

THE FREQUENCY OF ESCHERICHIA COLI AND ITS SENSITIVITY TO NITROFURANTOIN IN URINARY TRACT INFECTION

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ABSTRACT

Objective: This study is conducted to determine frequency of E-Coli and its sensitivity to nitrofurantoin in patients with urinary tract infection.

Material and Methods: The study was conducted at a tertiary care hospital of District Peshawar, i.e. Khyber Teaching Hospital (KTH), after reviewed and approved by the Committee for Ethical Review of Research involving Human Subjects of KTH. Non-random consecutive sampling technique was used for the collection of data and data collection was completed in 06 months' time i.e. from 20th February to 19th August 2018. The survey was conducted as a descriptive cross-sectional study using open Epi calculator, keeping confidence interval of 95%, sample size calculated is 148. Urine samples were collected in sterile containers and was sent to laboratory for routine examination, culture and sensitivity. A colony 10⁵ or more was considered E Coli growth. Nitrofurantoin was used to check the sensitivity for organisms as per operational definition. All the tests and examinations were carried out under the supervision of experienced medical specialist and microbiologist.

Results: In this study, 148 patients were studied. Average age was 41.86 years + 11.62SD. E coli was found in 91 (61.5%) of patients out of total 148 patients. Among UTI patients 78(85.7%) were sensitive to Nitrofurantoin.

Conclusion: High prevalence of drug-resistant urinary tract pathogens, particularly to Nitrofurantoin suggests cautious use of antibiotic therapy for the treatment of UTI.

Keywords: Urinary tract infection, Antibiotics, Common Bacteria, sensitivity.

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INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial illnesses in adults and is one of the most common indications for antibiotics. UTIs are a common cause of morbidity in women. The majority of cases involve only the lower urinary tract and the most common pathogen is Escherichia coli.

For uncomplicated infections, especially those without signs of upper tract infection, empirical therapy without culture and susceptibility analysis are recommended. Resistance to amoxicillin has been established for years and resistance to trimethoprim-sulfamethoxazole (TMP-SMX) has emerged more recently with rates of >20% in some areas. The Infectious Diseases Society of America recommends that in regions where resistance rates to TMP-SMX exceed 10% to 20%, TMP-SMX

should not be used for empirical therapy. Fluoroquinolones, in particular ciprofloxacin, are used increasingly but resistance to ciprofloxacin is also rising. Amoxicillin + clavulanate may be an alternative in uncomplicated UTIs caused by multidrug-resistant isolates if susceptibility is confirmed by laboratory findings. Nitrofurantoin, which currently retains activity against most multidrug-resistant strains may also be considered. A recent study reported 29.6% resistance to trimethoprim-sulfamethoxazole and 88.2% sensitivity to Fluoroquinolones particular ciprofloxacin with 100% sensitivity to Nitrofurantoin. The frequency of E-coli was observed in 56.42% of patients with 91.77% sensitivity to nitrofurantoin with urinary tract infection. The sensitivity of bacteria to antibiotics varies in relation to the geographical region, due to frequent use and misuse.

The emergence of resistance and consequent reduced efficacy of antibiotics in the management of UTIs is indeed a serious public health problem. This is particularly important in the developing countries like Pakistan, where apart from high level of poverty, ignorance and poor hygienic practices and drugs of questionable quality are often in circulation. The current study is designed in this regard to find statistics about the efficacy of nitrofurantoin for the treatment of UTIs in our local population. UTI poses significant financial stress and reduced quality of life due

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to non-availability sensitivity data. By finding individuals as well as community local statistics of antibiotics sensitivity will help empiric therapy early in our local population. Moreover, this study will help us gain knowledge about the type of pathogens responsible for UTIs. These results will be projected to various health care institutions for improvements in the current treatment in order to decrease the morbidity and mortality and better management of patients with UTIs.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted at a tertiary care hospital of District Peshawar, i.e. Khyber Teaching Hospital (KTH), after being reviewed and approved by the Committee for Ethical Review of Research involving Human Subjects of KTH. Non-random consecutive sampling technique was used for the collection of data and data collection was completed in 06 months' time i.e. from 20th February to 19th August 2018.

The sample size calculated is 148, calculated by using open Epi calculator, keeping confidence interval of 95%. The patients were recruited after obtaining a written informed consent. Data was collected while respecting the anonymity of the individual participants. Urine was collected in sterile containers and was sent to the laboratory for routine examination, culture and sensitivity testing. A colony 105 or more was considered E Coli growth. Nitrofurantoin was used to check the sensitivity for organisms as per operational definition. All the tests and examinations were carried out under the supervision of experienced medical specialist and microbiologist who had extensive experience in their respective fields i.e. a minimum of 5 years. Patients of either gender or age 18-60 years admitted or presenting to out-patient department during the days of data collection fulfilling the criteria of UTI as defined in operation definition were included. Out of them those who had taken antibiotics in last 48 hours of presentation or immunocompromised patients i.e. HIV, Diabetes Mellitus and patients on Immunosuppressive drugs or their urine culture showed mix bacterial growth were excluded from the study. Exclusion criteria were strictly followed to control confounders and bias in the study results. For the analysis of data SPSS version 23.0 was used. Frequencies and percentages were calculated for categorical variables like gender, education status, residence and sensitivity to nitrofurantoin. Mean ± Standard Deviation were computed for numerical variable like age and BMI. Effect modifiers like age, gender, education status, BMI and residence were dealt through stratification. Post stratification Chi square test was applied keeping P value ≤ 0.05 as significant.

RESULTS

A total of 148 patients with culture proven UTI with the age of 18-60 years were approached. There were 81 (54.73%) females and 67(45.27%) males. Male to female ratio was 0.63:1. Patients' age was divided in three categories, out of which majority presenting with culture proven UTI were of age more than or equal to 45 years which

were 65(43.9%), 55(37.2%) were of age 31-45years and 28(18.9%) patients had age range less than or equal to 30 years. The study included age range 18 to 60 years. Average age was 41.86 Years + 11.62SD. E coli was found in 91(61.5%) of patients out of total 148. Among UTI patients,78(85.7%) were sensitive to nitrofurantoin. Majority of our sample were having BMI less than 25kg/m2 while 54.1% of patients were literate having up to secondary level education and 54.7% of patients belonged to urban area of this locality. Stratification of sensitivity to nitrofurantoin showed that except for residence all the other factors were insignificant.

Age wise distribution of resistance to nitrofurantoin showed that old age was more prone as compared to younger age. The patients with age less than or equal to 30 years had sensitivity of 57.1%, age group 31-45 years had 54.5% sensitivity and patients with 45-60 years of age had 50.8% sensitivity in patients with UTI. Gender wise distribution of sensitivity showed that gender had no significant impact. There was 9.5% sensitivity in male and 9.4% in female patients.

Table 1: Age Wise Distribution of the Patients (N=148)

	Frequency	Percent	Mean + SD
<= 30.00	28	18.9	41.86+ 11.62
31.00 - 45.00	55	37.2	
46.00+	65	43.9	
Total	148	100.0	

Table 2: E Coli and Antibiotic Sensitivity Distribution (N=148)

Sensitivity to Nitrofurantoin		E-Coli		Total
		Yes	No	
Yes	Count	78	1	79
	% within E-Coli	85.7%	1.8%	53.4%
	% of Total	52.7%	.7%	53.4%
No	Count	13	56	69
	% within E-Coli	14.3%	98.2%	46.6%
	% of Total	8.8%	37.8%	46.6%
Total	Count	91	57	148
	% within E-Coli	100.0%	100.0%	100.0%
	% of Total	61.5%	38.5%	100.0%

Table 3: BMI, Educational status and Residence (N=148)

		Count	Table N %
BMI	<25	104	70.3%
	>=25	44	29.7%
Educational Status	Illiterate	37	25.0%
	Up to Secondary	80	54.1%
	Intermediate above	31	20.9%
Residence	Rural	67	45.3%
	Urban	81	54.7%

Table 4: Stratification of Sensitivity to Nitrofurantoin

		Sensitivity to Nitrofurantoin		P-value	
		Yes	No		
Gender	Male	33	34	0.360	
		49.3%	50.7%		
	Female	46	35		
		56.8%	43.2%		
BMI	<25	56	48		0.861
		53.8%	46.2%		
	>=25	23	21		
		52.3%	47.7%		
Educational Status	Illiterate	18	19	0.727	
		48.6%	51.4%		
	Up to Secondary	45	35		
		56.2%	43.8%		
	Intermediate above	16	15		
		51.6%	48.4%		
Residence	Rural	52	15	0.000	
		77.6%	22.4%		
	Urban	27	54		
		33.3%	66.7%		
age (in years)	30.00 - 18.00	16	12	0.832	
		57.1%	42.9%		
	45.00 - 31.00	30	25		
		54.5%	45.5%		
	60.00 - 46.00	33	32		
		50.8%	49.2%		

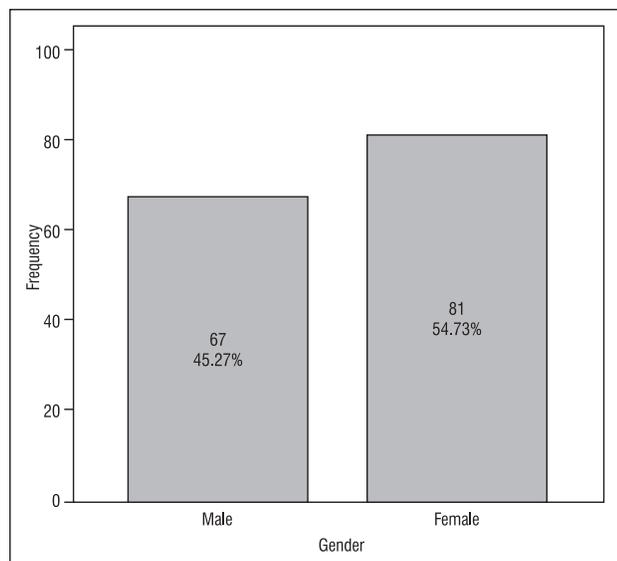


Fig 1: Gender Wise Distribution of the Patients (N=148)

DISCUSSION

Uncomplicated urinary tract infections (UTIs) are usually diagnosed in previously healthy women with no underlying disease or anatomical anomalies, whereas complicated UTIs refer to patients with co-morbidities, anatomical anomalies, and catheter-associated or hospital acquired infections . UTIs are a global financial burden and the emergence of resistance in uncomplicated and complicated uropathogens is of great concern . Escherichia coli (E. coli) is the most common uropathogen in both uncomplicated and complicated UTIs.¹⁶ There is a wide spectrum of pathogens causing complicated UTIs including E. coli, Klebsiella, Pseudomonas, Enterobacter, Enterococcus and Candida species .

Guidelines recommend a short course of trimethoprim-sulfamethoxazole (TMP-SMX) for the empiric treatment of uncomplicated UTIs if resistance is less than 20% . In South Africa, TMP-SMX is widely used for UTI prophylaxis and treatment and for Pneumocystis jirovecii prophylaxis in immunocompromised patients which has led to increased bacterial resistance . In a setting where more than 20% of E. coli cultures are resistant to TMP-SMX, guidelines recommend ciprofloxacin, nitrofurantoin or Fosfomycin . Nitrofurantoin is an effective urinary tract antiseptic that is not used for other kind of infections. It does not affect antibiotic use in any other infection and it has a resistance rate of less than 20% in this study. Therefore it should be used as first-choice treatment in uncomplicated UTIs in this hospital.

A very high rate of culture-negative urine samples was received at the laboratory. This might imply that samples are sent for culture inappropriately. Routine urine culture is not necessary . Cost effectiveness can be achieved by only sending cultures from patients with both symptoms of UTI and abnormality on urine dipstick. The dipstick strategy is most likely to be cost-effective. This criterion will also help to limit the unnecessary use of empiric antibiotics. TMP-SMX and amoxicillin are of no use in this population with UTIs. Nitrofurantoin should be the empiric choice for uncomplicated UTIs.

E. coli showed the highest sensitivity to nitrofurantoin in the current study, which are in line with those of previous studies in Saudi Arabia and other countries²¹. These data further support recommendations made in previous studies, in which, nitrofurantoin may be more effective than co-trimoxazole or amoxicillin in the empiric treatment of UTIs.

For nitrofurantoin, the prevalence of resistant isolates were higher among elderly patients. This match the results observed in earlier studies that found ciprofloxacin resistance was highest among patients older than 65 years (7.1%). However, nitrofurantoin resistance pattern in our study is contrary to that described by Sham's study, in which resistance to nitrofurantoin was constant irrespec-

tive of patient's age .

Antibiotic abuse and practicing incomplete antibiotic regimen has considerably promoted the multidrug resistant bacteria . Our study showed that E. coli had lower resistance for less commonly used drugs like imipenem, meropenem, amikacin and nitrofurantoin. This finding is supported by the study of Sharmin S which reported a good sensitivity for imipenem, ceftazidime and amikacin against UTI-isolates of E. coli in Bangladesh . Encarnacion A R also reported sensitivity of the UTI-isolates of E. coli for amikacin in Philippines. Although E. coli exhibits high sensitivity to nitrofurantoin, this antibiotic is not suggested for cases with serious upper urinary tract infections or systemic involvement. In the present study, sensitivity of E. coli to nitrofurantoin was less than that reported in other surveys performed in Iran and other parts of the world . In this regard, in a previous study by Ghorbani A E. coli was more susceptible to ciprofloxacin, amikacin, and nitrofurantoin . Comparison of the present findings with previous research showed that the prevalence of gentamicin and cephalothin resistance of E. coli isolates were much lower in our study as compared to the research by Khoshbakht R in Shiraz, Iran .

Our study revealed high rates of prior antibiotic use for UTIs and other unrelated infections such as upper respiratory tract infections. These prior antibiotics might have played a role in the current resistance profiles.

A meta-analysis showed that antibiotic use in primary care for respiratory or urinary infections leads to selection of resistance to that antibiotic and that this would lead to increased population carriage of resistant organisms and increased use of second-line antibiotics. It was also reported that infection with organisms with resistance after prior antibiotic use was greatest in the month immediately after treatment but could persist for up to 12 months .

A single centre cohort is the main limitation of this study. Multicentre randomized large trials are needed to generalize these study findings.

CONCLUSION

Increased resistance of urinary tract E. coli isolates to nitrofurantoin was demonstrated, suggesting re-evaluation of empirical therapy for the treatment of UTIs. Periodic monitoring of antimicrobial susceptibility both in the community and hospital settings is recommended.

REFERENCES

1. Naeem M, Khan MA, Qazi SM. Antibiotic susceptibility pattern of bacterial pathogens causing urinary tract infection in a tertiary care hospital. *Ann Pak Inst Med Sci*. 2010;6:214-8
2. Schmiemann G, Kniehl E, Gebhardt K, Matejczyk MM, Hummers-Pradier E. The Diagnosis of Urinary Tract Infection. A Systematic Review. *Dtsch Arztebl Int*.

2010;107:361-7

3. Bader MS, Hawboldt J, Brooks A. Management of complicated urinary tract infections in the era of antimicrobial Sensitivity. *Postgrad Med*.2010;122:7-15
4. Meister L, Morley EJ, Scheer D. History and physical examination plus laboratory testing for the diagnosis of adult female urinary tract infection. *Acad Emerg Med* 2013;20(7):631-45
5. Jiang T, Chen PS, Ouyang JA. Urine particles analysis: performance evaluation of Sysmex UF-1000i and comparison among urine flow cytometer, dipstick, and visual microscopic examination. *Scand J Clin Lab Invest* 2011;71(1):30-7
6. Abrahamian FM, Krishnadasan A, Mower WR. The association of antimicrobial Sensitivity with cure and quality of life among women with acute uncomplicated cystitis. *Infection* 2011;39(6):507-14
7. Habte TM, Dube S, Ismail N, Hoosen AA. Hospital and community isolates of uropathogens at a tertiary hospital in South Africa. *S Afr Med J*. 2009;99(8):584-7
8. Briscoe SE, McWhinney BC, Lipman J, Roberts JA, Ungerer JP. A method for determining the free (unbound) concentration of ten beta-lactam antibiotics in human plasma using high performance liquid chromatography with ultraviolet detection. *Journal of Chromatography B*, 2012;907:178-184
9. Kumar D, Singh AK, Ali MR, Chander Y. Antimicrobial Susceptibility Profile of Extended Spectrum β -Lactamase (ESBL) Producing Escherichia coli from Various Clinical Samples. *Infectious diseases*, 2014;7:1
10. Rashid M, Modi S, Shukla I, Chander Y. Prevalence and antibiogram of extended spectrum beta-lactamase producing Escherichia coli. *J Evol Med Dent Sci* 2013;14(2):1368-78
11. Mehr MT, Khan H, Khan TM, Iman N, Iqbal S, Adnan S. E coli urine super bug and its antibiotic sensitivity - a prospective study. *J Med Sci Jun* 2010;18(2):110-3
12. Hooton TM, Stamm WE. Diagnosis and treatment of uncomplicated urinary tract infection. *Infect Dis Clin North Am*. 1997;11(3):551-81
13. Guneysele O, Onur O, Erdede M, Denizbasi A. Trimethoprim/sulfamethoxazole resistance in urinary tract infections. *J Emerg Med*. 2009;36(4):338-41
14. Ronald A. The etiology of urinary tract infection: traditional and emerging pathogens. *Am J Med*. 2002;8 (113): 14S-9
15. Sobel JD, Kaye D. Urinary tract infections. In: Mandell GL, Bennett JE, Dolin R, eds. Principles and practice of Infectious diseases. 6th ed. Philadelphia, Pa.: Elsevier Churchill Livingstone;2005: 890
16. Huovinen P. Resistance to TMP-SMX. *Clin Infect Dis*. 2001;32:1608-14
17. Sanford J P, Gilbert DN, Moellering Jr RC, Eliopoulos GM, Sande MA, Chambers HF. The Sanford Guide to Antimicrobial Therapy. 38th ed. Sperryville, VA, 2008;27:30
18. Gupta K. Addressing antibiotic resistance. *Am J Med*. 2002;8(113):29S-34

19. Little P, Turner S, Rumsby K. Dipsticks and diagnostic algorithms in urinary tract infection: development and validation, randomised trial, economic analysis, observational cohort and qualitative study. *Health Technol Assess.* 2009;13(19):1-73
20. Al-Tawfiq JA, Anani AA. Antimicrobial susceptibility pattern of bacterial pathogens causing urinary tract infections in a Saudi Arabian hospital. *Chemotherap.* 2009;55(2):127-31
21. Gupta K, Scholes D, Stamm WE. Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women. *J Am Med Asso* 1999;281(8):736-8
22. Sahm DF. Multidrug-resistant urinary tract isolates of *Escherichia coli*: prevalence and patient demographics in the United States in 2000. *Antimicrob Agents Chemother.* 2001;45(5):1402-6.
23. Lee MG, Henry GL. Drug availability in Jamaica. *West Indian Med J.* 1989;38(2):105-9
24. Sharmin S, Alamgir F, Fahmida, Saleh AA. Antimicrobial sensitivity pattern of uropathogens in children. *Bangladesh J Med Microbiol.* 2009;03(1):18-22
25. Arabi FMZ, Banazadehi A. Prevalence and antimicrobial susceptibility patterns of uropathogens among patients referring to valieasr laboratory in Najafabad, Isfahan. *Iran Mid East J Sci Res.* 2013;13:85-90
26. Ghorbani A, Ehsanpour A, Roshanzamir N, Omidvar B. Alterations in antibiotic susceptibility of urinary tract infection pathogens. *J Nephropathol.* 2012;1(1):43-8
27. Khoshbakt R, Salimi A, Aski HS, Keshavazi H. Antibiotic susceptibility of bacterial strains isolated from urinary tract infections in Karaj, Iran. *Jundishapur J Microbiol.* 2012;6(1):86-90
28. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *Br Med J* 2010;340:2096.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

- Khan HA:** Study design, discussion, Manuscript writing.
- Yousaf SUM:** Concept, critical review Analysis, interpretation.
- Rashid A:** Bibliography.
- Abbas G:** Literature search .
- Shah BM:** Bibliography.
- Khan Z:** Statistical Analysis.
- Ali S:** Case collection.
- Arif U:** Case collection.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.