Abstract
Background and Objective: Urinary infection is one of the most common medical complications of pregnancy. It occurs in 5-10% of pregnant women and may lead to serious fetal morbidity like prematurity and low-birth-weight infants, and may result in maternal morbidity, like renal dysfunction, sepsis, respiratory insufficiency and even maternal death if it’s progressed to acute pyelonephritis. We retrospectively evaluated the prevalence of urinary infection, causing microorganisms, risk factors and complications in our population.

Methods: The medical files of 1934 patients who gave birth in our department within last two years have been retrospectively evaluated. 1326 women who had a routine antenatal care and at least one screening urine culture for bacteriuria had been included to the study. Women who had positive urine culture (n=106) had been compared with those who had negative result (n=1220) for demographic characteristics and maternal/fetal complications.

Results: 1326 pregnant women were studied, of whom 106 (16.98%) were identified to have asymptomatic bacteriuria. The level of education was lower in asymptomatic bacteriuria group, but the prevalence of preterm delivery, low-birth-weight infants and anemia were higher than the control group. Thirty cases of acute pyelonephritis (2.26%) were hospitalized during the study period.

Conclusion: Urinary tract infection during pregnancy can cause serious maternal and perinatal morbidity. All pregnant women should be screened for bacteriuria by urine culture at least once and they should be treated if the results are positive. Acute pyelonephritis during pregnancy is a serious problem which should be treated as inpatients with appropriate parenteral antibiotics.

Keywords: Pregnancy, urinary tract infection, asymptomatic bacteriuria, pyelonephritis.

Urinary Tract Infection in Pregnancy

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Gebelikte üriner enfeksiyon


Yöntem: Klinikimizde son 2 yıl içerisinde doğum yapan 1934 hastanın dosyaları retrospektif olarak tarandı. Bu kadınların gebelik takibi klinikimizde yapılabilecek birçok temel ve etkenin ötesine en az bir kez tama amaclı idrar kültürü yapılmış olan 1326 gebe çalışmaya dahil edildi. İdrar kültürünün pozitif raporlanan gebelerle (n=106), kültür sonucu negatif olanlar (n=1220) genel özellikleri ve maternal/fetal komplikasyonlar açısından birbirleri ile karşılaştırıldı.


Anahtar Sözcükler: Gebelik, üriner enfeksiyon, asemptomatik bakteriüri, pyelonefrit.

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Introduction

Urinary tract infection is one of the most common medical complications of pregnancy together with anemia and hypertension, and it occurs approximately in 5-10% of all pregnancies.1,2 Urinary infection can be defined as the proliferation of active microorganisms inside the urinary channel which are harmful to their environment. Bacteriuria is the isolation of bacteria in the urine specimen.3 Presence of 1x10^5 or more colony forming units (CFUs) of the same active microorganism per milliliter in 2 consecutive urine specimens has been a historically used threshold value for the diagnosis of bacteriuria.

Some physiological changes occurring during the pregnancy expedite the emergence of urinary infections and cause a higher incidence. As a result of hormonal changes, tonus of urinary bladder and ureter is reduced, and subsequently dilatation in the ureter and renal pelvis, incidence of urinary stasis and vesicourethral reflux increase. Increased plasma volume and glomerular filtration rate result in reduction in the urinary concentration. Furthermore, there is an increase in the incidence of glycosuria and aminoaciduria and a reduction in the resistance of urinary tract system against bacteria in pregnancy. Depending on all these developments, the incidence of symptomatic urinary tract infections is increased in pregnancy.4

Urinary tract infections can be seen in three different forms in pregnancy; asymptomatic bacteriuria, acute cystitis or acute pyelonephritis. The incidence of asymptomatic bacteriuria, which can be described as bacteriuria without specific symptoms of the urinary tract infection, has been reported between 2-13% in pregnancy in our population5 and all over the world, and this rate is not higher than the non-pregnant rate of the same age group.6 However, physiological changes in pregnancy lead to a severe course of the problem. It has been demonstrated that if untreated, asymptomatic bacteriuria increased the frequency of premature delivery and neonates with low birthweight7, and also it was likely to cause acute pyelonephritis at a rate of 15-30%.8 Acute pyelonephritis is a serious clinical presentation which can be seen in 1-2% of all pregnancies, and may cause critical fetal-maternal adverse effects.9

Based on all, we planned a retrospective study in order to identify the incidence of urinary tract infection and complications in the pregnant women followed-up by our clinic and to describe the potential risk factors and reveal the effectiveness of the treatment.

Methods

Files of 1934 patients who gave birth in our clinic over 24 week's gestation between 1 January 2003 and 31 December 2004 were retrospectively evaluated. As it is a routine to get urine specimen from all pregnant women presented to our clinic for antenatal follow-up, 1326 pregnant women, who visited the clinic at least twice for antenatal control and had her urine culture done at least once for screening purposes during the pregnancy and had no fetal anomaly, were included in the study. Since there was not a complete correlation between the results of cytometric urine analysis and the results of urine culture and detection of pyuria is not an efficient criteria to distinguish between symptomatic and asymptomatic urinary infections,11 detection of pyuria as a result of cytometric urine analysis was not admitted as a diagnosis of the urinary tract infection, and only patients with a result of urine culture were included. Then, clinic files of 1326 patients included in the study were individually examined, and data about demographic characteristics of patients, complications emerged during the course of pregnancy, incidence of asymptomatic bacteriuria and symptomatic urinary tract infection, birthweights of neonates and neonatal complications were collected. Deliveries earlier than 37 week's gestation were regarded as preterm; hematocrite value less than 30% detected during the labor as anemia; and birthweights less than 2500 gr as low birthweight. Results of the urine culture of patients included in the study were retrospectively screened by means of the automation programme of the hospital in coordination with the clinic of microbiology. The results were also evaluated in terms of incidence of the infecting organisms identified.

Urine specimens of the patients were obtained from the first urine in the morning in sterile cups following the appropriate cleaning as moderate-
flow urine specimen. Specimens were inoculated with a 0.001 ml calibrated loop onto a 5% sheep blood and eosin methylene blue (EMB) agar, and evaluated following an incubation at 37°C for 18 to 24 hours. Presence of 1x10^5 or more CFUs of the same active microorganism per each millimeter of the urine specimen was regarded as positive outcome. Pregnant women whose results of 2 subsequent urine cultures were positive, but who had no symptoms and clinical complaints were diagnosed with asymptomatic bacteriuria, and all those patients were treated by cephuroxime axetil (250 mg twice a day) for a period of 5 days if the organism was sensitive, but with appropriate antibiotics if it was insensitive. Patients who had positive or negative outcome of urine culture during the routine visit control, but presented with clinical symptoms and complaints such as fever higher than 38°C, flank pain and costovertebral angle tenderness, and diagnosed with acute pyelonephritis were all admitted to the hospital, and treated with parenteral antibiotics after obtaining specimens for urine culture. These patients received sodium cephotoraxime sodium (1 gr, iv, 2x1) as treatment agent which lasted 24 hours after the appearance of clinical findings. In patients with insufficient response to the treatment, parenteral treatment was continued with appropriate antibiotics after receiving the outcome of the urine culture. In all patients who were treated in accordance with the diagnosis of acute pyelonephritis, the treatment was continued with oral antibiotics after the acute period, and those patients were evaluated again with urine culture two weeks after the end of the treatment. In this control, the pregnant women who had a positive urine culture, but no clinical symptoms were prophylactically treated with nitrofurantoin (100 mg, per-oral, 1x1) during the rest of their pregnancy, and this treatment lasted until the 37 week's gestation. Patients who had a negative urine culture before the parenteral treatment in spite of clinical diagnosis of acute pyelonephritis, as there may be some organisms like U.urealyticum ve M. hominis present other than routinely examined bacteria, they were also examined for such organisms. Mycoplasma-IST (bio Merieux, Fransa) media was inoculated in accordance with the instructions of the manufacturer and the growth was evaluated following an incubation of 24 to 48 hours at 37°C. The patients with U. urealyticum and M. hominis were treated with erytromicine (250 mg, per-oral, 4x1) for a period of 14 days.

1326 pregnant women who were included in the study were divided into two groups as with/without asymptomatic bacteriuria, and then compared in terms of overall characteristics and maternal/fetal complications. Also pregnant women who were treated due to acute pyelonephritis were evaluated in aspects of overall characteristics and complications, but no statistical comparison was made with normal pregnant women due to restricted number of cases. Only ratios reflective of our population were calculated.

Statistical analyses were made by SPSS Ver. 10.0 (Chicago, IL, ABD) programme using Fisher exact, Chi-square and matched t-test, and p<0.05 was considered statistically significant.

Results

A total of 1934 medical files were retrospectively evaluated, and 1326 pregnant women who met the study criteria were included in the study. Evaluations showed that a total of 110 (8.9%) cases had preterm delivery, 98 (7.39%) cases had preeclampsia/eclampsia, 93 (7.01%) cases had anemia, 101 (7.61%) had low birthweight and 25 (1.8%) cases had perinatal infant death. Of pregnant women included in the study, 510 (38.46%) had caesarean delivery, and the remaining 816 (61.54%) had normal vaginal delivery. Analysis of culture results showed that a total of 106 (7.99%) pregnant women had positive urine culture, and they comprised the group diagnosed with asymptomatic bacteriuria. The most common causative organism in pregnant women with bacteriuria was E. coli (84.9%) in 90 women, followed by Staphylococcus saprophyticus (5.66%) in 6 women, methicillin-resistant Staphylococcus aureus (3.77%) in 4 women, methicillin-sensitive Staphylococcus aureus (2.83%) in 3 women and other Enterobacteria (2.83%) in 3 women respectively.

Of 1326 pregnant women included in the study, comparison of 106 women whose routine
urine culture was positive, i.e. who received the diagnosis of asymptomatic bacteriuria, with 1220 pregnant women with negative urine culture in terms of demographic characteristics showed that there was no significant difference between the groups except for the educational level (p>0.05), and the educational level was significantly lower in the group of pregnant women with asymptomatic bacteriuria (p=0.032), (Table 1). When maternal and fetal complications in both groups were compared, no significant difference was observed in delivery method, incidence of preeclampsia/eclampsia, incidence of pyelonephritis and peripartum fetal death rates (p>0.05) (Table 2). However, 16.87% of pregnant women with asymptomatic bacteriuria had a preterm delivery earlier than the week 37 while this ratio was found 7.29% in the group without asymptomatic bacteriuria and intergroup Odds Ratio was calculated as 2.50 (95% confidence interval = 1.44-4.34) (p=0.001) (Table 2). When both groups were compared in the incidence of low birthweights, the intergroup Odds Ratio was found 1.98 (95% confidence interval=1.08-3.62) (p=0.024) (Table 2). Furthermore, when the incidence of anemia was compared between both groups, it was observed that the incidence of anemia was higher in pregnant women with asymptomatic bacteriuria (12.26%) than in the group without asymptomatic bacteriuria (6.55%) (Odds Ratio= 1.99) (95% confidence interval= 1.06-3.71) (p=0.027) (Table 2).

Of 106 pregnant women with diagnosis of asymptomatic bacteriuria, 65 (61.3%) came back for culture control 2 weeks after the treatment while 41 women (38.7%) didn't show up for control until the delivery. The bacteria was not isolated in 38 cultures (92.7%) following the treatment, and thus the treatment was considered succesful in these pregnant women. In the remaining two women, one had a reinfection with another microorganism, but an analysis showed that her specimen was inappropriate, therefore, it was concluded that growth of bacteria was resulting from contamination. In the other woman with persistant infection, there was a history of urinary stone.

Among 1326 pregnant women included in the study, a total of 30 (2.26%) patients were admitted to our clinic and treated with a diagnosis of acute pyelonephritis during that period. Four of those patients were among the group of patients who had positive urine culture and had been diagnosed with asymptomatic bacteriuria, and thus received prophilactic treatment. The previous urine culture was negative in the remaining 26 patients. The incidence of acute pyelonephritis was slightly higher in the group with asymptomatic bacteriuria with 3.77% compared to the group without asymptomatic bacteriuria (2.13%), but the difference was not statistically significant (Odds ratio = 1.80), (95% confidence interval=0.61-5.26), (p=0.214). Of those, the number of patients who had a positive urine culture reprocessed upon their presentation to the clinic with a diagnosis of acute pyelonephritis was 19 (63.3%). Also, in spite of clinical diagnosis of acute pyelonephritis, eight of 11 patients with a negative urine culture in the repeated test had U. urealyticum while one had M. hominis . In two patients, no growth was observed in the urine culture although the clinical findings were in com-

**Table 1.** Overall characteristics of the pregnant with and without asymptomatic bacteriuria.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>With asymptomatic bacteriuria n=106</th>
<th>Without asymptomatic bacteriuria n=1220</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years±SD)</td>
<td>26.4±4.5</td>
<td>27.2±5.6</td>
<td>0.436</td>
</tr>
<tr>
<td>Mean parity (±SD)</td>
<td>0.6±0.7</td>
<td>0.59±0.7</td>
<td>0.474</td>
</tr>
<tr>
<td>Mean educational level (years±SD)</td>
<td>7.3±3.03</td>
<td>8.8±3.44</td>
<td>0.032</td>
</tr>
<tr>
<td>Previous preterm delivery (&lt;37 hf)</td>
<td>5 (%4.71)</td>
<td>49 (%4.01)</td>
<td>0.726</td>
</tr>
<tr>
<td>Concomittant medical disorders (Diabetes etc.)</td>
<td>4 (%3.77)</td>
<td>41 (%3.36)</td>
<td>0.484</td>
</tr>
</tbody>
</table>

SD: Standard deviation
pliance with the presentation of acute pyelonephritis. Overall characteristics and complications of the pregnant women with acute pyelonephritis are shown at Table 3.

**Table 3.** General characteristics and complications of the pregnant women with acute pyelonephritis.

<table>
<thead>
<tr>
<th></th>
<th>With asymptomatic bacteriuria</th>
<th>Without asymptomatic bacteriuria</th>
<th>Odds Ratio (95% confidence interval)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm delivery (&lt;37 week)</td>
<td>18 (%16.98)</td>
<td>92 (%7.54)</td>
<td>2.50 (1.44-4.34)</td>
<td>0.001</td>
</tr>
<tr>
<td>Caesarean delivery</td>
<td>45 (%42.45)</td>
<td>465 (%38.11)</td>
<td>1.19 (0.80-1.79)</td>
<td>0.379</td>
</tr>
<tr>
<td>Preeclampsia/eclampsia</td>
<td>9 (%8.49)</td>
<td>89 (%7.29)</td>
<td>1.17 (0.57-2.41)</td>
<td>0.652</td>
</tr>
<tr>
<td>Acute pyelonephritis</td>
<td>4 (%3.77)</td>
<td>26 (%2.13)</td>
<td>1.80 (0.61-5.26)</td>
<td>0.214</td>
</tr>
<tr>
<td>Anemia (&lt;30% hematocrite)</td>
<td>13 (%12.26)</td>
<td>80 (%6.55)</td>
<td>1.99 (1.06-3.71)</td>
<td>0.027</td>
</tr>
<tr>
<td>Low birthweight (&lt;2500 gr)</td>
<td>14 (%13.20)</td>
<td>87 (%7.13)</td>
<td>1.98 (1.08-3.62)</td>
<td>0.024</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>2 (%1.88)</td>
<td>23 (%1.88)</td>
<td>1.0008 (0.23-4.30)</td>
<td>0.607</td>
</tr>
</tbody>
</table>

**Discussion**

Urinary tract infection is one of the most common medical complications of pregnancy, and it presents as asymptomatic bacteriuria in nearly 2 to 13%, and symptomatic infection in 1 to 2% of all pregnant women. Although symptomatic urinary tract infections consist of acute cystitis and acute pyelonephritis presentations, it is not easy to distinguish symptoms of cystitis and asymptomatic bacteriuria due to frequent complaints of suprapubic pain and polyuria in pregnancy. Also, infecting organisms leading to asymptomatic bacteriuria and acute cystitis are frequently different, and asymptomatic bacteria can progress into pyelonephritis, but it is not a cause of cystitis. Therefore, we considered conventional acute pyelonephritis as the presentation of symptomatic urinary infection, and pregnant women who had no or unspecific complaints and bacteriuria in the urine culture processed for screening purposes were considered having asymptomatic bacteriuria. Based on this, frequency of asymptomatic bacteriuria and acute pyelonephritis is 7.99% and 2.26% respectively in our population. In another study conducted in our country, the reported frequencies for asymptomatic bacteriuria and symptomatic urinary infection were 10.6% and 4.6% respectively. Uncu et al. found an asymptomatic bacteriuria rate of 9.3%, and also an acute pyelonephritis frequency rate of 0.5% in the group who underwent routine screening and treatment while it was 2.1% in the group without any screening. We have found a slightly higher rate of acute pyelonephritis compared to the results of Uncu et al. It may result from the detection of U. urealyticum and M. hominis induced infections that cannot be determined by routine culture processings, but by special mycoplasma culture, in nearly one third of the patients diagnosed with acute pyelonephritis.

Although it has been recently reported that a few tests like catalase activity, nitrite or Gram’s staining can be used to evaluate the urine specimen for the diagnosis of urinary tract infections, culture of moderate-sterile urine has become the golden standard in the diagnosis of bacteriuria as the specificity and sensitivity of above tests are insufficient. Only half of the pregnant women with bacteriuria are diagnosed with pyuria evaluation in
the urine alone. According to the commonly accepted description, presence of 10^5 or more CFUs of the same active microorganism per 1 milliliter of the sterile urine specimen obtained at least 2 consecutive times is necessary to make a diagnosis for asymptomatic bacteriuria. However, it has been proposed that a single urine culture from the specimen obtained during the first trimester of pregnancy would be sufficient in order to identify the frequency of bacteriuria in pregnancy and treat it, if necessary, and thus all pregnant women should be screened at least once. On the other hand, if the conditions are appropriate, and it is certain that the pregnant woman will re-visit for control purposes, it would be a better approach to confirm the diagnosis with a second urine culture in women whose urine culture was positive due to high risk of contamination. Also, it is cost effective to conduct a routine screening in populations where incidence of bacteriuria is over 2% and risk for developing acute pyelonephritis in those with bacteriuria is over 13%. Therefore, all pregnant women who present to our clinic for routine pregnancy follow-up are required to give at least one urine specimen, and we used the urine culture as a criteria in the diagnosis of urinary tract infections in our study.

E. coli is responsible for approximately 90% of urinary tract infections in sexually active women, which is followed by Staphylococcus saprophyticus. It is almost the case in pregnant women, and the most common organisms of the urinary tract infection in pregnancy include E. coli, Staphylococcus saprophyticus, Proteus mirabilis, Klebsiella pneumoniae, group B streptococci and rarely U. urealyticum and M. hominis. The most common organism in our study was E. coli, followed by Staphylococcus saprophyticus, metcillin-resistant Staphylococcus aureus, metcillin-sensitive Staphylococcus aureus and other Enterobacteria respectively, which is a parallel finding to the literature.

Many studies conducted so far reported that both inefficiently treated asymptomatic bacteriuria and acute pyelonephritis may lead to preterm delivery, low birth weight, and even perinatal death, which have been also supported by several meta-analyses. In a very recent systematic review, it has also been reported that treatment of asymptomatic bacteriuria in pregnant women with antibiotics reduced the risk for acute pyelonephritis and potential preterm delivery. As a result, in case asymptomatic bacteriuria is detected in pregnancy, it must be properly treated in order to avoid any maternal and fetal complications that may develop. We also treated all pregnant women diagnosed with asymptomatic bacteriuria. However, the ratio of preterm delivery before 37 week's gestation, delivery of neonates less than 2500 gr and anemia was higher in pregnant women with asymptomatic bacteriuria in our study. It may be associated with non-attendance of a major part of pregnant women (38.7%) who were included in the study and treated due to asymptomatic bacteriuria for the control visit after receiving the treatment until the delivery, non-attendance for control culture after the treatment or non-compliance with the treatment. It is already indicated in the literature that risk for recurrent bacteriuria is higher in a later period in spite of treatment, and it should be monitored with follow-up cultures. Also, it has been found that the educational level of pregnant women in the asymptomatic bacteriuria group is significantly lower. Therefore, it may be considered that the frequency of preterm delivery, low birthweight and anemia in this group may not be directly associated with asymptomatic bacteriuria, but it may be related with lower socioeconomic status and insufficient antenatal care.

It is well known that in case asymptomatic bacteriuria is detected in pregnancy, it should be treated, however it is still controversial which treatment agent should be used and how long the treatment should last. Based on this, a systematic review carried out in 2004 showed that although a wide variety of antibiotics has been used in the past, almost all of the agents used were effective, and no superiority has been demonstrated for any of them. Besides, the most commonly used agents are mainly penicillins and cephalosporins whose teratogenic effect has not been demonstrated yet, and β-lactam antibiotics, phosphomycin and nitrofurantoin. Such infections can be successfully treat-
ed by oral cephalosporins even tough there is a high level of resistance to penicillins in recent years. All pregnant women with bacteriuria in our study was treated by cephuroxim axetil (250 mg, twice a day for 5 days), which resulted in 92.7% success. Different results exist regarding the treatment period of asymptomatic bacteriuria in the literature. Some studies report that a single dose therapy is efficient, some others suggest three, five or seven days of treatment periods. A systematic review showed that there is not enough evidence so that it can not be exactly described, however Infectious Diseases Society of America recommends that duration of antimicrobial therapy should be 3-7 days. In our study, a successful outcome was achieved with a five-day treatment, and bacteriuria was eradicated in most of the patients (92.7%).

Acute pyelonephritis can be described as the acute, bacterial infection of the kidney presenting with tremor, fever and mostly flank pain. It has been reported that acute pyelonephritis develops in 1-2% of pregnancies, and presence of previous asymptomatic bacteriuria or any renal disease increases the risk for development of pyelonephritis, and also possibility to develop acute pyelonephritis is reduced at less than 5% in case pregnant women with asymptomatic bacteriuria are treated. In our population, the frequency of acute pyelonephritis was 3.77% in the group with asymptomatic bacteriuria and 2.13% in the group without asymptomatic bacteriuria, and no significant difference was found between the two groups. The reason for higher acute pyelonephritis rate in spite of timely treatment of asymptomatic bacteriuria may be higher non-attendance rates of patients for post-treatment controls and perhaps insufficient compliance with the therapy. But, it is difficult to interpret because of restricted number of cases. Nearly one third of the cases with acute pyelonephritis included in the study had preterm delivery, low birthweight and anemia. Hill et al. reported 8% preterm delivery, 7% low birthweight and 23% anemia in their population. Our rates for preterm delivery and low birthweight were slightly higher. However, the rate for preterm delivery was only 3% in the Hill et al. study while our rate was 16.6%. Furthermore, the rate of hypertensive pregnant women was 13.3%. Therefore, higher rates of preterm delivery and low birthweight in our group of 30 patients may not be associated with the presentation of acute pyelonephritis, but with the nature of the patient population carrying a risk for preterm delivery. We followed up the patients diagnosed with acute pyelonephritis at mean 4.5 days as inpatients, and treated them with cephalosporin group of antibiotics for 4 days, and none of the patients developed more severe maternal complications such as respiratory failure, renal failure or sepsis. Such severe complications had been reported in very high rates (21%) at the beginning of 1980s, but they were highly reduced along with improvement in the monitoring and treatment facilities in recent years.

**Conclusion**

Urinary tract infection in pregnancy is a very frequent medical problem, and if untreated on time or inefficiently treated it may lead to severe maternal and fetal complications. Therefore, all pregnant women should be screened at least once by urine culture for asymptomatic bacteriuria throughout their antenatal controls, during early pregnancy, if possible, and when the result is positive, they should be treated by oral antibiotics for a period of 3-7 days. Those women should also be followed-up for recurrent infection after the treatment by means of periodic culture processing. And pregnant women who were diagnosed with acute pyelonephritis must be treated aggressively as inpatients, and appropriate, parenteral antibiotics should be selected for treatment.

**References**


