole (25µg) (Hi-Media Lab Ltd, Mumbai). Resistance data was interpreted according to Clinical laboratory Standards Institute guidelines¹⁰

RESULTS AND DISCUSSION

Out of 4533 urine specimens, 3417 (75.38%) were sterile and 1116 (24.62%) depicted bacterial growth. Gram negative bacteria 648 (58.06%) outnumbered gram positive pathogens 468 (41.94%). E.coli remained the most common isolate 349 (53.86%) followed by Citrobacterspp 89(13.73), Pseudomonas 74 (11.42%), Acinetobacter 64 (9.87%) and Klebsiellapneumoniae 42 (6.48%). E.coli isolates reflected maximum sensitivity to Nitrofurantoin (87.12%) followed by Amikacin (86.53%), Gentamicin (68.19%). The resistance rate of urinary E.coli isolated was highest for Cefazolin (86.82%) followed by Norfloxacin (84.53%), Amoxycylav (82.23%), Cotrimoxazole (82.23%), Ciprofloxacin (76.22%) and Cefuroxime (74.21%) shown in Table 1. Maximum number of E.coli was isolated from Gynae and Obstetrics department (53.62%) followed by General Surgery department (23.19%) & Pediatrics department (12.32%) among inpatients as shown in Table 2. As regards Nitrofurantoin sensitivity, most of the isolates from Gynae& obstetrics department (94.59%) remained sensitive whereas 75% and 82.35% of isolates remained sensitive to nitrofurantoin respectively from general surgery and pediatrics department. Among outpatients, predominant E.coli isolates were from General surgery (47.39%) which depicted 79% sensitivity to nitrofurantoin, followed by gynae and obstetrics department (33.18%)

in which sensitivity remained 92.86% as shown in Table 3. As regards gender, females (61.03%) were more commonly infected with E.coli as compared to males (38.97%) and Nitrofurantoin sensitivity was better in females (90.61%) as compared to males (83.09%) as depicted in Table 4. E.coli isolates were predominant in age group of 21-30 years (41.31%) among females followed by 31- 40 years (16.43%) and 11-20 years (12.77%) whereas in males E.coli isolates were maximum in age group of 61-70 years (33.09%) followed by 51-60 years (17.65%) and 0-10 years (15.44%) as shown in Table 5. While historically it was believed that the causative organism in UTIs differed between men and women, more recent data has shown that for both sexes the primary causative pathogen is *Escherichia coli*, which accounts for 75-90% of UTIs^{11,12}. With the increases in antibiotic resistance among *E. coli* and other *Enterobacteriaceae* over the past several decades, surveillance data have become critical for appropriate empiric selection of antibiotic therapy. U.S. guidelines specify that TMP/SMX should be avoided for empiric treatment of uncomplicated acute cystitis or pyelonephritis in populations where non-susceptibility to this agent exceeds 20% in uropathogens. Antibiotic treatment is typically selected empirically, based on the patient clinical presentation, medical history and local patterns of antibiotic susceptibility¹³. In the present study gram negative pathogens (58.06%) outnumbered gram positive organisms (41.94%) which is comparable to study done by Khoshbakht R et al 2013 who reported predominance of gram negative bacilli (83.17%) while gram positive organisms as 21.73%¹⁴. Among gram negative uropathogens *E.coli* remained predominant isolate (53.86%) which is in agreement with the findings of Khoshbakht R et al 2013, Shalini et al 2011 and Kibret M &Abera B 2014 who also reported *E.coli* as most predominant pathogen isolated from urine samples with prevalence of 66.08% ,64.33% and 63.6% respectively^{14,15,16}. Isolates exhibited high resistance to Norfloxacin (84.53%) and Ciprofloxacin (76.22%) which is comparable to study done by AshaPai KB et al 2011, who also reported high resistance for Ciprofloxacin 72.59% &Norfloxacin 73.49%¹⁷. Generalized prescription of fluoroquinolones as empirical treatment for cystitis should be abandoned. This common practice facilitates the emergence of strains resistant to this class of antibiotics and promotes the emergence of multidrug-resistant strains in the community¹⁸. Another factor could be the generalized use of fluoroquinolones in animal feed in the country (especially in poultry intensive breeding), and the subsequent transmission of resistant strains from animals to humans¹⁹. Majority of *E.coli* isolates were susceptible to Nitrofurantoin (87.12%), with resistant isolates only 12.89%, which is similar to results documented by Shalini et al 2011 ,Kibret M &Abera B 2014 and Rijal A et al 2012, in which sensitive isolates were 93.48%, 96.2% and 96.5% with only 6.52% , 3.8% and 3.5% resistant isolates^{15,16,20}. NFT is a specific antibiotic for

infections of the urinary tract. It is bacteriostatic at low concentrations and bactericidal at high concentrations. The oral form of NFT is absorbed well. Approximately 60% is bound to plasma proteins and is metabolized in the liver; 30–50% of the given dosage is excreted via the urine. After oral administration, drug concentrations of NFT in urine range between 50µg/mL and 250µg/mL which exceeds the MIC for susceptible organisms. Its disadvantages include the requirement of dosing q6h and low tissue concentrations. Major adverse events of NFT are related to the gastrointestinal system and skin ⁵.The drug of choice as depicted by the findings of present study remains Nitrofurantoin as 87.12% isolates were sensitive, with only 13.47% isolates resistant. Nitrofurantoin has been used for more than five decades for the treatment of uncomplicated cystitis and it was found to remain active against most of the uropathogens, but its popularity was hampered by a recommended seven day dosing regimen and concerns about its efficacy and tolerance. A study which was conducted by Gupta K et al 2007 has revealed that, a 5-day course of nitrofurantoin was equivalent clinically and microbiologically to a 3-day course of Cotrimoxazole and that it should hence be considered as an effective fluoroquinolones-sparing alternative for the treatment of acute cystitis in women ²¹.The consistent and high-level susceptibility of *E. coli* to nitrofurantoin may be influenced by Nitrofurantoin's narrow spectrum of activity, limited indication, narrow tissue distribution, and limited contact with bacteria outside the urinary tract ²².In present study aminoglycosides depicted high susceptibility as regards Amikacin (86.53%) and Gentamicin(68.19%) which is similar to those reported by Shalini et al 2011 &AshaPai KB et al 2011 as Amikacin 98.91% ,Gentamicin 66.30% and Amikacin 88.56% respectively^{15,17}.Aminoglycosides are effective against most of the bacteria which cause cystitis. They have a relatively narrow margin of safety between the therapeutic and the toxic concentrations. They exhibit ototoxicity and nephrotoxicity ²³.Since the route of administration is parenteral, so patient compliance becomes a factor of consideration as regards outpatients whereas these drugs can be a good treatment modality among inpatients for treating uncomplicated cystitis as present study is reflecting high sensitivity for both Amikacin (86.53%) and Gentamicin (68.19%).The antimicrobial susceptibility pattern of present study is clearly indicating that Norfloxacin, Ciprofloxacin, Cotrimoxazole and Amoxyclav are virtually useless as regards their efficacy against urinary *E.coli* isolates with only 15.47%, 17.77% and 17.77% and 23.78% isolates being sensitive. In context of gender, females (61.03%) were more commonly infected with *E.coli* as compared to males (38.97%) which are comparable to Khoshbakht R et al 2013who mentioned 89.5% isolates in females and 10.5% in males ¹⁴. Most infections are caused by retrograde ascent of bacteria from fecal flora to bladder and kidney via urethra, especially in fe-

males whom the urethra is shorter and wider²⁴. Anatomical structure of female urethra and vagina make them susceptible to trauma during sexual intercourse and bacterial passage through urethra up to the bladder during pregnancy and delivery^{25, 26}. Males are less prone to UTIs possibly because of their longer urethra and the presence of antimicrobial substances in prostatic fluid²⁷. E.coli isolates from females (9.39%) showed relatively less resistance than males (16.91%). So nitrofurantoin usage can be more promising in females as compared to males. The absorption of oral nitrofurantoin is 40-50% and hence, it is enhanced when it is taken with food. The drug has minimal side effects on shortcourse therapy. It can be used for treating uncomplicated cystitis, including the treatment of cystitis during pregnancy when it is clearly indicated²⁸. Age specific distribution of E.coli isolates among females showed highest rate in the age group of 21-30 years (41.31%) followed by 31-40 years (16.43%) and 11-20 years (12.77%) whereas in men the highest number of E.coli isolates were in the age group of 61-70 (33.09%) followed by 51-60 years (17.65%) and 0-10 years (15.44%) which is similar to the findings of Rijal A et al 2012 who observed E.coli preponderance in males over 61 years (18.6%)²⁰. As suggested by the literature there was a female preponderance except in the elderly age group (more than 69 years) which showed a high male percentage^{29,30}. The cause of urinary tract infections in elderly male may be because of conditions leading to bladder outflow obstruction. UTIs are often treated with different broad-spectrum antibiotics, one with a narrow spectrum of activity may be appropriate because of emerging concerns about infection with resistant organisms, and antimicrobial susceptibility testing of the urinary pathogens constitutes the basis for antibiotic therapy. However, in view of the increasing bacterial resistance, regular monitoring of resistance patterns is necessary to improve guidelines for empirical antibiotic therapy³¹.

Table 1:Antibiogram of Escherichia coli

Antibiotic	Sensitive (percentage)	Resistant (percentage)
Cotrimoxazole	62 (17.77)	287 (82.23)
Nitrofurantoin	304 (87.12)	45 (12.89)
Amoxyclav	62 (17.77)	287 (82.23)
Gentamicin	238 (68.19)	111 (31.81)
Amikacin	302 (86.53)	47 (13.47)
Ciprofloxacin	83 (23.78)	266 (76.22)
Norfloxacin	54 (15.47)	295 (84.53)
Cefazolin	46(13.18)	303 (86.82)
Cefuroxime	90 (25.79)	259 (74.21)
Cefotaxime	154(44.13)	195(55.87)

Table 2: Distribution of E.coli isolates and Nitrofurantoin sensitivity among inpatients

Department	Number of isolates (%age)	Resistant (%age)	Sensitive (%age)
General Surgery	32 (23.19)	8 (25)	24(75)
Orthopedics	3 (2.17)	1(33.33)	2(66.66)
Gynecology and Obstetrics	74 (53.62)	4(5.41)	70 (94.59)
Medicine	10 (7.25)	2(20)	8(80)
Pediatrics	17 (12.32)	3(17.65)	14(82.35)
Medical ICU	2 (1.45)	1 (50)	1(50)
Total	138 (100)	19	119

Table 3.Distribution of E.coli isolates and Nitrofurantoin sensitivity pattern among outpatients

Department	Number of isolates (%age)	Resistant (%age)	Sensitive (%age)
General Surgery	100 (47.39)	21 (21)	79 (79)
Orthopedics	01 (0.47)	0	1 (100)
Gynecology and Obstetrics	70(33.18)	5 (7.14)	65 (92.86)
Medicine	16 (7.58)	1 (6.25)	15 (93.75)
Pediatrics	23 (10.90)	2 (8.70)	21(91.30)
Ophthalmology	01 (0.47)	0	1 (100)
Total	211	29	182

Table 4.Gender-wise distribution and Nitrofurantoin susceptibility of E.coli

Gender	Number of isolates (%age)	Resistant (%age)	Sensitive (%age)
Female	213(61.03)	20(9.39)	193 (90.61)
Male	136(38.97)	23(16.91)	113(83.09)
Total	349(100)	43(12.32)	306(87.68)

Table 5.Age- specific distribution of E.coli isolates among female and male

Age	Female	Male
	Number of isolates	Number of isolates
0-10	11 (5.16%)	21 (15.44%)
11-20	27 (12.77%)	8 (5.88%)
21-30	88 (41.31%)	9 (6.62%)
31-40	35 (16.43%)	15 (11.03%)
41-50	24 (11.27%)	14 (10.29%)
51-60	16 (7.51%)	24 (17.65%)
61-70	12 (5.63%)	45 (33.09%)
Total	213 (100%)	136 (100%)

CONCLUSION

E.coli remained the predominant isolate among gram negative organisms, more commonly in females presenting to our hospital. In developing countries self-medication because of on counter availability of antibiotics and secondly the unwanted prescriptions of antimicrobials by physicians make the situation worst. The in vitro activity of Nitrofurantoin found in the present study suggests that this drug would provide adequate fluoroquinolones sparing alternative therapy at places where

Cotrimoxazole use is no longer prudent because of high rates of resistance .A review of antibiotic policy pertaining to treatment of urinary tract infections is necessary, which shall require interactions of various departments. A common working policy has to be formulated using local surveillance data to guide the empiric selection of antibiotic therapy as well as prevention of development of resistant strains.

REFERENCE

1. Sussman M. Urinary Tract Infections. In, Topley and Wilson's Microbiology and Microbial Infections. Hausler Jr, Sussman M (eds) . 9th ed., Arnold; 1998: 601-21.
2. Tasbakan MI, Pullukcu H, Sipahi OR, Yamazhan T, Arda B, Ulusoy S. A pooled analysis of the resistance patterns of *Escherichia coli* strains isolated from urine cultures in Turkey: A comparison of the periods 1997–2001 and 2002–2007. *Turk J Med Sci* 2011; 41(3):557–64.
3. Arjunan M, Al-Salamah AA and Amuthan M. Prevalence & Antibiotics Susceptibility of Uropathogens in patients from a Rural Environment, Tamil Nadu. *Am J Infect Dis* 2010; 6 (2): 29-33.
4. Coskun O, Erdem H, Avcı A. Management of community-acquired acute bacterial cystitis in Turkey. *Turk J Med Sci* 2011; 41(1):149–57.
5. Hooper DC. Urinary tract agents: nitrofurantoin and methenamine. In, Mandell GL, Bennett JE, Dolin R (editors). *Principles and practice of infectious diseases*. 7thed, Philadelphia, PA: Churchill Livingstone; 2010: 515–20.
6. Pullukcu H, Aydemir S, Tasbakan S, Sipahi OR, Cilli F, Ulusoy S. In vitro efficacy of nitrofurantoin on *Escherichia coli* strains isolated from urine cultures. *Turk J Infect* 2007; 21:197–200.
7. Leegaard TM, Caugant DA, Froholm LO, Hoiby EA. Apparent differences in antimicrobial susceptibility as a consequence of national guidelines. *Clin Microbiol Infect* 2000; 6(6): 290-93.
8. Cheesbrough M. *Medical laboratory manual for tropical countries: Microbiology Vol 2*. Butterworth-Heinemann Ltd, Kent, U.K 2006; 23-78.
9. Bauer AW, Kirby WM, Sherris JC, Turck M. Antibiotic susceptibility testing by standardized single disk method. *Am J Clin Pathol* 1996; 45(4): 493-96.
10. CLSI. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; 21st informational supplement .CLSI document M100-S21. Wayne, PA 2011.
11. Ulleryd P. Febrile urinary tract infection in men. *Int J Antimicrob Agents* 2003; 22(2):89–93.

12. Gupta K, Hooton TM, Stamm WE. Increasing antimicrobial resistance and the management of uncomplicated community-acquired urinary tract infections. *Ann Intern Med* 2001; 135(1):41–50.
13. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011; 52(5): 103–20.
14. Khoshbakht R, Salimi A, Aski HS, Keshavarzi H. Antibiotic susceptibility of bacterial strains isolated from urinary tract infections in Karaj,Iran. *Jundishapur J Microbiol* 2013; 6(1):86-90.
15. Shalini, Joshi MC, Rashid MK, Joshi HS. Study of Antibiotic Sensitivity Pattern in Urinary Tract Infection at a Tertiary Hospital. *Nat J Integr Res Med* 2011; 2(3):43-6.
16. Kibret M, Abera B. Prevalence and antibiogram of bacterial isolates from urinary tract infections at Dessie Health Research Laboratory, Ethiopia. *Asian Pac J Trop Biomed* 2014; 4(2): 164-68.
17. AshaPai KB, Rai R, Sanjeev H, Karnaker VK, Krishna Prasad MS. Nitrofurantoin: An Alternative Therapy for Uncomplicated Cystitis in the Era of Antimicrobial Resistance. *J ClinDiag Res* 2011; 5(5):964-66.
18. Karlowsky JA, Hoban DJ, Decorby MR, Laing NM ,Zhanel GG. Fluoroquinolone-resistant urinary isolates of *Escherichia coli* from outpatients are frequently multidrug resistant: results from the North American Urinary Tract Infection Collaborative Alliance-Quinolone Resistance study. *Antimicrob Agents Chemother* 2006; 50(6): 2251-54.
19. Miller LG,Tang AW. Treatment of uncomplicated urinary tract infections in an era of increasing antimicrobial resistance. *Mayo ClinProc* 2004; 79(8):1048-54.
20. Rijal A, Ghimire G, Gautam K, Barakoti A. Antibiotic Susceptibility of Organisms Causing Urinary Tract Infection in Patients Presenting to a Teaching Hospital. *J Nepal Health Res Counc* 2012; 10(20):24-27.
21. Gupta K, Hooton TM, Roberts PL, Stamm WE. Short course nitrofurantoin for the treatment of acute uncomplicated cystitis in women. *Arch Intern Med* 2007; 167(20):2207-2212.
22. James AK, Laurie J, Clyde T, Mark EJ, Daniel FS. Trends in Antimicrobial Resistance among Urinary Tract Infection Isolates from Female Outpatients in the United States. *Antimicrob Agents Chemother* 2002; 46(8): 2540-45.
23. Tripathi KD. Aminoglycosides. In, Tripathi M, Tripathi V (editors). *Essentials of Medical Pharmacology*. New Delhi: Jaypee brothers; 1999; 730-38.

24. Inabo HI, Obanibi HBT. Antimicrobial susceptibility of some urinary tract clinical isolates to commonly used antibiotics. *Afr J Biotechnol* 2006; 5(5):487-89.
25. Al Sweih N, Jamal W, Rotimi VO. Spectrum and antibiotic resistance of uropathogens isolated from hospital and community patients with urinary tract infections in two large hospitals in Kuwait. *Med Princ Pract* 2005; 14(6):401-7.
26. Kolawole A, Kolawole O, Kandaki-Olukemi Y, Babatunde S, Durowade K, Kolawole C. Prevalence of urinary tract infections (UTI) among patients attending DalhatuAraf Specialist Hospital, Lafia, Nasarawa State, Nigeria. *Int J Medicinal Med Sci* 2009; 1(5):163-67.
27. Farajnia S, Alikhani MY, Ghotaslou R, Naghili B, Nakhband A. Causative agents and antimicrobial susceptibilities of urinary tract infections in the northwest of Iran. *Int J Infect Dis* 2009; 13(2):140-44.
28. Garau J. Other antimicrobials of interest in the era of extended spectrum beta-lactamases: fosfomicin, nitrofurantoin and tigecycline. *Clin Microbiol Infect* 2008; 14(1): 198-202.
29. Orrett FA. Urinary tract infections in general practice in a rural community in South Trinidad. *Saudi Med J* 2001; 22(6):537-40.
30. Acharya A, Gautam R, Subedee L. Uropathogens and their antimicrobial susceptibility pattern in Bharatpur, Nepal. *Nepal Med Coll J* 2011; 13(1):30-33.
31. Kripke C. Duration of therapy for women with uncomplicated UTI. *Am Fam Physician* 2005; 72(11): 2219

AJPTR is

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: editor@ajptr.com

