

Full Length Research Paper

Bacterial profile and drug susceptibility pattern of urinary tract infection in pregnant women with ureteral stones and hydronephrosis

Murat Atar^{1*}, Yasar Bozkurt¹, Ahmet Ali Sancaktutar¹, Haluk Soylemez¹, Necmettin Penbegul¹, Muhammet Erdal Sak², Recep Tekin³, Mehmet Nuri Bodakci¹ and Namik Kemal Hatipoglu¹

¹Department of Urology, University of Dicle, Diyarbakir, Turkey.

²Department of Obstetrics and Gynecology, University of Dicle, Diyarbakir, Turkey.

³Department of Infectious Diseases, University of Dicle, Diyarbakir, Turkey.

Accepted 28 February, 2012

The aim of this study is to identify bacterial agents and their antibiotic susceptibility patterns isolated from pregnant women with symptomatic ureterolithiasis. Seventeen patients who had proven ureteral stones, positive urine cultures and underwent intervention for ureterolithiasis treatment between January, 2008 to December, 2011 were included in this study. Bacteriuria was defined as accounts of 10^5 cfu/ml in urine culture. The mean age and gestational period was 24.5 years and 25.5 weeks. The major symptoms were renal colic, hematuria and fever-chills. The overall prevalence of urinary tract infection (UTI) in pregnancy with ureteral stones was 17/65 (26.2%). *Escherichia coli* are the most common etiological agent (64.7%), followed by *Klebsiella* and *Staphylococcus*. The rate of resistance of *E. coli* to amoxicillin-clavulanate, ampicillin, cefotaxime, ciprofloxacin, trimethoprim/sulfamethoxazol, ceftriaxone, piperacillin/tazobactam and imipenem were 50, 45.5, 100, 18, 36.4, 28.6, 36.4, 0%, respectively. The rate of resistance of *Klebsiella* to Ampicillin were 80% and Amoxicillin-Clavulanate, Cefazolin, Cefepime, Ceftazidim were 60%. There were no resistance of *Klebsiella* to ciprofloxacin, gentamicin, meropenem and amikacin. Significant bacteriuria was observed in these patients and we recommend urine cultures in all pregnant women with ureteral stones during pregnancy. Ceftriaxone is recommended for the patients who have UTI with ureteral stones during pregnancy because of its high specificity and sensitivity.

Key words: Pregnancy, urine culture, bacteriuria, antibiotic susceptibility.

INTRODUCTION

Asymptomatic bacteriuria is one of the most common infectious complications of pregnancy and the prevalence is between 2 to 8% of cases (Fiadjoe et al., 2010). Though, the prevalence is the same as in the non-pregnant women, there is a higher progression rate leading to pyelonephritis in 30% of pregnant women (Duarte et al., 2008). However, the prognosis is often good if there is prompt evaluation and immediate treatment (Fiadjoe et al., 2010). An inflammatory reaction

to a stone or infection can lead to pyuria so that coexisting urinary tract infection (UTI) must be evaluated. UTI is the most common nonobstetric complication of urolithiasis in pregnancy and treatment of UTI will prevent about 40% of pyelonephritis and a two-fold higher premature birth rate (Saidi et al., 2005). Several anatomical and physiological changes that occur during pregnancy affect the entire urinary tract. Mild hydronephrosis is accepted as a normal phenomenon and may be present in up to ninety percent of pregnancies (Goldfarb et al., 1989). Stones or many other obstruction factors may cause decompensation of ureteral function, progressing to symptomatic acute hydronephrosis (Puskar et al., 2001) which occurs in 3% of cases

*Corresponding author. E-mail: atarsmail@yahoo.com. Tel: 0090412248 8001. Fax: 0090412248 8523

(Rasmussen and Nielsen, 1988). After UTI, urolithiasis is the most common cause of urological-related abdominal pain in pregnancy (Charalambous et al., 2009). The incidence of urolithiasis in pregnancy has been reported, that is similar to normal population (Cheriachan et al., 2008; Fiadjoe et al., 2010). If acute hydronephrosis is not treated, it can progress to life-threatening infection which may endanger the life of mother and the fetus. Preterm birth, that is associated with renal colic is rare but may develop. Treatment modalities for urolithiasis during pregnancy range from conservative treatment to more invasive procedures (Cheriachan et al., 2008).

The aim of this study was to identify bacterial agents and their antibiotic susceptibility pattern isolated from pregnant women with symptomatic persistent hydronephrosis due to ureteral stones during pregnancy. As far as we know, this is the first study on the literature about this issue.

MATERIALS AND METHODS

In this retrospective study, we reviewed 65 cases of pregnant women, who had been treated due to ureteral stones and symptomatic persistent hydronephrosis during pregnancy in our center between January, 2008 and December, 2011. Hospital charts of the patients were retrospectively reviewed and patients' data including patient's age, presenting symptoms, diagnostic methods, previous urological interventions, grade of hydronephrosis, localization and size of stone and stage of pregnancy were recorded.

An obstetric physical examination and ultrasonography (US), was performed to all patients for determining gestational stage and excluding obstetric complications. The diagnosis of ureteral obstruction in pregnancy was made on the basis of the clinical presentation, presence of microscopic hematuria in urinalysis, and transabdominal USG. Routine laboratory investigations (complete blood count, urea and creatinine) were done.

Conservative treatment such as intravenous fluids and analgesics were given to all patients following admission to hospital. Second or third generation cephalosporines were given in cases with infection after urine culture collected. Significant bacteriuria was defined as urine specimen with one bacterial species isolated in counts of 10^5 colony forming units (cfu)/ml (Delzell et al., 2000) and microscopic pyuria was defined as white blood cells ≥ 10 mm³ in the uncentrifuged urine (Usta et al., 2011; Nicolle et al., 2005).

For bacterial cultures midstream, clean catch urine samples were collected from pregnant patients. The urine samples of the patients' preliminary diagnosis at urinary tract infections and the patient, who have leukocyte in urine were inoculated quantitatively onto 5% sheep blood agar and Eosin-Methylen Blue (EMB) agar (Merck KGaA, Darmstadt, Germany). Then, media plates were incubated aerobically at 37°C for 18 to 24 h. Isolates with urine cultures yielding growth of $\geq 10^5$ cfu/ml were included in this study. Identification and antimicrobial susceptibility testing of all isolates were performed by conventional methods and the BD Phoenix™ 100 (Becton Dickinson, MD, USA) fully automated microbiology system. Antimicrobial susceptibility testing results were confirmed with Kirby-Bauer's disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) interpretive breakpoint.

The patients who are pregnant above 18 years of age and at least 12 weeks of gestation with typical symptom of ureteral stones (renal colic, fever-chills- sweat, hematuria and pyuria), had

symptomatic persistent hydronephrosis during pregnancy, had positive results from urine culture (10^5 cfu/ml) before intervention, admitted to hospital with suspected ureteral stones and without antibiotic treatment for any reason were included to study. Patients who did not meet all of the inclusion criteria and had negative results from urine culture were excluded from the study. Also, the patients who had no ureteral stones detected on USG findings or during URS procedure were excluded from the study.

URS was performed with a 9.5-F semi-rigid ureteroscope after confirming that the urinary tract infection was treated and the urinary culture was sterile. The calculi was fragmented with a holmium laser and then extracted with forceps. A JJ stent was applied to patients who had apparent edema of the ureter, large residual stones, stone impaction, or probable ureteral trauma during the URS procedure. The position of the JJ stent in the renal pelvis was confirmed by ureteroscopic examination or by US during the process. Fluoroscopic imaging modalities were not used. Under local anesthesia, the percutaneous nephrostomy (PCN) tube was inserted in the flank position with ultrasonographic guidance, and a JJ stent was inserted with a 22-F cystoscope. Fifteen days after operation and/ or postpartum, USG was repeated and the JJ stent was removed endoscopically if not required to remain.

RESULTS

Over a period of 4 years, positive urinary cultures were observed in 17 of 65 patients (26.2%) and were enrolled in the present study. The mean age of patients was 24.5 years (range 18 to 39), and the gestational period was 25.5 weeks (range 12 to 35). The mean CRP, sedimentation and WBC was 9.2 mg/dl, 71.1 and 13.6 K/UL, respectively. The patients' characteristics are listed in Table 1. The major symptoms were renal colic (100%), hematuria (100%), microscopic pyuria (88.2%) and fever-chills (64.7%).

E. coli was the most common pathogen (64.7%), followed by *Klebsiella pneumoniae* (29.4%) and *Staphylococcus haemolyticus* (5.9%). The rate of resistance of *E. coli* to amoxicillin-clavulanate, ampicillin, cefotaxime, ciprofloxacin, trimethoprim/ sulfamethoxazol, ceftriaxone, piperacillin/ tazobactam and imipenem were 50, 45.5, 100, 18, 36.4, 28.6, 36.4, 0%, respectively. The rate of resistance of *K. pneumoniae* to amoxicillin-clavulanate, ampicillin, cefazolin and cefepime were 60, 80, 60 and 60%, respectively. There were no resistance of *K. pneumoniae* to ciprofloxacin, gentamicin, imipenem, meropenem and amikacin. The *S. haemolyticus* (methicillin resistant, in one patient) was resistance to ampicillin, oxacillin, penisilin G, and it was sensitive to linezolid, rifampin, trimethoprim/sulfamethoxazol and vancomycin. The susceptibility to antimicrobial agents of pregnant's pathogens is shown in Table 2.

Thirteen patients had right side, 3 patients had left side and one patient had bilateral hydronephrosis. The US findings were diagnostic for obstructive ureteral calculi in 10 (58.8%) patients. In the remaining 7 patients, the URS procedure was used both for diagnosis and treatment. Under spinal anaesthesia, the URS procedure was performed to 10 patients, while under local anesthesia the JJ stent was inserted to 5 and PCN tube was inserted

Table 1. The data of the 17 pregnant patients with positive urine culture.

| Characteristic | Mean±SD (range) or N (%) |
|-------------------------------|--------------------------|
| Age (year) | 24.52±6.43 |
| Gestation (weeks) | 25.52±6.32 (12-35) |
| Number of pregnancy | 1.70±1.10 (1-4) |
| Stone diagnosed by USG | 10 (58.8) |
| Mean grade of hydronephrosis | 2.47±1.28 |
| Mean ESR | 71.14±29.08 |
| Mean CRP (mg/dl) | 9.17±15.26 |
| Mean WBC (K/UL) | 13.64±5.09 |
| Positive urine nitrite | 13 (76.5) |
| Mean serum creatinine (mg/dl) | 1.11±1.78 |
| Mean hematocrite (%) | 31.76±2.98 |
| Symptoms | |
| Pain and renal colic | 17 (100) |
| Fever, chills, sweat | 11 (64.7) |
| Hematuria | 17 (100) |
| Microscopic pyuria | 15 (88.2) |

USG: Ultrasonography, WBC: white blood count, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate.

Table 2. Resistance rates of isolated bacteria from positive urine culture to antibiotics.

| Antibiotics | <i>E. coli</i> , n = 11, % (Resistance/total) | <i>Klebsiella pneumonia</i> Spp. n = 5, % (Resistance/total) |
|------------------------------|---|--|
| Amikacin | 9 | 0 |
| Amoxicillin-Clavulanate | 50 (5/10) | 60 |
| Ampicilin | 45.5 | 80 |
| Cefazolin | 54.5 | 60 |
| Cefepime | 54.4 | 60 |
| Cefotaxime | 100 (4/4) | - |
| Cefuroxime | 28.6 (2/7) | 50 (2/4) |
| Cefoxitin | 10 (1/10) | 0 |
| Ceftriaxone | 28.6 (2/7) | 40 |
| Ceftazidime | 50 (5/10) | 60 |
| Ciprofloxacin | 18 | 0 |
| Gentamicin | 33 (3/9) | 0 |
| Imipenem | 0 | 0 |
| Meropenem | 0 (0/9) | 0 |
| Nitrofurantoin | 0 (0/4) | 20 |
| Norfloxacin | 0 (0/4) | 20 |
| Piperacillin/Tazobactam | 36.4 | 20 |
| Trimethoprim/Sulfamethoxazol | 36.4 | 20 |

to 2 pregnant women. Cefazolin was given to 6 and ceftriaxone was given to 11 pregnant women for conservative treatment before urine culture (Table 3). Intraoperatively, there was no ureteral perforation or obstetric complication.

DISCUSSION

Bacteriuria is defined as the presence of bacteria in the

urine culture of more than 10^5 cfu/ml (Cunningham and Lucas, 1994), and has been associated with an increased risk of preterm birth and perinatal mortality (Patterson and Andriole, 1997; Delzell et al., 2000). However, bacterial counts as low as 10^2 cfu should also be considered significant in pregnant women and must be treated appropriately (Thomas et al., 2010). In this retrospective study, we defined the bacteriuria as the presence of bacteria in the urine of more than 10^5 cfu/ml

Table 3. Characteristics of pregnant, bacteria isolated from positive urine culture and the treatment modality.

| Patient No. | Diagnosis | Hydronephrosis (Grade) | Co-morbidity | Bacteria | Conservative antibiotic (Day) | Therapy and duration (Day) | The intervention |
|-------------|-----------|------------------------|--------------|------------------------|-------------------------------|--------------------------------|------------------|
| 1 | LUS | 1 | - | <i>E. coli</i> | Ceftriaxone iv, 3 | Cefoxitin im, 7 | URS |
| 2 | RUS | 2 | - | <i>E. coli</i> | Cefazolin im, 3 | Amoxicillin-Clavulanate po, 7 | JJ stent |
| 3 | RUS | 2 | - | <i>E. coli</i> | Ceftriaxone iv, 3 | Cefoxitin im, 8 | JJ stent |
| 4 | RUS | 3 | - | <i>E. coli</i> | Cefazolin im, 2 | Amoxicillin-Clavulanate po, 10 | URS+JJ stent |
| 5 | RUS | 2 | - | <i>E. coli</i> | Cefoxitin im, 3 | Amoxicillin-Clavulanate po, 7 | URS+JJ stent |
| 6 | RUS | 2 | HT | <i>S. haemolyticus</i> | Ceftriaxone iv, 3 | Amoxicillin-Clavulanate po, 10 | JJ stent |
| 7 | RUS | 1 | - | <i>K. pneumoniae</i> | Ceftriaxone iv, 3 | Ceftriaxone im, 7 | JJ stent |
| 8 | RUS | 2 | - | <i>K. pneumoniae</i> | Cefazolin im, 3 | Meropenem iv, 7 | URS+JJ stent |
| 9 | LUS | 2 | - | <i>E. coli</i> | Cefazolin im, 2 | Meropenem iv, 7 | URS+JJ stent |
| 10 | RUS | 3 | - | <i>K. pneumoniae</i> | Ceftriaxone iv, 3 | Cefoxitin im, 7 | PCN tube |
| 11 | RUS | 2 | - | <i>K. pneumoniae</i> | Ceftriaxone iv, 3 | Piperacillin/Tazobactam, 7 | URS+JJ stent |
| 12 | RUS+LUS | 2/2 | DM | <i>K. pneumoniae</i> | Ceftriaxone iv, 3 | Amoxicillin-Clavulanate po, 7 | Bil. JJ stent |
| 13 | RUS | 2 | - | <i>E. coli</i> | Ceftriaxone iv, 3 | Cefoxitin im, 7 | URS+JJ stent |
| 14 | RUS | 2 | - | <i>E. coli</i> | Cefazolin im, 2 | Amoxicillin-Clavulanate po, 7 | URS |
| 15 | RUS | 1 | - | <i>E. coli</i> | Ceftriaxone iv, 3 | Amoxicillin-Clavulanate po, 7 | PCN tube |
| 16 | RUS | 3 | - | <i>E. coli</i> | Cefazolin im, 3 | Amoxicillin-Clavulanate po, 7 | URS+JJ stent |
| 17 | LUS | 2 | - | <i>E. coli</i> | Ceftriaxone iv, 3 | Cefoxitin im, 7 | URS |

URS: Ureteroscopy, L: left, R: right, IV: intravenous, IM: intramuscular, PO: perorally, HT: hypertension, DM: diabetes mellitus, *K. pneumoniae*: *Klebsiella pneumoniae*, *S. haemolyticus*: *Staphylococcus haemolyticus*, PCN: percutaneous nephrostomy, RUS: right ureteral stone, LUS: left ureteral stone Bil: bilateral.

and the overall prevalence of bacteriuria among pregnant women with ureteral stones was 26.2%. This is higher than the prevalence of symptomatic (17.9%), and asymptomatic bacteriuria (13%) was seen in pregnancy (Olsen et al., 2000). This is likely to be attributed to ureteral stones and symptomatic persistent hydronephrosis with pregnancy.

Urinary tract pathogens in pregnant patient are similar to those in non-pregnant patient and *E. coli* is the most common, followed by *Klebsiella* (Millar and Cox, 1997). *E. coli* is responsible from 75 to 90% of bacteriuria during pregnancy (Fiadjoe et al., 2010). Kehinde et al. (2001) have found that *Klebsiella* accounted from 38.1% of the causative agents identified, followed by *E. coli* 31.3% in pregnant patients. It has been found that both

Klebsiella species and *E. coli* were responsible for UTI, especially in people with a reduced immune system, as seen in pregnancy (Wolday and Erge, 1997). In this study, *E. coli* was seen in 64.7%, *Klebsiella* was seen in 29.4% and *Staphylococcus* was seen in 5.9% of our patients. This is likely to be attributed to ureteral stones, hydronephrosis and pregnancy with low socioeconomic status of our pregnant patients.

Acute pyelonephritis complicates 1 to 2% of pregnant women, which the most common renal complication during pregnancy (Sharma and Thapa, 2007). Asymptomatic bacteriuria, cystitis, urinary tract malformation and urinary calculi are risk factors for pyelonephritis. It presents with fever, flank pain and cystitis symptoms, typically. Management involves midstream urine

examination for culture and also blood culture if indicated. Treatment should be aggressive, consisting of rehydration and appropriate intravenous antibiotics (Fiadjoe et al., 2010; Bozkurt et al., 2012). Up to 42% of pregnant women with renal colic and urolithiasis have pyuria on urinalysis (Stothers and Lee, 1992). In this study, renal colic and hematuria were seen in all patients. Microscopic pyuria was seen in 15 patients and fever-chills were seen in 11 of pregnant. All of *E. coli* isolated from pregnant women was found to be sensitive to imipenem, meropenem, nitrofurantoin, norfloxacin and most of *E. coli* was found to be sensitive to amikacin, cefoxitin, ceftriaxone and ciprofloxacin in our study. Since, ciprofloxacin and norfloxacin are not recommended in pregnancy nitrofurantoin,

amoxicillin-clavulanate and cephalosporins remain drug of choice as it is safe to use in pregnancy. These drugs are recommended for both asymptomatic and symptomatic bacteriuria in pregnancy (Masinde et al., 2009).

The rate of resistance of *E. coli* to amoxicillin-clavulanate, ampicillin, cefotaxime, ciprofloxacin, trimethoprim/ sulfamethoxazol, ceftriaxone and piperacillin/ tazobactam were 50, 45.5, 100, 18, 36.4, 28.6, 36.4%, respectively in our study. In a study by Masinde et al. (2009), the rate of resistance of *E. coli* to ampicillin, sulfamethaxazole/trimethoprim, ciprofloxacin, nitrofurantoin, and ceftriaxone were 53, 64.7, 11.8, 5.9 and 29.4%, respectively.

In a retrospective study, *Klebsiella* was sensitive to ceftriaxone (53.54%), followed by gentamicin (52.53%), nitrofurantoin (48.38%), and ciprofloxacin (40.12%). All *K. pneumonia* isolated from our 5 patients were found to be sensitive to amikacin, sefoxitin, ciprofloxacin, gentamicin, imipenem and meropenem (Sharma et al., 2007). The rate of resistance of *Klebsiella* to ampicillin were 80% and amoxicillin-clavulanate, ceftazidim, cefepime, ceftazidim were 60%.

Conclusion

Because of the high risk of complications (hydronephrosis, UTI and pyelonephritis), the treatment of pregnant women with ureteral stones, should be aggressive, hospitalized and intravenous antibiotics. However, when failure of conservative treatment, surgical drainage is recommended, because of high incidence of positivity for urine culture (26.2%), we recommend urine culture to prevent adverse outcome for the mother and foetus. *E. coli* was the most common pathogen, followed by *Klebsiella* and Staphylococcus. Majority of *E. coli* are resistant to Cefotaxime, Cefazolin, Cefepime and Ampicillin. Because of its high safety (both for mother and foetus) and sensitivity to uropathogens in pregnancy, ceftriaxone should be the first choice for the treatment of UTI with symptomatic ureteral stones during pregnancy.

REFERENCES

- Bozkurt Y, Penbegul N, Soylemez H, Atar M, Sancaktutar AA, Yildirim K, Sak ME (2012). The efficacy and safety of ureteroscopy for ureteral calculi in pregnancy: our experience in 32 patients, Urol. Res., [Epub ahead of print]
- Charalambous S, Fotas A, Rizk DE (2009). Urolithiasis in pregnancy. Int. Urogynecol. J. Pelvic Floor Dysfunct., 20(9): 1133-1136.
- Cheriachan D, Arianayagam M, Rashid P (2008). Symptomatic urinary stone disease in pregnancy. Aust. NZ J. Obstet. Gynaecol., 48(1): 34-39.
- Cunningham FG, Lucas MJ (1994). Urinary tract infections complicating pregnancy, Baillieres Clin. Obstet. Gynaecol., 8(2): 353-373.
- Delzell JE, Jr, Lefevre ML (2000). Urinary tract infections during pregnancy. Am. Fam. Physician, 61(3): 713-721.
- Duarte G, Marcolin AC, Quintana SM, Cavalli RC (2008). [Urinary tract infection in pregnancy], Rev. Bras. Ginecol. Obstet., 30(2): 93-100.
- Fiadjoe P, Kannan K, Rane A (2010). Maternal urological problems in pregnancy, Eur. J. Obstet. Gynecol. Reprod. Biol., 152(1): 13-17.
- Goldfarb RA, Neerhut GJ, Lederer E (1989). Management of acute hydronephrosis of pregnancy by ureteral stenting: risk of stone formation, J. Urol., 141(4): 921-922.
- Kehinde A, Adedapo K, Aimakhu C, Odugokbe A T, Olayemi O, Salako B (2011). Urinary pathogens and drug susceptibility patterns of urinary tract infections among antenatal clinic attendees in Ibadan, Nigeria. J. Obstet. Gynaeco. Res., 38(1): 280-284.
- Masinde A, Gumodoka B, Kilonzo A, Mshana SE (2009). Prevalence of urinary tract infection among pregnant women at Bugando Medical Centre, Mwanza, Tanzania, Tanzan J. Health Res., 11(3): 154-159.
- Millar LK, Cox SM (1997). Urinary tract infections complicating pregnancy, Infect. Dis. Clin. North Am. 11(1): 13-26.
- Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM (2005). Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults, Clin. Infect. Dis., 40(5): 643-654.
- Olsen BE, Hinderaker SG, Lie RT, Gasheka P, Baerheim A, Bergsjø P, Kvale G (2000). The diagnosis of urinary tract infections among pregnant women in rural Tanzania; prevalences and correspondence between different diagnostic methods. Acta Obstet. Gynecol. Scand., 79(9): 729-736.
- Patterson TF, Andriole VT (1997). Detection, significance, and therapy of bacteriuria in pregnancy. Update in the managed health care era, Infect. Dis. Clin. North Am., 11(3): 593-608.
- Puskar D, Balagovic I, Filipovic A, Knezovic N, Kopjar M, Huis M, Gilja I (2001). Symptomatic physiologic hydronephrosis in pregnancy: incidence, complications and treatment, Eur. Urol. 39(3): 260-263.
- Rasmussen PE, Nielsen FR (1988). Hydronephrosis during pregnancy: a literature survey, Eur. J. Obstet. Gynecol. Reprod. Biol., 27(3): 249-259.
- Saidi A, Delaporte V, Lechevallier E (2005). [Urological problems encountered during pregnancy], Prog. Urol., 15(1): 1-5.
- Sharma P, Thapa L (2007). Acute pyelonephritis in pregnancy: a retrospective study, Aust N Z J Obstet. Gynaecol., 47(4): 313-315.
- Stothers L, Lee LM (1992). Renal colic in pregnancy, J. Urol. 148(5): 1383-1387.
- Thomas A A, Thomas A Z, Campbell SC, Palmer JS (2010). Urologic emergencies in pregnancy. Urology, 76(2): 453-460.
- Usta TA, Dogan O, Ates U, Yucel B, Onar Z, Kaya E (2011). Comparison of single-dose and multiple-dose antibiotics for lower urinary tract infection in pregnancy. Intl. J. Gynaecol. Obstet. 114 (3): 229-233.
- Wolday D, Erge W (1997). Increased incidence of resistance to antimicrobials by urinary pathogens isolated at Tikur Anbessa Hospital, Ethiop. Med. J., 35(2): 127-135.