

Uropathogens and Gestational Outcomes of Urinary Tract Infections in Pregnancies that Necessitate Hospitalization

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Key Words

Urinary tract infection • Pregnancy • Uropathogens • *Escherichia coli*

Abstract

Background and Objectives: Our aim is to identify uropathogens that cause urinary tract infections (UTIs) that necessitate hospitalization, and analyze outcomes of gestational UTIs. **Methods:** This study consisted of 30 pregnant women who necessitate hospitalization because of UTI (7.8% of gestational UTIs during the same period of time). UTI that necessitates hospitalization is defined as clinical complaints, urination problems, urine analysis and culture positivity, fever and uterine discomfort. Patients with at least two positive cultures ($\geq 100,000$ cfu/ml) were included to this study. Antimicrobial susceptibility tests were obtained in all cases in order to determine antimicrobial resistance and to choose the ideal antibiotics for treatment. **Results:** In our study, we have found that *Escherichia coli* is the most common microorganism (56.7%). *Enterococcus faecalis* (13.3%) and *Klebsiella pneumonia* (10%) were other frequently observed microorganisms. In this series, mean gestational week at birth was 35 weeks 5 days (range 23–40 weeks). Mean birthweight was 2,656 g (range 500–3,700 g). Twenty-three cases (76.7%) were hospitalized before 37th gestational week and preterm delivery rate was 56.3%. Maternal risk factors and coexisting diseases were detected in 11 (36.7%) patients as follows: diabetes mellitus in 4, thrombophilia in 3, thyroid disorders in 3 and hydroureteronephrosis in 1 case. Cesarean section rate

was 65.2%. **Conclusions:** Knowing uropathogens of patient population is beneficial in the management of patients and better planning of future medical treatments. Preterm labor seems to be an important complication in pregnancies with UTIs going together with fever and urination problems.

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Introduction

The prevalence of bacteriuria in women has previously been reported as 3–20 % in various studies [1]. Untreated urinary tract infections (UTIs) during pregnancy is associated with an increased risk of multiple maternal and neonatal complications, such as preeclampsia, preterm birth, intrauterine growth restriction and low birth weight [2–5]. Gestational UTIs are complicated when the infection is accompanied by risk factors such as urolithiasis, recurrent UTI, urinary tract abnormalities, chronic inflammatory diseases, autoimmune disorders, renal parenchymal diseases, and diabetes mellitus [6–10]. Therefore, time is of the essence in treating gestational UTIs [9, 11, 12]. Furthermore, identifying the uropathogens in the obstetric populations is important in order to optimize the antibiotic regimens used for the empiric treatment [13–16]. In this study, we have demonstrated the uropathogens and the pregnancy outcomes of the UTIs that necessitate hospitalization within the framework of our antenatal care program.

Table 1. Microorganisms responsible from the UTIs of the study subjects

Isolate	n	%
<i>E. coli</i>	17	56.7
<i>K. pneumonia</i>	3	10
<i>E. faecalis</i>	4	13.3
Others	4	13.3
<i>S. hemolyticus</i>	2	6.7
<i>S. epidermidis</i>	1	3.3
<i>S. mitis</i>	1	3.3
Mixed	2	6.7
Total	30	100

Table 2. Microorganisms and the antimicrobial resistance profile of 14 cases

Isolate	Resistance
<i>E. coli</i>	amoxicillin-clavulanate, ciprofloxacin, ampicillin, trimethoprim-sulfamethoxazole, piperacillin-tazobactam
<i>E. coli</i>	ceftazidime, ampicillin, cefixime, ciprofloxacin, amoxicillin-clavulanate
<i>E. coli</i>	fosfomycin
<i>E. coli</i>	ampicillin, cefixime, cefuroxime
<i>E. coli</i>	ampicillin, gentamycin, cefixime, cefroxime, ceftizoxime, cephoitin
<i>E. coli</i>	ampicillin, trimethoprim-sulfamethoxazole
<i>E. faecalis</i>	tetracycline, clindamycin, trimethoprim-sulfamethoxazole
<i>E. faecalis</i>	ampicillin, benzilpenicillin
<i>E. faecalis</i>	clindamycin, trimethoprim-sulfamethoxazole
<i>K. pneumoniae</i>	ampicillin, piperacillin-tazobactam, cefixime, cefroxime
<i>K. pneumoniae</i>	ampicillin, fosfomycin
<i>K. pneumoniae</i>	ampicillin, fosfomycin, nitrofurantoin
<i>S. epidermidis</i>	benzilpenicillin, erythromycin, cephoitin
<i>S. haemolyticus</i>	benzilpenicillin, clindamycin, ertapenem, fosfomycin, imipenem, cephoitin

Materials and Methods

We have used our institutional database of antenatal care program to identify 387 patients who were treated for a community acquired gestational UTI. Thirty patients were hospitalized due to a UTI. Patients were hospitalized in the presence of urinary symptoms (dysuria, frequency, nausea, vomiting and/or costovertebral region sensitivity), positive urine tests (urinalysis and culture), fever and uterine discomfort (irregular contractions or increased sensitivity).

Patients with at least two positive cultures [$\geq 100,000$ colony forming units per milliliter (cfu/ml)] were included to this study (pre- and post-hospitalization). Urine cultures were performed at our institution between January 1, 2015 and December 31, 2016. Contaminated urine cultures were repeated or excluded from the study.

Antimicrobial susceptibility tests were done in all cases in order to determine antimicrobial resistance profile and to choose the ideal antibiotics for empiric and definitive treatment. Antibiotics tested in the antibiogram included meropenem, amikacin, amoxicillin clavulanate, ampicillin, ertapenem, fosfomycin, gentamycin, nitrofurantoin, piperacillin-tazobactam, cefixime, cefuroxime, ciprofloxacin, trimethoprim-sulfamethoxazole and ceftriaxon.

Statistical analysis were performed with the Statistical Package for the Social Sciences (SPSS.22, IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). The percentages of microorganisms responsible from the UTIs of the study subjects were calculated.

Written informed consent was obtained from all the patients, and the study was approved by the institutional ethics committee of Hacettepe University. The study was performed in accordance with the ethical standards described in an appropriate version of the 1975 Declaration of Helsinki, as revised in 2000. No funding was used for this study.

Results

A total of 387 patients had a positive culture during the study period, in which 30 patients were hospitalized. The rate of hospitalization was 7.8%. There were 14 primiparous and 16 multiparous women. Mean age was 29 years (range 22–38 years) at the time of diagnosis. Maternal risk factors and coexisting diseases were detected in 11 (36.7%) patients as follows: diabetes mellitus in 4, thrombophilia in 3, thyroid disorders in 3 and hydroureteronephrosis in 1 case.

Twenty-three cases (76.7%) were hospitalized before 37th gestational week (1 case was in the first trimester, 5 cases were in the second trimester and 17 cases were in the third trimester), while remaining cases ($n = 7$) were hospitalized at term pregnancy. Seven patients were delivered at other centers due to various reasons and delivery data could not obtained for them.

There were 15 (65.2%) cesarean section and 8 (34.8%) vaginal deliveries among the 23 deliveries. The mean gestational week at birth was 35 weeks 5 days (range 23–40 weeks) for these patients. The mean birthweight was found to be 2,656 g (range 500–3,700 g). Term delivery (≥ 37 th gestational week) rate was 43.7%. There were 3 extremely preterm cases that died after birth. For the remaining 18 liveborn neonates, mean APGAR score was 8.8 and 9.4 at 1st and 5th minute, respectively.

Table 1 shows the microorganisms responsible from the UTIs of the study subjects. *E. coli* was the main microorganism responsible from the UTIs. *K. pneumonia*, *E. faecalis*, *S. epidermidis*, *S. haemolyticus*, *S. mitis* and *C. albicans* were the other uropathogens. We have ob-

served 2 mixed infections (*E. coli* + *K. pneumonia* and *C. albicans* + *S. mitis*) in our series. There were no antimicrobial susceptibility in 16 cases and table 2 shows the microorganisms and the antimicrobial susceptibility results of the remaining 14 cases.

Discussion

Untreated UTIs has been reported to be associated with multiple pregnancy complications like preeclampsia, preterm birth, intrauterine growth restriction and low birth weight [2–6]. In our cohort, preterm delivery rate was 56.3%. UTIs may also be the cause of various obstetrical complications which can be prevented by appropriate treatment protocols [17–19]. Preeclampsia and preterm premature rupture of membranes should especially be the concern of the obstetricians in the presence of UTIs [20, 21].

Maternal problems such as urolithiasis, chronic recurrent urinary infections, urinary tract abnormalities, chronic inflammatory diseases, autoimmune disorders, renal diseases (nephrotic syndrome, glomerular diseases etc) and diabetes mellitus were the risk factors for UTI in pregnancies [6–9]. In this small series, 16.7 % of cases were with such risk factors (4 diabetes mellitus and 1 hydroureteronephrosis).

Knowing the uropathogens of each obstetric population is particularly important in the management of UTIs. There are various studies related to the most frequently observed microorganisms in UTIs during pregnancy. *Escherichia coli* is reported to be the most critical microorganisms which should be kept in mind [20–23]. In our study, we also have found that *E. coli* is the most common microorganism responsible from the UTI. *K. pneumonia*, *E. faecalis*, *S. epidermidis*, *S. haemolyticus*, *S. mitis* and *C. albicans* were the other microorganisms responsible from the infection in our study group.

K. pneumoniae is a common cause of UTIs during pregnancy. It has been reported that *K. pneumonia* was isolated in 21.5% of the urine samples in pregnancies with asymptomatic bacteriuria [24]. *E. faecalis* is reported to be a less common uropathogen in pregnant women with UTI although it has been found to be relatively more frequent in our series [25].

S. Epidermidis seems to be a nosocomial infection and must be the concern of physicians in patients with long-term hospitalisation [24, 26]. *S. haemolyticus* which goes together with significant clinical symptoms is also an important uropathogen causing obstetrical complications

[27]. *S. mitis* has been considered a relatively benign oral streptococcus and a member of the oral commensal flora. Nevertheless, it can cause infection especially in immune-compromised patients [28]. Infection of the urinary tract due to *C. albicans* is uncommon. Prolonged use of antibiotics and diabetes mellitus may be associated with fungal UTIs [29].

Antibiotic susceptibility tests are very important in order to have successful therapy and low cost management. The choice of treatment should be guided by antimicrobial susceptibility testing in UTIs. Recently, increasing numbers of urinary pathogens are developing resistance to antibiotics [30, 31]. In our series, there were no antimicrobial susceptibility in 16 cases and table 2 shows the microorganisms and the antimicrobial susceptibility results of the remaining 14 cases.

Single center experience, small number of patients and retrospective design of the study were the main limitations in our study.

Conclusion

In conclusion, knowing the uropathogens of the patient population is beneficial in the management of patients and better planning of future medical treatments. Preterm labor seems to be an important complication in pregnancies with UTIs going together with fever and urination problems.

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References

- 1 Priscilla R, Latha G, Rajan D, Sultana M: Prevalence and antimicrobial resistance pattern of bacterial strains isolated from patients with urinary tract infection. *MOJ Public Health* 2017;5:32–35.
- 2 Gilstrap LC 3rd, Ramin SM: Urinary tract infections during pregnancy. *Obstet Gynecol Clin North Am* 2001;28:581–591.
- 3 Cram LF, Zapata MI, Toy EC, Baker B 3rd: Genitourinary infections and their association with preterm labor. *Am Fam Physician* 2002;65:241–248.
- 4 Millar LK, Cox SM: Urinary tract infections complicating pregnancy. *Infect Dis Clin North Am* 1997;11:13–26.
- 5 Kalinderi K, Delkos D, Kalinderis M, Athanasiadis A, Kalogiannidis I: Urinary tract infection during pregnancy: current concepts on a common multifaceted problem. *J Obstet Gynaecol* 2018;38:448–453.
- 6 Lewis DF, Robichaux AG, Jaekle RK, Marcum NG, Stedman CM: Urolithiasis in pregnancy: diagnosis, management, and pregnancy outcome. *Obstet Gynecol Surv* 2003;58:446–447.
- 7 Hou S, Orłowski J, Pahl M, Ambrose S, Hussey M, Wong D: Pregnancy in women with end-stage renal disease: treatment of anemia and premature labor. *Am J Kidney Dis* 1993;21:16–22.
- 8 Chou CY, Ting IW, Lin TH, Lee CN: Pregnancy in patients on chronic dialysis: a single center experience and combined analysis of reported results. *Eur J Obstet Gynecol Reprod Biol* 2008;136:165–170.
- 9 Kremery S, Hromec J, Demesova D: Treatment of lower urinary tract infection in pregnancy. *Int J Antimicrob Agents* 2001;17:279–282.
- 10 Cunningham FG, Lucas MJ: Urinary tract infections complicating pregnancy. *Baillieres Clin Obstet Gynaecol* 1994;8:353–373.
- 11 Hooton TM, Stamm WE: Diagnosis and treatment of uncomplicated urinary tract infection. *Infect Dis Clin North Am* 1997;11:551–581.
- 12 Vazquez JC, Villar J: Treatments for symptomatic urinary tract infections during pregnancy. *Cochrane Database Syst Rev* 2003;4:CD002256.
- 13 Nicolle LE: Urinary tract infection: traditional pharmacologic therapies. *Dis Mon* 2003;49:111–128.
- 14 Gupta K, Hooton TM, Stamm WE: Increasing antimicrobial resistance and the management of uncomplicated community-acquired urinary tract infections. *Ann Intern Med* 2001;135:41–50.
- 15 Arslan H, Azap OK, Ergönül O, Timurkaynak F: Risk factors for ciprofloxacin resistance among *Escherichia coli* strains isolated from community-acquired urinary tract infections in Turkey. *J Antimicrob Chemother* 2005;56:914–918.
- 16 Bouza E, San Juan R, Muñoz P, Voss A, Kluytmans J: A European perspective on nosocomial urinary tract infections I. Report on the microbiology workload, etiology and antimicrobial susceptibility (ESGNI 003 study). *Clin Microbiol Infect* 2001;7:523–531.
- 17 Foxman B: Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am J Med* 2002;113(suppl 1A):5S–13S.
- 18 Schieve LA, Handler A, Hershov R, Persky V, Davis F: Urinary tract infection during pregnancy: its association with maternal morbidity and perinatal outcome. *Am J Public Health* 1994;84:405–410.
- 19 Mazor-Dray E, Levy A, Schlaeffer F, Sheiner E: Maternal urinary tract infection: is it independently associated with adverse pregnancy outcome? *J Matern Fetal Neonatal Med* 2009;22:124–128.
- 20 Hsu C, Witter F: Urogenital infection in preeclampsia. *Int J Gynecol Obstet* 1995;49:271–275.
- 21 Banhidly F, Acs N, Puhó EH, Czeizel AE: Pregnancy complications and birth outcomes of pregnant women with urinary tract infections and related drug treatments. *Scand J Infect Dis* 2007;39:390–397.
- 22 Sheiner E, Mazor-Drey E, Levy A: Asymptomatic bacteriuria during pregnancy. *J Matern Fetal Neonatal Med* 2009;22:423–427.
- 23 Delzell JE Jr, Lefevre ML: Urinary tract infections during pregnancy. *Am Fam Physician* 2000;61:713–720.
- 24 Akerele J, Abbulimen P, Okonofua F: Prevalence of asymptomatic bacteriuria among pregnant women in Benin City, Nigeria. *J Obstet Gynaecol* 2001;21:141–144.
- 25 Turpin C, Minkah B, Danso K, Frimpong E: Asymptomatic bacteriuria in pregnant women attending antenatal clinic at Komfo Anokye Teaching Hospital, Kumasi, Ghana. *Ghana Med J* 2007;41:26–29.
- 26 Cho SH, Naber K, Hacker J, Ziebuhr W: Detection of the *icaADBC* gene cluster and biofilm formation in *Staphylococcus epidermidis* isolates from catheter-related urinary tract infections. *Int J Antimicrob Agents* 2002;19:570–575.
- 27 Loh K, Sivalingam N: Urinary tract infections in pregnancy. *Malays Fam Physician* 2007;2:54–57.
- 28 Mitchell J: *Streptococcus mitis*: walking the line between commensalism and pathogenesis. *Mol Oral Microbiol* 2011;26:89–98.
- 29 Fisher JF, Chew WH, Shadomy S, Duma RJ, Mayhall CG, House WC: Urinary tract infections due to *Candida albicans*. *Rev Infect Dis* 1982;4:1107–1118.
- 30 Smaill F, Vazquez JC: Antibiotics for asymptomatic bacteriuria in pregnancy. *Cochrane Database Syst Rev* 2007;2:CD000490
- 31 Patterson TF, Andriole VT: Detection, significance, and therapy of bacteriuria in pregnancy: update in the managed health care era. *Infect Dis Clin North Am* 1997;11:593–608.