

A Cross Sectional Study on Distribution of Urinary Tract Infection and Their Antibiotic Utilisation Pattern In Kerala

Arul Prakasam K.C.^{1*}, K. G. Dileesh Kumar¹, M. Vijayan²,

¹ Department of Pharmacy Practice, JKKMMRF's Annai Sampoorani Ammal College of pharmacy, B. Komarapalayam, Namakkal District, Tamil Nadu, India -638183.

² Assistant Surgeon and Medical Officer, CHC Cheruvadi, Calicut district, Kerala, India -673661.

*Corres. Author : kcarul2000@gmail.com
Mobile No.: +919842778531

Abstract: Urinary tract infection is the one of the most common bacterial infection in humans and a major cause of morbidity. It is also a common reason for outpatients consults. However the etiology of UTI and their antibiotic sensitivity pattern vary from time to time and across different areas. The objective of the study was to determine the distribution, clinical, laboratory profile and antibiotic utilization pattern. It is a cross sectional hospital based study conducted on 200 outpatients with symptoms of UTI for a period of 6 months. This study shows that young married females (65%) are more prone to the risk of UTI. Complicated UTI is more common in males. *E. coli*, the predominant organism isolated shows maximum susceptibility to meropenem and amikacin. Diabetes mellitus appears to be predominant risk factor of UTI in our study. The risk of acquiring UTI in diabetic subjects significantly increases in long standing diabetes, male gender and with poor glycemic control. Dysuria and fever are the most common clinical manifestation. Ciprofloxacin is the most commonly prescribed antibiotic for general population and amoxicillin in pregnant females. The diagnosis is mainly based on clinical presentation and rarely confirmed by culture and sensitivity. The isolated organism shows resistance towards commonly used antibiotics (fluoroquinolones and cephalosporins) which may be due to indiscriminate prescription and lack of patient's compliance.

Key Words: Urinary tract infection, drug utilization, antibiotic susceptibility, *E. coli*.

INTRODUCTION

Urinary tract infection is caused by pathogenic invasion of the urinary tract which leads to an inflammatory response of the urothelium. The clinical manifestation of UTI depend upon the portion of the urinary tract involved, the etiologic organism, the severity of the infection and patients ability to mount an immune responds to it¹. Signs

and symptoms include fever, dysuria, and urinary urgency, cloudy or malodorous urine.

UTI is an extremely common condition that occurs in both male and female of all the ages. The prevalence and incidence of UTI is higher in women than in men due to several clinical factors including anatomic differences, hormonal effects and behavioral pattern. Malnutrition, poor hygiene, low socioeconomic status are associated with UTI and

these factors are rife in rural settings². Complicated UTI is defined as that which occurs in patients with anatomically abnormal urinary tract or significant medical or surgical co morbidities³. UTIs are a common burden in patients with diabetes mellitus. Cystitis, ascending infection leading to pyelonephritis, impaired leucocyte function, recurrent vaginitis, emphysematous complications and renal/perinephric abscesses are well recognized in this group of patients if glycemic control is poor⁴. Infections particularly in pregnancies and in the elderly can be asymptomatic, but asymptomatic bacteriuria is associated with an increased risk of intrauterine growth retardation and low birth weight babies. Furthermore, untreated asymptomatic bacteriuria leads to development of cystitis in approximately 30% of cases, and can lead to the development of pyelonephritis in about 50% of cases. Thus it is important to identify and treat UTI to avoid such complication⁵.

Any impediment to the free flow of urine – tumor, stricture, stone, prostatic hypertrophy results in hydronephrosis and greatly increases the risk of UTI. Infection superimposed on urinary tract obstruction may lead to rapid destruction of renal tissue. It is of utmost importance, therefore when infection is present, to identify and repair obstructive lesions. A large prospective study of sexually active young women showed that recent sexual intercourse, use of diaphragm with spermicide and alteration of vaginal flora by OCP use was strong risk factors for UTI development. Bacteriuria develops in at least 10-15% of hospitalized patients with indwelling urethral catheters.

UTI is mostly caused by gram negative aerobic bacilli found in GI tract. Included in this family are the *E. coli*, *Klebsilla*, *Enterobactor*, *Citrobacter*, *Proteus and serratia species*. Other common pathogens include *Staphylococcus epidermidis*, *Staphylococcus saprophyticus* and *Enterococcus species* which presumably result in UTI following colonization of the vagina or perianal skin. Less common organism such as *Gardenella vaginalis*, *Mycoplasma species* and *Ureaplasma urealyticum* may infect patients with intermittent or indwelling catheters⁶.

Therapeutic decision should be based on accurate and up-to-date antimicrobial susceptibility. The antibiotic drugs which have been used for the treatment of the UTI include penicillins, cotrimoxazole, older quinolones such as nalidixic acid and cephalosporins. Newer fluorinated quinolone (ofloxacin, ciprofloxacin), gentamicin, amikacin and imipenem demonstrated excellent effectiveness against the organisms, but are best reserved for treatment failures and more complicated

infections since overuse of these agents can lead to resistance. The present study was undertaken to retrospectively identifying the common pathogens and drug sensitivity pattern of the isolate among patients who attended the outpatients department so as to guide empirical treatment.

The aim is to study the distribution of UTI and their antibiotic utilization pattern. The objectives are the study of age and gender wise distribution of UTI, study of major symptoms and predisposing factors, evaluation of uropathogens and their antibiotic sensitivity and resistance pattern and to study the pattern of empirical antibiotic therapy.

MATERIAL AND METHODS

This was a hospital based descriptive cross sectional study conducted in the out patients department of a community health centre, Calicut, Kerala a period August 2011 – January 2012. All symptomatic lower urinary tract infection in adult males and females of age group 18-70 years is included in this study. Catheter associated (nosocomial) UTI, pediatric UTI, UTI in chronic debilitated (bedridden) patients and asymptomatic UTI are excluded from this study.

All the necessary and relevant information are collected from prescription, laboratory reports and interviewing the patients in a suitable date collection form. The data analyzed by using SPSS version 16.1. Descriptive results were expressed as frequency and percentage. Pearson chi square test was used to test for significant correlation. P value < 0.05 were accepted as statistically significant.

RESULTS

Out of 200 patients, female patients were 130 (65%) and male were 70 (35%). The incidence of UTI in male patients was more in patients with age group of 51-60 (54.28%) and least in the age group of 21-30 (10%). There was no incidence of UTI in the age group of 31-40 in male patients. Among female patients higher prevalence observed in the age group of 31-40 (27.5%) and 51-60 (26.5%). Among 200 patients 73.5% are married, 36% belongs to middle class family (1000-5000 Rs/month), 26.5% belong to low class (<1000 Rs/month).

Out of 200 patients 64% have complicated UTI, while 36% have uncomplicated UTI. Among 70 males 60 (85.7%) have risk factors predisposing to UTI ($p=0.000$). Among 130 females 47.7% presented with uncomplicated UTI and remaining 68 (52.3%) have risk factors. Among males 53.6% are smokers, 34.3% have diabetes ($p=0.001$), 17.1% have BPH, 15.7% had recurrent UTI and 7% was suffering from nephrolithiasis ($p=0.012$). Among

females 17.7% have recurrent UTI, 16.2% are pregnant, 16.2% are users of OCP/IUCD, 13.8% have diabetes, 13.1% are postmenopausal ladies and 0.8% had renal stone shown in the Figure: 1. Among pregnant ladies 2nd trimester (61.9%) was more prone to the risk of UTI followed by 1st trimester (23.8%). Incidence of UTI in 3rd trimester is only 14.28%. Thus among 200 patients diabetes mellitus (21%) was the predominant risk factors and renal stone (3%) was the least common risk factors as shown in Figure: 1. Among 42 diabetic subjects UTI is more prevalent in long standing cases (64.28%). 59.52% had poor glycemic control, this composed of 17 males and 8 females. Thus UTI is more prevalent in male patients with long standing diabetes and poor glycemic control shown in the Table: 1.

Among 200 patients the 68% presented with dysuria, 60.5% with fever, 46.5% with urgency and 29% with lower abdominal pain. Foul smelling urine, rigor and haematuria present in <5% patients. Among 200 patients only 153 (76.5%) patients done urine analysis, out of these only 44.4% had significant pyuria, 55.5% had insignificant pyuria and remaining 4.5% had haematuria explained in the Table: 2. No correlation is found between sex and pyuria ($p=0.621$). Disappointingly only 36 (18%) confirmed by urine culture and sensitivity. Out of 31 positive culture results 19 from females and 12 from males. 3 patients report negative culture, but no correlation is found between culture positivity and gender ($p=0.325$). Among 31 positive culture cases 96.7% isolates are gram negative, which composed of 83.9% *E.coli*, 9.7% *Klebsiella* and 3.2% *Proteus*. Only 3.2% isolates are gram positive *Staphylococcus saprophyticus* shown in the Figure: 2. Among 31 culture positive cases 25.8% had insignificant bacteriuria and 74% had significant bacteriuria. Out of 26 *E.coli* isolates, 24 (92.3%) are sensitive to meropenem, 15 (57.69%) to amikacin, 11 (42.3%) to gentamicin, 8 (30.76%) to cefotaxim, 6 (23.07%) to ciprofloxacin and norfloxacin and 4 (15.38%) to cotrimoxazole. Out of 26 *E.coli* isolates, 76.9% resistant to cefotaxim, 61.5% to ciprofloxacin, 57.69% to norfloxacin, 53.84% to gentamicin

19.23% to amikacin 26.9% to cotrimoxazole and zero resistance to meropenem. The sensitive antibiotic to *Klebsiella* isolates are meropenem (100%), gentamicin (66.6%), piperacillin tazobactam (66.6%), cefotaxim (33.3%) and ciprofloxacin (33.3%). *Proteus* is sensitive to gentamicin and *Staphylococcus saprophyticus* is sensitive to cotrimoxazole shown in the Figure: 3. *Proteus* shows 100% resistance to ciprofloxacin and norfloxacin. *Staphylococcus* shows resistance to gentamicin. The resistant antibiotics for *Klebsiella* isolates are norfloxacin (100%), amikacin (100%), cefotaxim (66.6%), ciprofloxacin (66.6%), gentamicin and cotrimoxazole (33.33%).

Among 200 patients, 147 (73.5%) are prescribed with fluoroquinolones followed by cotrimoxazole (9.5%), cephalosporin (8.5%), penicillin (6.5%), aminoglycoside (1%) and nitrofurantoin (1%). Overall uses of antibiotics are as follows. 63 (31.5%) were prescribed with ciprofloxacin, 22.5% with norfloxacin, 19.5% with ofloxacin, 9.5% with cotrimoxazole, 5.5% with cefadroxil, 3.5% with amoxicillin, 3% with ampicillin, 2% with cefixim, 1% with gentamicin and 1% with cephalixin explained in the Table: 3. Among pregnant ladies 7 (33.3%) were treated with amoxicillin, 6 (28.5%) with ampicillin, 5 (23.8%) with cefadroxil, 2 (9.5%) with nitrofurantoin and remaining 1 (4.8%) were prescribed with cefixim. 99% of patients received oral antibiotics while 1% with parenteral antibiotics. Generally the duration of empirical antibiotic therapy is seven days (66%) followed by five days (28.5%). In our study majority of patients receive non antibiotic supportive treatment such as paracetamol (80%), mefenamic acid (15%), diclofenac sodium (5%), phenazopyridine (17%) and disodium hydrogen citrate (28.5%).

Among 200 patients, 68% lost to follow up, 15% not respond to empirical antibiotic, 3.5% had relapse UTI and 13.5% patients are completely cured both symptomatically and urine analysis shown in the Table: 4.

Table 1: Glycemic control and UTI

Glycemic status	No. males (%) N=24	No. of females (%) N=18
Good glycemic control	7(16.7%)	10(23.80%)
Poor glycemic control	17(40.47%)	8(19.04%)

Table 2: Urine analysis:

Urine report	No. Of patients (%)
Significant pyuria	68(44.4%)
Insignificant pyuria	85(55.5%)
Haematuria	7(4.57%)

Figure 1: Distribution of predisposing factors:

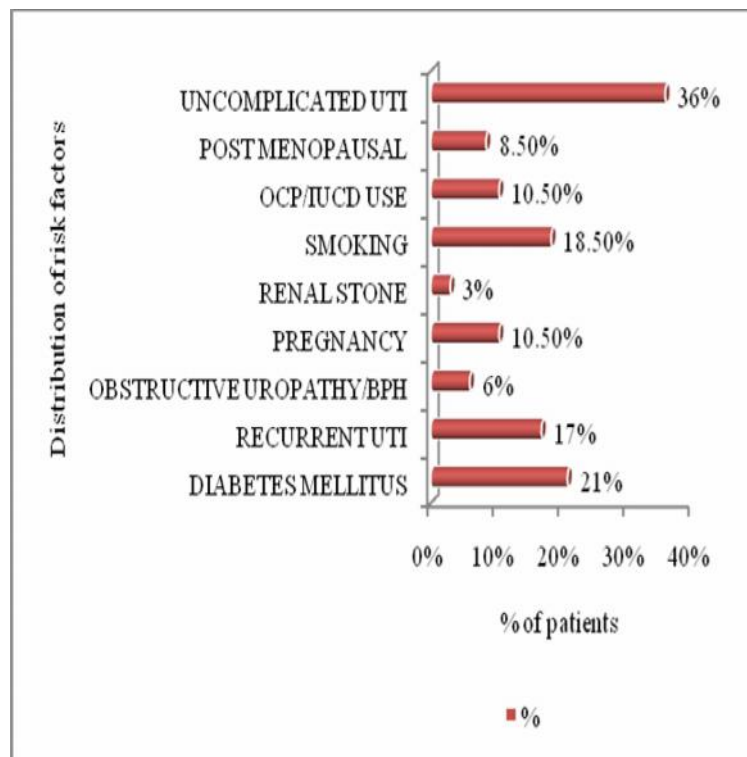


Table 3: Overall use of antibiotics:

Antibiotic	Total no. Prescribed (%) N=200
Ampicillin	6(3.0%)
Amoxicillin	7(3.5%)
Ciprofloxacin	63(31.5%)
Norfloxacin	45(22.5%)
Ofloxacin	39(19.5%)
Gentamicin	2(1.0%)
Cotrimoxazole	19(9.5%)
Cefadroxil	11(5.5%)
Cephalexin	2(1.0%)
Cefixime	4(2.0%)
Nitrofurantoin	2(1.0%)

Table 4: Disposition on follow-up

Disposition	No. of males (%) N=70	No. of females (%) N=130
Completely cured	12(6%)	15(7.5%)
Relapse UTI	3(1.5%)	4(2%)
Not respond to empirical antibiotic	12(6%)	18(9%)
Lost to follow up	43(21.5%)	93(46.5%)

Figure 2: Organism obtained from urine culture

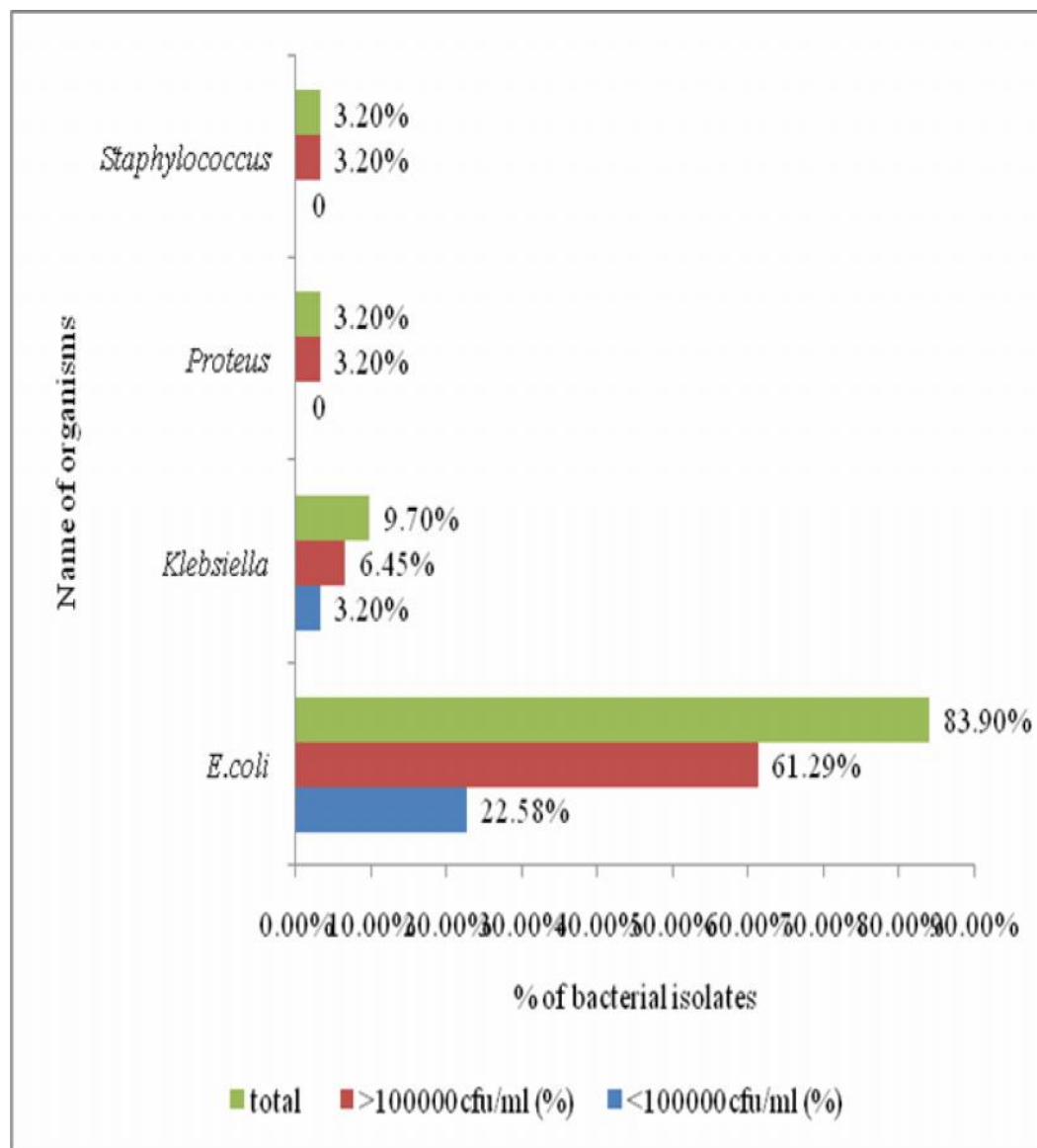
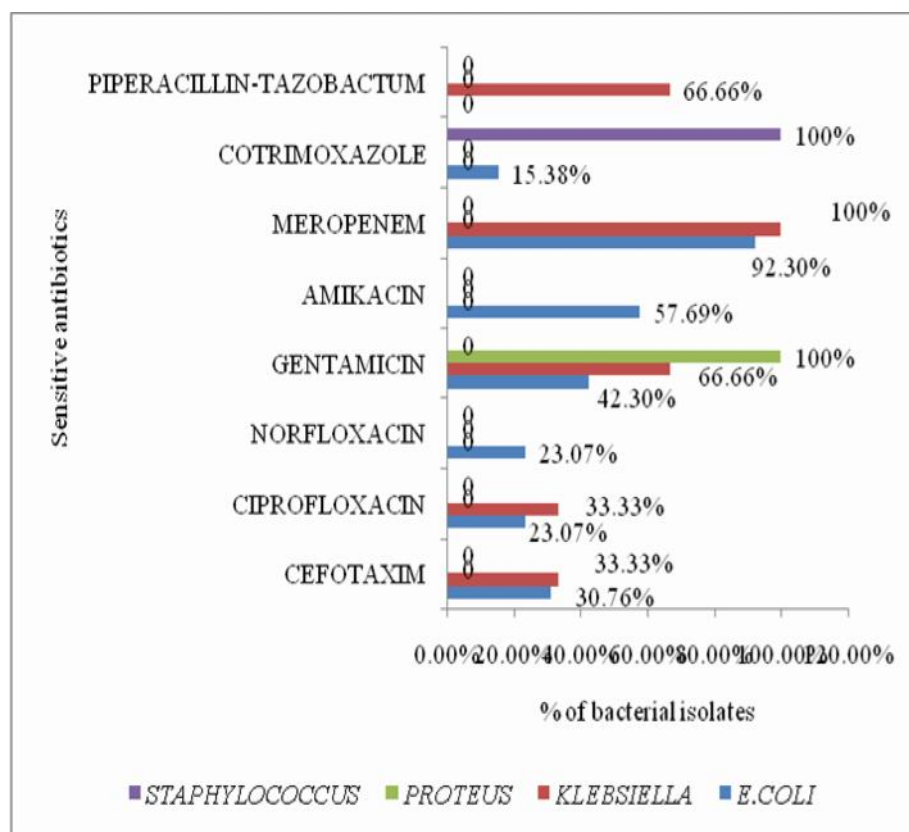


Figure 3: Antibiotic susceptibility pattern of bacterial isolates:

DISCUSSION

The study observes that the prevalence of UTI was high among the females (65%) than males (35%). Among females highest prevalence is seen in reproductive age group, 21-30 (23%), and 31-40 (42%). Close proximity to female urethral meatus to anus, shorter urethra and sexual intercourse have been reported as factors that influences this higher prevalence in women. Among males an increased prevalence of UTI was recorded among the elderly age group, 51-60 (54.28%), and 41-50 (22.85%) than among young age patients (10%). Increasing frequency of prostate disease in males and diabetes mellitus are responsible for increasing the incidence of UTI in elderly patients³. Our study shows that higher prevalence of UTI among married individual (73.5%) than unmarried (15.5%). Betsy Foxman, 1999 found a clear association between frequent sexual intercourse, use of OCP/IUCD and UTI. Our study observes that majority of UTI patients belongs to low (26.5%) and middle (36%) class family. Malnutrition, poor hygiene, low socioeconomic status are associated with UTI and these factors are rife in rural setting².

Our study observes that high prevalence of complicated UTI in males (85.7%) compared to females (68/130, 52.3%) and it is statistically significant ($p=0.000$). This is in agreement with results obtained by Mahesh E. et.al 2010. Of the total 128 (64%) cases of complicated UTI, diabetes mellitus (21%) was the most common risk factor. A statistically significant association is found between male gender (34.3%) and UTI among diabetic subjects ($p=0.001$). UTI in diabetic patients is more prevalent with long standing (>5 year) diabetes (64.3%) and with poor glyceemic control (59.5%). This result is in agreement with other reports which showed that UTI is more common in diabetic male patients with poor glyceemic control⁷. Among males smoking appears to be the predominant risk factors followed by diabetes (34.3%) and BPH (17.1%). Renal stone (7.1%) is the least common risk factor in males. But a statistically significant correlation exist between male gender and nephrolithiasis ($p=0.012$). Smoking alters the normal physiology of urinary tract and predispose to recurrent UTI. Among young females recurrent UTI (17.7%) is the most common risk factors followed by OCP/IUCD use and pregnancy (16.2%). No significant correlation is found between female gender and recurrent UTI ($p=0.722$). Various researchers found

a significant association between IUCD use and UTI. Among elderly ladies diabetes and post menopausal estrogen deficiency were found to be the major risk factors. Our study observes that 2nd trimester is more prone to the risk of UTI followed by 1st trimester.

The diagnosis of UTI is based on the clinical presentation of the patients it often time supported by urine analysis and rarely confirmed by urine culture and sensitivity. Dysuria (68%) and fever (60.5%) were the most common symptoms of UTI in the present study as with similar studies worldwide. Only 153 patients had done urine analysis and a mere 44.4% had significant pyuria. Disappointingly only 36 (18%) had done urine culture and 23 were confirmed to have significant bacteriuria. Out of 36 samples, 31 are positive for bacterial growth. The gram negative bacilli constituted 96.7% of bacterial isolates implicated in UTI cases. *E.coli* (83.8%) was the most prevalent bacterial agent causing UTI. *Klebsiella species* (9.6%) was the next common isolate obtained⁷. *E. coli* shows very high susceptibility to meropenem (92.3%) followed by amikacin (57.6%) and gentamicin (42.3%). *E.coli* shows poor susceptibility to fluoroquinolones (23.07%), cotrimoxazole (15.38%) and cefotaxime (30%).

All the UTI suspects were treated with empirical antibiotics. Fluoroquinolones are the most widely prescribed antibiotics for the empirical therapy of UTI followed by cotrimoxazole, cephalosporins and penicillin. Nitrofurantoin and gentamicin are the least commonly used antibiotics for community acquired UTI. Among fluoroquinolones ciprofloxacin and norfloxacin are preferred than ofloxacin. In pregnancy amoxicillin, ampicillin and cefadroxil are the most preferred antibiotics in decreasing order. A. M. Al Haddad, 2005 states that

amoxicillin, ampicillin and cephalosporin are the safe antibiotics that can be used in UTI in pregnancy. Among 200 subjects 68% did not come back for a follow up⁸. 15% (30/200) of the patients not respond to empirical antibiotic therapy. 13.5% reported symptomatic relief and remaining 3.5% complaint of relapse UTI. The high resistance of *E.coli* to commonly used antibiotics may be due to poor patient compliance, indiscriminate prescription and high prevalence of ESBL producing organism causing complicated UTI.

CONCLUSION

To conclude the prevalence rate of uncomplicated UTI in general practice is high among young females in reproductive age groups. Complicated UTI is more common in extremes of age in both males and females. Predominant risk factors to complicated UTI include diabetes mellitus, BPH, and recurrent UTI. OCP/IUCD use pregnancy and sexual activity are the risk factors in young females. 2nd trimester is more prone to the risk of UTI among pregnant ladies. *E. coli* was found to be the most common cause of UTI in all age groups. This isolates shows resistance to commonly used antibiotics and susceptible only to injectable antibiotics. Fluoroquinolones (ciprofloxacin) is the most widely prescribed antibiotic for general population and amoxicillin is the major antibiotics used for pregnant ladies. In our settings, only low percentage of patients comes back for a follow up. Relapse UTI and treatment failure are the major problem encountered in the management. More over the study concludes that *E. coli* and other isolates were more sensitive to meropenem and amikacin compared to other antibiotics tested and therefore these may be the drug of choice for complicated urinary tract infections.

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