Int J Clin Exp Med 2016;9(6):12039-12045
www.ijcem.com /ISSN:1940-5901/IJCEM0023214

Original Article

Which antibiotoc is better to select empirically for lower urinary tract infections in pregnant women?

Migraci Tosun[1], Emel Kurtoglu Ozdes[1], Keramettin Yanik[2], Arif Kokcu[1], Erdem Ozhan[3]

[1]Department of Obstetrics and Gynecology, Ondokuz Mayis University, Samsun, Turkey; [2]Department of Medical Microbiology, Ondokuz Mayis University, Samsun, Turkey; [3]Havza State Hospital, Samsun, Turkey

Received January 4, 2016; Accepted April 1, 2016; Epub June 15, 2016; Published June 30, 2016

Abstract: We evaluated the bacterial profiles and antibiotic sensitivities presenting in each trimester of pregnant women diagnosed with lower urinary tract infection. *Escherichia coli* was the most common isolated uropathogen (77.8%, 75%, and 52%, respectively), followed by *Klebsiella pneumoniae* (0%, 3.6%, and 16%, respectively), and *Enterococcus faecalis* (3.7%, 14.3%, and 8%, respectively). Ciprofloxacin was found to have sensitivity for all uropathogens, with 92.8% sensitivity for *Escherichia coli* and 100% for *Klebsiella pneumoniae*. Norfloxacin also exhibited high sensitivity for almost all bacterial agents, except *Acinetobacter baumannii*, with 91.4% sensitivity for *Escherichia coli* and 100% for *Klebsiella pneumoniae*. Phosphomycin had the highest sensitivity, 100%, for the two most common uropathogens, *Escherichia coli* and *Klebsiella pneumoniae*. Because empirical antimicrobial choices play a critical role in the prevention of unwanted complications, lower urinary tract infection in pregnancy can be treated with empirically selected phosphomycin.

Keywords: Antibiotic sensitivity pattern, empirical treatment, pregnancy, trimester, urinary tract infection, uropathogen

Introduction

Urinary tract infection (UTI), which is diagnosed when there is a bacterial count of 10^5/mL in a quantitative urine culture, is one of the most common bacterial infections in pregnancy [1-3]. While the overall incidence rate of UTI in pregnancy is approximately 8%, it has a wide range in different parts of the world [4, 5]. UTI may be symptomatic in the form of acute cystitis, complicated, and result in pyelonephritis, or it may remain asymptomatic [2].

Apart from several factors that increase the incidence of UTI, such as poor socioeconomic status, sickle cell trait, increased age, high parity, diabetes mellitus, neurogenic bladder, urinary tract abnormality, and increased sexual activity, significant physiologic changes in pregnancy facilitate pathogenic colonization [6, 7]. These changes include urinary stasis and vesicoureteric reflux due to progesterone-induced ureteral dilatation and pressure from the expanding uterus, reduced immune function, difficulty with hygiene due to a gravid abdomen, and medical interventions such as urethral catheterization [3, 4, 8, 9].

UTI, particularly when it remains untreated, leads to significant maternal and fetal morbidity, such as pyelonephritis, hypertension/preeclampsia, preterm delivery, prematurity, low birth weight, intrauterine growth restriction, and sepsis, and even to fetal death [2, 4, 10-12].

Escherichia coli accounts for 80-90% of the bacteria that cause urinary infection in pregnancy [5-11]. Other frequently cultured uropathogens include *Proteus mirabilis, Klebsiella pneumoniae, Staphylococcus aureus*, and streptococcus species [11, 13]. Because UTI can lead to severe maternal and perinatal complications, empirical antibiotics are needed in cases of acute infection while waiting for urine culture and antibiotic sensitivity results. Therefore, knowledge regarding the most frequent uropathogens and antibiotic sensitivity patterns particular to each trimester are of great importance. The aim of this study was to investigate the

Table 1. Demographic features of the study group according to three trimesters of the pregnancy

Features	1st trimester (≤13 weeks) (n=27)	2nd trimester (14-27 weeks) (n=28)	3rd trimester (28-41 weeks) (n=50)	*p*-value
Age	26.8±5.6	30.0±4.7	27.5±5.1	0.052†
Gravida	2 (1-5)	3 (1-7)	2 (1-6)	0.068‡
Parity	1 (0-4)	1 (0-4)	1 (0-3)	0.383‡

†One-Way ANOVA. ‡Kruskal Wallis test.

bacterial profiles and antibiotic sensitivities present in each trimester in pregnant women diagnosed with lower urinary tract infection (LUTI).

Materials and methods

The study included 105 pregnant patients who attended Ondokuz Mayis University Hospital between January 2012 and January 2013 with symptoms suggestive of LUTI (urgency, frequency, dysuria, suprapubic pain) and diagnosed with LUTI after evaluation of a midstream urine culture. Patients who had used antibiotics within the previous two weeks and patients with a recent history of instrumentation were excluded. Demographic data features, including age, gravidity, parity, gestational age at diagnosis, trimester, identified uropathogens, and antibiotic sensitivity, were analyzed retrospectively. Antibiotics were classified according to the United States Food and Drug Administration (FDA) pregnancy categories. In category B, either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk in later trimesters). In category C, either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal or other) and there are no controlled studies in women, or studies in women and animals are not available; drugs should be given only if the potential benefit justifies the potential risk to the fetus. In category D, there is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective) [14].

The study was approved by the Committee for Medical Research Ethics at Ondokuz Mayis University (No: B.30.2.ODM.0.20.08/1456).

Statistical analyses were carried out using the SPSS for Windows program, version 11.5. The Kolmogorov-Smirnov test was used to determine whether the distribution of discrete numeric variables was close to a normal distribution. Definitive statistics were identified as discrete numeric variables, mean ± standard deviation, or median (minimum-maximum); nominal and ordinal variables were identified as case number and percentage (%).

Statistical significance between groups in terms of mean value was determined using one-way analysis of variance, and statistical significance between groups in terms of median value was determined using the Kruskal-Wallis test. Categorical variables were determined by Pearson's Chi-Square test, Fisher's exact test, or probability ratio test. A *p* value less than 0.05 was considered statistically significant.

Results

In this study, we analyzed retrospectively 105 pregnant patients with confirmed LUTI in terms of demographic features, isolated uropathogens, and antibiotic sensitivity patterns in each trimester. **Table 1** showed the demographic features of the study group. There were no differences among trimesters in terms of age, gravidity or parity (**Table 1**).

When causative agents of UTI were determined in each of the three trimesters, *Escherichia coli* was the most common isolated uropathogen (77.8%, 75%, and 52%, respectively), followed by *Klebsiella pneumoniae* (0%, 3.6%, and 16%, respectively), and *Enterococcus faecalis* (3.7%, 14.3%, and 8%, respectively). *Escherichia coli* was isolated significantly more frequently in the first two trimesters when compared to the last trimester (P=0.032) (**Table 2**).

There were no statistically significant differences among the trimesters in terms of overall antibiotic sensitivity, with the exception of pipe-

Table 2. Isolated uropathogens in three trimesters of the pregnancy

Isolated uropathogens	1st trimester (n=27)	2nd trimester (n=28)	3rd trimester (n=50)	*p*-value
Acinetobacter baumannii	1 (3.7)	0 (%0.0)	0 (%0.0)	0.254†
Citrobacter koseri	0 (0.0%)	0 (0.0%)	1 (2.0%)	0.474†
Enterobacter cloacae	1 (3.7%)	0 (0.0%)	0 (0.0%)	0.254†
Enterococcus faecalis	1 (3.7%)	4 (14.3%)	4 (8.0%)	0.363†
Enterococcus hirae	0 (0.0%)	0 (0.0%)	1 (2.0%)	0.474†
Escherichia coli	21 (77.8%)[a]	21 (75.0%)[b]	26 (52.0%)[a,b]	0.032‡
Klebsiella oxytoca	0 (0.0%)	0 (0.0%)	1 (2.0%)	0.474†
Klebsiella pneumoniae	0 (0.0%)[a]	1 (3.6%)	8 (16.0%)[a]	0.012†
Coagulase negative staphylococci	0 (0.0%)	1 (3.6%)	2 (4.0%)	0.402†
Proteus mirabilis	2 (7.4%)	0 (0.0%)	3 (6.0%)	0.197†
Proteus vulgaris	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Staphylococcus aureus	0 (0.0%)	1 (3.6%)	2 (4.0%)	0.402†
Staphylococcus epidermidis	1 (3.7%)	0 (0.0%)	1 (2.0%)	0.485†
Staphylococcus sciuri	0 (0.0%)	0 (0.0%)	1 (2.0%)	0.474†

†Probability ratio test. ‡Pearson's Chi-Square test. a: the difference between patients with ≤13 weeks of gestation and 28-41 weeks is significant (p<0.005); b: the difference between patients with 14-27 weeks of gestation and 28-41 weeks is significant (p<0.005).

Table 3. Overall antibiotic (FDA pregnancy category B) sensitivity pattern in the three trimesters of pregnancy

Antibiotics	≤13 weeks	14-27 weeks	28-41 weeks	*p*-value
Amoxicillin/clavulanic acid	23/26 (88.5%)	25/32 (78.1%)	43/50 (86.0%)	0.505‡
Ampicillin	14/25 (56.0%)	17/33 (51.5%)	31/54 (57.4%)	0.864‡
Ampicillin/Sulbactam	1/1 (100.0%)	-	0/1 (0.0%)	1.000¶
Daptomycin	1/1 (100.0%)	4/4 (100.0%)	7/7 (100.0%)	-
Erythromycin	0/1 (0.0%)	1/1 (100.0%)	2/7 (28.6%)	0.214†
Ertapenem	7/7 (100.0%)	17/17 (100.0%)	26/27 (96.3%)	0.525†
Phosphomycin	17/18 (94.4%)	25/26 (96.2%)	42/43 (97.7%)	0.819†
Clindamycin	1/1 (100.0%)	1/1 (100.0%)	5/7 (71.4%)	0.560†
Meropenem	27/27 (100.0%)	32/32 (100.0%)	52/53 (98.1%)	0.471†
Nitrofurantoin	23/27 (85.2%)	37/39 (94.9%)	55/63 (87.3%)	0.330†
Oxacillin	1/1 (100.0%)	2/2 (100.0%)	3/7 (42.9%)	0.142†
Penicillin	1/2 (50.0%)	5/7 (71.4%)	6/13 (46.2%)	0.542†
Piperacillin	2/4 (50.0%)	2/3 (66.7%)	1/3 (33.3%)	0.712†
Piperacillin/Tazobactam	27/27 (100.0%)[a]	29/32 (90.6%)	45/53 (84.9%)[a]	0.030†
Cefazolin	20/26 (76.9%)	23/29 (79.3%)	43/52 (82.7%)	0.821†
Cefepime	26/27 (96.3%)	28/32 (87.5%)	50/53 (94.3%)	0.384†
Cefoxitin	24/25 (96.0%)	32/32 (100.0%)	48/50 (96.0%)	0.338†
Cefotaxime	4/5 (80.0%)	11/11 (100.0%)	22/22 (100.0%)	0.120†
Ceftazidime	24/26 (92.3%)	28/30 (93.3%)	45/50 (90.0%)	0.861†
Ceftriaxone	23/26 (88.5%)	25/31 (80.6%)	44/50 (88.0%)	0.612†
Cefuroxime	21/25 (84.0%)	24/31 (77.4%)	43/49 (87.8%)	0.473‡
Cefuroxime axetil	3/5 (60.0%)	6/8 (75.0%)	7/8 (87.5%)	0.523†
Cefuroxime sodium	2/2 (100.0%)	-	1/1 (100.0%)	1.000¶

†Probability ratio test. ‡Pearson's Chi-Square test. ¶Fisher's exact test. a: the difference between the patients with <13 weeks of gestation and 28-41 weeks is significant (p=0.046).

Table 4. Overall antibiotic (FDA category C, D) sensitivity pattern in the three trimesters of pregnancy

Antibiotics	≤13 weeks	14-27 weeks	28-41 weeks	*p*-value
High level Gentamicin	1/1 (100.0%)	5/5 (100.0%)	6/6 (100.0%)	-
Amikacin	27/27 (100.0%)	32/32 (100.0%)	52/53 (98.1%)	0.471†
Fusidic acid	1/1 (100.0%)	-	2/2 (100.0%)	1.000¶
Gentamicin	25/27 (92.6%)	31/34 (91.2%)	55/60 (91.7%)	0.980†
Imipenem	28/28 (100.0%)	32/32 (100.0%)	53/54 (98.1%)	0.471†
Chloramphenicol	5/5 (100.0%)	6/6 (100.0%)	19/19 (100.0%)	-
Colistin	3/3 (100.0%)	5/5 (100.0%)	8/8 (100.0%)	-
Levofloxacin	7/9 (77.8%)	10/10 (100.0%)	21/22 (95.5%)	0.150†
Linezolid	2/2 (100.0%)	7/7 (100.0%)	13/13 (100.0%)	-
Moxifloxacin	1/1 (100.0%)	-	2/2 (100.0%)	1.000¶
Norfloxacin	23/26 (88.5%)	35/39 (89.7%)	59/63 (93.7%)	0.660†
Rifampisin	1/1 (100.0%)	2/2 (100.0%)	7/7 (100.0%)	-
Ciprofloxacin	25/27 (92.6%)	35/39 (89.7%)	62/66 (93.9%)	0.742†
Teicoplanin	2/2 (100.0%)	7/7 (100.0%)	13/13 (100.0%)	-
Tetracycline	1/3 (33.3%)	2/7 (28.6%)	8/14 (57.1%)	0.409†
Tigecycline	2/2 (100.0%)	-	2/3 (66.7%)	1.000¶
Trimethoprim/Sulfamethoxazole	19/28 (67.9%)	24/33 (72.7%)	48/61 (78.7%)	0.530‡
Vancomycin	2/2 (100.0%)	7/7 (100.0%)	13/13 (100.0%)	-
High level Streptomycine	4/4 (100.0%)	-	4/6 (66.7%)	0.467¶

†Probability ratio test. ‡Pearson's Chi-Square test. ¶Fisher's exact test.

racillin/tazobactam, which was found to have significantly lower sensitivity in the last trimester. The sensitivity of tetracycline was lower than 50% in the first and second trimesters, and erythromycin had lower sensitivity in the third trimester; almost all other antibiotics had sensitivities close to 100% in each trimester. The antibiotics were shown in **Tables 3** and **4**.

When the antibiotic sensitivity patterns of the isolated uropathogens were identified, *Escherichia coli*, the most common isolated agent, showed 100% sensitivity to amikacin, phosphomycin, imipenem, chloramphenicol, colistin, meropenem, cefoxitin, cefoperazone/sulbactam, and cefuroxime sodium. *Klebsiella pneumoniae*, the second most common causative agent of UTI, showed 100% sensitivity to most of the antibiotics, including amikacin, phosphomycin, ertapenem, gentamicin, imipenem, chloramphenicol, colistin, meropenem, levofloxacin, norfloxacin, ciprofloxacin, cefotaxime, cefoperazone/sulbactam, cefuroxime axetil, and trimethoprim/sulfamethoxazole.

Ciprofloxacin was found to have sensitivity for all uropathogens, with 92.8% sensitivity for *Escherichia coli* and 100% for *Klebsiella pneumoniae*. Norfloxacin also exhibited high sensitivity for almost all bacterial agents, except *Acinetobacter baumannii*, with 91.4% sensitivity for *Escherichia coli* and 100% for *Klebsiella pneumoniae.* Phosphomycin had the highest sensitivity, 100%, for the two most common uropathogens, *Escherichia coli* and *Klebsiella pneumonia* (**Table 5**).

Discussion

It has long been known that UTI in pregnancy, even if asymptomatic, is associated with significant maternal and fetal morbidity and mortality. Therefore, it is essential to treat it urgently and effectively. Empirical antimicrobial therapy should be administered, then reviewed and changed if necessary following antimicrobial sensitivity testing. However, some factors affecting the bacterial profile and therapy, as well as factors such as socioeconomic status and gestational age at infection, have been identified in previous studies [15-17].

Identifying the most common causative agents for a population contributes to the accuracy of treatment. For instance, the percentage of *E. coli* was found to be 50.8% which is less than previous findings in studies done in developed

Table 5. Antibiotic sensitivity pattern of detected uropathogens

	Amoxicillin/clavulanic acid	Ampicillin	Ampicillin/sulbactam	Daptomycin	Erythromycin	Ertapenem	Phosphomycin	Imipenem	Clindamycin	Meropenem	Nitrofurantoin	Oxacillin
Acinetobacter baumannii	-	-	50.0	-	-	-	-	50.0	-	50.0	-	-
Citrobacter koseri	100.0	0.0	-	-	-	-	-	100.0	-	100.0	100.0	-
Enterobacter cloacae	0.0	0.0	-	-	-	-	0.0	100.0	-	100.0	100.0	-
Enterococcus faecalis	-	100.0	-	100.0	100.0	-	87.5	100.0	0.0	-	91.0	-
Enterococcus hirae	-	-	-	-	-	-	-	-	-	-	100.0	-
Escherichia coli	89.0	60.5	-	-	-	97.8	100.0	100.0	-	100.0	95.2	-
Klebsiella oxytoca	100.0	0.0	-	-	-	-	100.0	100.0	-	100.0	100.0	-
Klebsiella pneumoniae	60.0	0.0	-	-	-	100.0	100.0	100.0	-	100.0	86.7	-
Coagulase negative staphylococcus	-	-	-	100.0	0.0	-	-	-	100.0	-	100.0	50.0
Proteus mirabilis	85.7	71.4	-	-	-	-	0.0	100.0	-	100.0	14.3	-
Proteus vulgaris	100.0	100.0	-	-	-	-	-	100.0	-	100.0	0.0	-
Staphylococcus aureus	-	-	-	100.0	100.0	-	-	-	100.0	-	100.0	66.7
Staphylococcus epidermidis	-	-	-	100.0	0.0	-	100.0	100.0	50.0	-	100.0	100.0
Staphylococcus sciuri	-	-	-	-	0.0	-	100.0	100.0	100.0	-	-	0.0

	Penicillin	Piperacillin	Piperacillin/Tazobactam	Cefazolin	Cefepime	Cefoxitin	Cefoperazone/Sulbactam	Cefotaxime	Ceftazidime	Ceftriaxone	Cefuroxime	Cefuroxime axetil	Cefuroxime sodium
Acinetobacter baumannii	-	50.0	50.0	-	50.0	-	50.0	-	50.0	-	-	-	-
Citrobacter koseri	-	0.0	0.0	100.0	100.0	100.0	-	100.0	-	100.0	100.0	-	-
Enterobacter cloacae	-	-	100.0	100.0	100.0	0.0	-	-	-	100.0	100.0	-	-
Enterococcus faecalis	91.0	-	-	-	-	-	-	-	-	-	-	-	-
Enterococcus hirae	100.0	-	-	-	-	-	-	-	-	-	-	-	-
Escherichia coli	-	66.7	92.9	82.7	94.0	100.0	100.0	96.6	92.6	86.6	85.0	73.7	100.0
Klebsiella oxytoca	-	-	100.0	100.0	100.0	100.0	-	100.0	100.0	100.0	100.0	-	-
Klebsiella pneumoniae	-	0.0	86.7	60.0	86.7	86.7	100.0	100.0	85.7	71.4	64.3	100.0	-
Coagulase negative staphylococcus	25.0	-	-	-	-	-	-	-	-	-	-	-	-
Proteus mirabilis	-	-	85.7	100.0	100.0	100.0	-	100.0	100.0	100.0	100.0	-	-
Proteus vulgaris	-	-	100.0	0.0	100.0	100.0	-	-	100.0	100.0	100.0	-	-
Staphylococcus aureus	0.0	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus epidermidis	0.0	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus sciuri	0.0	-	-	-	-	-	-	-	-	-	-	-	-

countries. However, it was higher than recent findings in developing countries like Lafia (30.56%), northern Nigeria, Benin (38%), southern Nigeria, Ile-Ife (42.2%), southwest Nigeria, Ilorin (47.5%) and southwest Nigeria, Addis Ababa (44%) [15]. In the present study, *Escherichia coli* was the most common isolated uropathogen, followed by *Klebsiella pneumoniae* and *Enterococcus*, in pregnant patients with LUTI symptoms at our university hospital, which is a reference center in the Black Sea Region of Turkey.

While gestational age has been identified as another important factor affecting bacterial profile and antimicrobial sensitivity, it has not been the topic of much interest in previous studies [16]. Because each trimester of pregnancy has its own physiological features, including alterations in urinary system functions, hormone levels, and bacterial colonization, it is important to determine the most common uropathogens in each trimester. *Escherichia coli* and *Klebsiella spp*. were reported as prominent causative bacterial agents isolated from the urine cultures of pregnant patients in Afyon, western Turkey, in each trimester [16]. However, we found *Escherichia coli* to be the most common bacterial agent in the first and second trimesters, and *Klebsiella pneumoniae* to be the predominant agent in the last trimester in pregnant patients living in Samsun, northern Turkey.

Prompt empirical treatment is essential in pregnant patients with symptomatic UTI to prevent serious complications and to provide relief; therefore, antimicrobial sensitivity needs to be determined in order to administer the appropriate treatment afterwards. Previous studies have reported that cephalosporins, quinolones, and phosphomycin are effective against the causative agents in pregnant patients with symptomatic UTI [15-17]. Consistent with those studies, we found ciprofloxacin (92.8% sensitivity for *Escherichia coli* and 100% for *Klebsiella pneumoniae*) and norfloxacin (91.4% sensitivity for *Escherichia coli* and 100% for Klebsiella pneumoniae) to exhibit high sensitivity for almost all bacterial agents. Phosphomycin displayed the highest sensitivity (100%) for the two most common uropathogens, *Escherichia coli* and *Klebsiella pneumoniae*.

It must be noted that when we evaluated the antibiotics according to FDA pregnancy category, because ciprofloxacin and norfloxacin are classified as group C, phosphomycin, which is classified as group B, seemed to be safer for first-line treatment. Furthermore, when we analyzed the antimicrobial agents by trimester, phosphomycin seemed to be highly effective for treatment in each trimester, as were ciprofloxacin and norfloxacin. In other words, LUTI in pregnancy can be treated with empirically selected phosphomycin.

Disclosure of conflict of interest

None.

Address correspondence to: Emel Kurtoglu Ozdes, Department of Obstetrics and Gynecology, Ondokuz Mayis University, Samsun, Turkey. Tel: +90 505 260 02 39 Ext. +903623121919/2562; E-mail: emel-0022@mynet.com

References

[1] Addo VN. Urinary tract infection in pregnancy. Comprehensive Obstetrics in the Topics. In: Kwawukume EY, Emuveyan EE, editors. Dansoman: Asente and Hittscher Printing Press Limited; 2001. pp. 261-267.

[2] Cunningham FG, Gant NF, Leveno KJ, Gilstrap LC III, Hauth JC, Wenstrom KD. Renal and urinary tract disorders. Williams Obstetrics, 21st edn. In: Andrea Seils, Noujaim SR, Daris K, editors. New York: McGraw-Hill Medical Publishing Division; 2001. pp. 1251-1272.

[3] McCormick T, Ashe RG, Kearney PM. Urinary tract infection in pregnancy. The Obstetrician and Gynaecologist 2008; 10: 156-162.

[4] Patterson TF, Andriole VT. Bacteriuria in pregnancy. Infect Dis Clin North Am 1987; 1: 807-22.

[5] Mikhail MS, Anyaegbunam A. Lower urinary tract dysfunction in pregnancy: a review. Obstet Gynecol Surv 1995; 50: 675-83.

[6] Gilstrap LC 3rd, Cunningham FG, Whalley PJ. Acute pyelonephritis in pregnancy: an anterospective study. Obstet Gynecol 1981; 57: 409-13.

[7] Asscher AW, Sussman M, Waters WE, Davis RH, Chick S. Urine as a medium for bacterial growth. Lancet 1966; 2: 1037-41.

[8] Schieve LA, Handler A, Hershow R, Persky V, Davis F. Urinary tract infection during pregnancy: its association with maternal morbidity and perinatal outcome. Am J Public Health 1994; 84: 405-10.

[9] Olusanya O, Okpere, EE, Ezimokhai M. The importance of social class in voluntary fertility control in a developing country. West African Journal of Medicine 1985; 4: 205-207.

[10] Nnatu S, Essien EE, Akinkugbe A, Odum CU. Asymptomatic bacteriuria in pregnant Nigerian patients. Clin Exp Obstet Gynecol 1989; 16: 126-9.
[11] Abdul IF, Onile BA. Bacterial isolates from urine of women in Ilorin and their antibiotic susceptibility patterns. Trop J Obstet Gynaecol 2001; 8: 61-65.
[12] Ezechi OC, Fasubaa OB, Dare FO. Antibiotic sensitivity patterns of microbial isolates from urine of pregnant women with urinary tract infections. Trop J Obstet Gynaecol 2003; 20: 113-115.
[13] Arias F. Abnormalities of the urinary system during pregnancy. Practical guide to high risk pregnancy and delivery. In: Daftary SN, Bhidc AG, editors. A south asian perspective. 3rd edition. New Delhi: Elsevier; 2008. pp. 489-505.
[14] Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling available online at http://federalregister.gov/a/2014-28241 Accessed 26 January 2015.
[15] Onoh R, Umeora O, Egwuatu V, Ezeonu P, Onoh T. Antibiotics sensitivity pattern of uropathogens from pregnant women with urinary tract infection in Abakaliki, Nigeria. Infect Drug Resist 2013; 6: 225-233.
[16] Unlu BS, Yildiz Y, Keles I, Kaba M, Kara H, Tasin C, Erkılınc S, Yildirim G. Urinary tract infection in pregnant population, which empirical antimicrobial agent should be specified in each of the three trimesters? Ginekol Pol 2014; 85: 371-6.
[17] Akarsu S, Kara C, Bozkurt OF, Cizmeci Z, Akdemir N, Unsal A. The clinical efficacy of fosfomycin trometamol versus amoxicillin-clavulanic acid in the treatment of symptomatic and asymptomatic bacteriuria in 3rd trimester pregnancy. J Turk Soc Obstet Gynecol 2010; 7: 107-112.