

Original Research Article

Comparison of empirical antibiotics used with microbiological sensitivity pattern among patients admitted with urinary tract infection

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ABSTRACT

Background: Symptomatic urinary tract infection (UTI) is among the most common infection described in hospital settings. This study compares common empirical antibiotics used with their clinical outcomes and microbiological sensitivity pattern among patients admitted with UTI in a tertiary care hospital.

Methods: It was a cross sectional study conducted in inpatients of a tertiary care hospital, in south Kerala. Those patients satisfying the inclusion criteria was recruited into the study after obtaining informed consent. Symptoms on the day of admission was assessed using the questionnaire for clinical profile. Primary outcome was matching of empirical antibiotics with culture and sensitivity pattern. Secondary outcomes were symptom resolution on third day with empirical antibiotics and profile organisms causing UTI.

Results: Out of 106 patients there were 47 males, 59 females. Sixty were above 61 years of age. Most common antibiotic used was piperacillin + tazobactam (47%) followed by ceftriaxone (45%). Empirical antibiotics matched with culture and sensitivity in 75% of subjects. Most common isolated organisms were *E. coli* (61%) and *Klebsiella pneumoniae* (15%). When matched empirical antibiotics were used, symptoms of dysuria, urinary frequency, urgency, abdominal pain and lower back pain resolved in 97%, 94%, 86%, 96%, 96% cases respectively.

Conclusions: Symptomatic resolution occurred in majority of cases where the empirical antibiotic was sensitive than compared to resistant case. As the agreement with empirical antibiotics became low, hospital antibiotic policies must reviewed and change according to resistance pattern and type of organism that is locally prevalent.

Keywords: Antibiotic resistance, Empirical antibiotics, Microbiological sensitivity, Urinary tract infection

INTRODUCTION

Urinary tract infections (UTIs) considered as severe public health problem and are caused by a range of pathogens, but most commonly by *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus faecalis* and *Staphylococcus saprophyticus*.¹ High recurrence rates and increasing antimicrobial resistance among uropathogens threaten to greatly increase the economic burden of these infections. UTIs encompass infections of the urethra (urethritis), bladder (cystitis), ureters (ureteritis), and kidney (pyelonephritis).² The incidence of cystitis is significantly higher in women than

men, likely the result of anatomic differences.² Clinically, UTIs are categorized as uncomplicated or complicated. Uncomplicated UTIs typically affect individuals who are otherwise healthy and have no structural or neurological urinary tract abnormalities.^{3,4} Urinary infections are also differentiated into lower UTIs (cystitis) and upper UTIs (pyelonephritis).^{3,4} Several risk factors are associated with cystitis, including female gender, a prior UTI, sexual activity, vaginal infection, diabetes, obesity and genetic susceptibility.^{3,4}

Patients suffering from a symptomatic UTI are commonly treated with antibiotics; these treatments can

result in long-term alteration of the normal micro-biota of the vagina and gastrointestinal tract and in the development of multidrug-resistant microorganisms. Also inappropriate use of antibiotics initiated before the laboratory results of urine culture contribute to increasing resistance to antibiotics in uropathogens. Awareness of the disease, knowledge of the spectrum of antibiotics and common complication of UTI will help to reduce morbidity and mortality. The use of appropriate empirical antibiotics will reduce treatment duration and hospital stay, improves symptom resolution, reduce incidence of antibiotic resistance and economic burden for patients. This was a cross sectional study that compares matching empirical antibiotics, their clinical outcome and microbiological sensitivity pattern.

METHODS

This was a cross sectional study conducted in inpatients of tertiary health facility from January 2017 to June 2018 in South Kerala. Assuming 50% of organism will show sensitivity to empirical antibiotic therapy with a relative precision of 20% and alpha error of 5%, sample size was calculated as 100.

Inclusion criteria

Subjects aged above 18 years of age presenting with symptoms of lower urinary tract infection with urine culture showing growth and willing to participate in study. Symptoms of lower urinary tract infection are dysuria, urinary urgency, urinary frequency, low back ache and abdominal pain.⁵⁻⁷

Exclusion criteria

Patients who were catheterized or underwent urinary procedures in last two weeks or known urinary tract abnormality was excluded from study.

After a written and informed consent obtained from the patient, required details were recorded in the proforma. A questionnaire which includes details regarding patient’s clinical profile, symptoms related to urinary infection, results of sensitivity was used in the study.

Patients satisfying inclusion criteria were approached to recruit into study. The nature of the study was well explained to them and written consent was obtained. Those giving consent were included into study. Cases with urine culture showing growth were given questionnaires detailing symptoms on first day of therapy and third day of therapy. Endpoint for study was comparison of agreement in antibiotics between empirical treatment and sensitivity from urine culture sensitivity report, symptom resolution on third day with empirical antibiotic treatment and profile of organisms causing UTI.

The data entry was done on MS excel and analysed using SPSS version 20. Categorical variables were expressed as

frequency and percentages and the mean (SD) was found for continuous variables. Percentage of samples having agreement between empirical antibiotics and culture and sensitivity pattern was found by Wilcoxon Signed Rank Test and chi square tests. Test of significance was applied for gauge differences between the groups.

RESULTS

Total of 106 inpatients were recruited into study. There were 47 males and 59 females. 7 were aged between 21-40 years of age, 60 belonged to the age group 61-80. 76 subjects were diabetic. Out of 47 males 26 patients had prostatomegaly. The most common empirical antibiotics used was piperacillin tazobactam (50) followed by ceftriaxone (48), levofloxacin (3), Meropenam (2), Nitrofurantoin (1) (Figure 1). Out of 106 patients 79 patient received empirical antibiotics that is matched by microbiological sensitivity pattern (Figure 2).

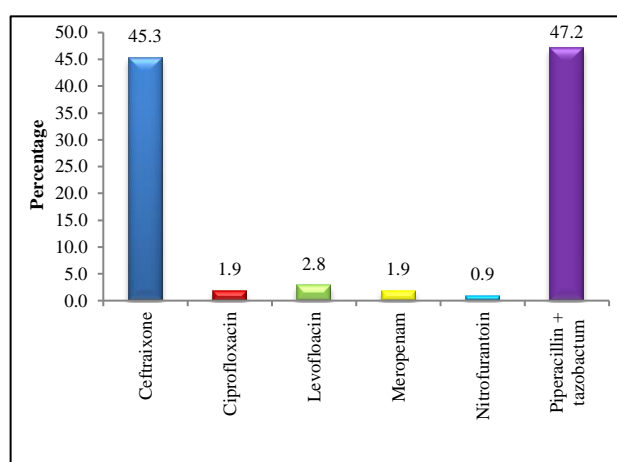


Figure 1: Percentage distribution of the sample according to empirical antibiotic use.

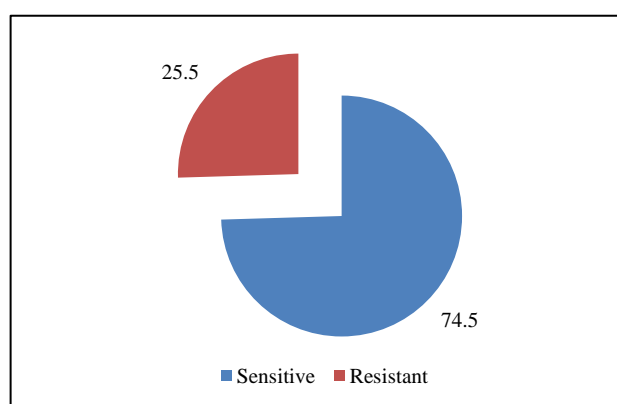


Figure 2: Percentage distribution of Sensitivity pattern in urine culture among patients admitted with Urinary tract infection.

The most common organism causing UTI in the present study was *E. coli* (65) followed by *Kleibseilla pneumonia* (16), *Pseudomonas* (6), *Enterobacter specius* (4),

Staphylococci (3), *Proteus mirabilis* (3) *Enterococcus faecium* (2), *Enterococcal faecalis* (2), *Citrobacter* (2), *Streptococcus agalactiae*, nonfermenting rods (1) and yeast like organism (1) (Table 1).

During the time of hospital admission 104 had dysuria, 89 had increased frequency of micturation, 79 had urgency, 64 had abdominal pain and 37 had back pain. With sensitive empirical antibiotic therapy there was substantial reduction in symptoms of dysuria (75 versus 8, p value <0.01), urinary frequency (63 versus 6, p value <0.01), urinary urgency (48 versus 6, p value <0.01), abdominal pain (42 versus 13, p value <0.01), back pain (30 versus 13, p value <0.01) for the patients when compared with resistant antibiotic at 3rd day of admission (Table 2). Twenty eight patients had ESBL positive microbial urinary infection and two had carbapenamase positive microbial infection.

Table 1: Percentage distribution of the sample according to organism.

Organism	Frequency	Percent
<i>Escherichia coli</i>	65	61.3
<i>Staphylococcus aureus</i>	3	2.8
<i>Enterococcus faecium</i>	2	1.9
<i>Enterobacter species</i>	4	3.8
<i>Klebsiella pneumonia</i>	16	15.1
Yeast like organism	1	0.9
<i>Citrobacter species</i>	2	1.9
<i>Proteus mirabilis</i>	3	2.8
Non fermenting gram negative rods	1	0.9
<i>Enterococcus faecalis</i>	2	1.9
<i>Pseudomonas aeruginosa</i>	6	5.7
<i>Streptococcus agalactiae</i>	1	0.9

Table 2: Empirical therapy and symptom at day 1 and day 3 of admission.

Symptom	Culture	Days	Yes		No		Z [#]	P value
			Frequency	Percent	Frequency	Percent		
Dysuria	Sensitive	Day 1	77	97.5	2	2.5	8.66	<0.01
		Day 3	2	2.5	77	97.5		
	Resistant	Day 1	27	100	0	0	2.83	0.005
		Day 3	19	70.4	8	29.6		
Frequency of micturition	Sensitive	Day 1	67	84.8	12	15.2	7.94	<0.01
		Day 3	4	5.1	75	94.9		
	Resistant	Day 1	22	81.5	5	18.5	2.45	0.014
		Day 3	16	59.3	11	40.7		
Urgency	Sensitive	Day 1	59	74.7	20	25.3	6.93	<0.01
		Day 3	11	13.9	68	86.1		
	Resistant	Day 1	20	74.1	7	25.9	2.45	0.014
		Day 3	14	51.9	13	48.1		
Abdominal pain	Sensitive	Day 1	45	57	34	43	6.48	<0.01
		Day 3	3	3.8	76	96.2		
	Resistant	Day 1	19	70.4	8	29.6	3.61	<0.01
		Day 3	6	22.2	21	77.8		
Back pain	Sensitive	Day 1	33	41.8	46	58.2	5.48	<0.01
		Day 3	3	3.8	76	96.2		
	Resistant	Day 1	17	63	10	37	3.61	<0.01
		Day 3	4	14.8	23	85.2		

[#]Wilcoxon Signed Rank Test

DISCUSSION

In the present study majority of the patient belonged to more than 65 age. As the age increases incidence of UTI also increases. Presence of multiple co morbidities is pointed out as one of the reason. UTI is also common in young reproductive female. Theras et al concluded that UTI is the most frequently diagnosed infection in long-term care residents, accounting for over a third of all nursing home-associated infections.⁸⁻¹⁰ It is second only

to respiratory infections in hospitalized patients and community-dwelling adults over the age of 65 years.^{10,11} As our population ages, the burden of UTI in older adults is expected to grow, making the need for improvement in diagnostic, management and prevention strategies critical to improving the health of older adults.¹¹ In the present study female are more than male. Even though UTI is most common in young female, incidence of male and female UTI is almost equal after the age of 65.⁸ Since majority of patient belonged to older age group present study is in line with previous literatures.

Majority of patient belonged to diabetic group. In our study resistant organisms grow in diabetic population, of total 28 resistant samples 20 cases (72 percent) belong to the diabetics. Study also showed increase in resistance among non-diabetics, this may be due to the fact that majority of patients belonged old age i.e. >60 years, and had other co morbidities other than diabetics like prostatomegaly. Ours being tertiary care centre majority of inpatient admission had history recurrent UTI which was not assessed by the study.

About 62 million adults are affected by diabetes in India.¹² Mean age for adult diabetes in India is 42.5 years.¹² Nitzan et al found out that urinary tract infections are more common, more severe, and carry worse outcomes in patients with type 2 diabetes mellitus, mostly by resistant pathogens.¹³ Various impairments in the immune system, poor metabolic control, and incomplete bladder emptying due to autonomic neuropathy may all contribute to the enhanced risk of urinary tract infections in these patients.¹³ Symptoms of urinary tract infection are similar to patients without diabetes, though some patients with diabetic neuropathy may have altered clinical signs.¹³

The most common antibiotic used in the present study as empirical antibiotic was piperacillin tazobactam followed by ceftriaxone and quinolones. Reasons of using much higher antibiotics are considered as ours being a tertiary care centre and majority cases admitted in the hospital represents complicated UTI which require broad spectrum antibiotics. Second recurrent UTI in setting of diabetes and resistant organism is being common, physicians being forced to use higher generation antibiotics. Even with the use of these antibiotics there was only 75 percent agreement with empirical antibiotics with incidence of resistant organism getting high in the field. For complicated UTI empirical antibiotics ranges from oral nitrofurantoin, fosfomycin, gentamycin, piperacillin tazobactam, carbapenams or polymixin antibiotics based on patient condition.¹⁴ The antibiotics of choice of uncomplicated UTI are oral cotrimoxazole, nitrofurantoin, ciprofloxacin and beta lactams. Wilbur et al studied ceftriaxone a third generation cephalosporin antibiotics with ertapenam a carbapenam antibiotic for complicated UTI found out that both almost same efficacy in obtaining a favourable microbiological response, but on combined analysis ertapenam was more superior to ceftriaxone.¹⁵

Most common etiological agent found out in the present study was *E. coli* followed by *Klebsiella pneumoniae*, *Pseudomonas*, *Staphylococci* and other gram negative organisms. This was consistent with previous studies. The most common type of resistant encountered in the study was extended spectrum beta lactamase (ESBL). The most common organism producing the same was *E. coli*.^{16,17} A survey done on uncomplicated UTI, most common pathogenic bacteria was found out to be *E. coli*,

Klebsiella and third was variable during different seasons.^{16,17}

Symptomatic relief of UTI with antibiotics may occur. General consensus is that with sensitive antibiotic complete symptom resolution starts by 3rd day therapy. Even though many cases may take up to 7 days to respond.⁷ In our study we have observed that symptom resolution had occurred even with empirical therapy resistant cases. The cause of which may be attributed to the in vivo sensitivity of these agents in UTI. When broad spectrum antibiotics were used as empirical therapy, had better agreement with microbiological culture sensitivity and also had a better symptom resolution.

Study had its limitations with few sample size. It also does not take account of other medications like NSAIDs given for symptomatic relief. It also did not differentiated recurrent UTIs with multiple antibiotic therapy history in the past. Study also didn't quantify the severity of the infection the patient had.

CONCLUSION

Study concludes empirical broad spectrum antibiotics had easy resolution of symptoms and had better agreement with microbiological sensitivity pattern. After the age of 60 incidence of urinary infection is almost equal in male and female. It also concluded resistance organism were more prevalent in diabetic population which is in line with previous studies. The most common organism causing urinary infection is *E. coli*. It should be noted that when agreement with empirical antibiotic and microbiological sensitivity becomes low, hospital antibiotic policies must be reviewed and change according to resistance pattern and type of organism that is locally prevalent.

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