



Asymptomatic Bacteriuria in Pregnancy: Prevalence, Antibiotic Susceptibility, and Related Demographic Factors

Lebriz Hale AKTÜN¹, Nilay KARACA², Yaşam Kemal AKPAK³

¹Medipol University Faculty of Medicine, Department of Gynecology and Obstetrics, İstanbul, Turkey

²Gaziosmanpaşa Medicalpark Hospital, Clinic of Gynecology and Obstetrics, İstanbul, Turkey

³Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Gynecology and Obstetrics, Ankara, Turkey

ABSTRACT

Objective: The aim of this study was to establish the prevalence of asymptomatic bacteriuria (ABU) in pregnancy. It is the most common urinary infection among pregnant women in our area.

Methods: Our study was conducted in 980 pregnant women. Gestational age of each woman was less than 20 weeks. Patients with any urinary tract infection symptoms, suprapubic pain, painful and frequent urination, urinary incontinence, smelly vaginal discharge indicating prolonged or recent antibiotic use, history of kidney disease or kidney stones, or gestational diabetes were excluded from this study. Urine culture and antibiogram of mid-stream urine were performed. The pregnant women diagnosed as having bacteriuria were treated with antibiotics for 7 days.

Results: There was no statistical significant association among age, gravida, parity, and sex activity in 749 pregnant women screened for ABU. Among 749, 53 pregnant women presented with ABU (7.1%). Among these 53 patients, *Escherichia coli* was the most frequently isolated microorganism that was detected in 36 women (69%). *E. coli* is sensitive to 99.3% fosfomycin and 85% cefuroxime. *Klebsiella pneumoniae*, the second most common microorganism, is sensitive to 86% fosfomycin and 100% cefepime and ceftriaxone. *Enterococcus species*, the third most common microorganism, is sensitive to 100% ampicillin and fosfomycin.

Conclusion: Pregnant women should be screened for ABU. The most appropriate period for screening is between 9 and 17 weeks of pregnancy, preferably 16. Gestational age should be measured using mid-stream urine culture. Fosfomycin is the preferred treatment because it has high sensitivity rate and is safe and easy-to-use.

Keywords: Pregnancy, asymptomatic bacteriuria, prevalence, antibiotic susceptibility, related risk factors

Introduction

Urinary tract infection is the most common bacterial infection that requires treatment in pregnancy (1). The risk of infection increases as a result of physiological and anatomical changes such as ureter dilatation during pregnancy, decrease in urethral peristalsis and bladder tonus, increase in plasma volume, decrease in urine concentration, and increase in urine estrogen and progesterone (2). Asymptomatic bacteriuria (ABU) is defined as

the presence of at least 10^5 organisms / mL in the urine culture taken from medium-flow urine in a patient without any local or systemic symptoms of the urinary tract (3). It is seen in 2-15% of pregnant women and the most important etiological agent is the coliform bacteria such as *Escherichia coli* (*E. coli*) as in non-pregnants (4).

If asymptomatic bacteriuria is not treated, it may cause either symptomatic acute cystitis at a rate of 20-40% or acute

Address for Correspondence: Nilay KARACA, Gaziosmanpaşa Medicalpark Hospital, Clinic of Gynecology and Obstetrics, İstanbul, Turkey

E-mail: karacanilay@hotmail.com

Received: 24.02.2017

Accepted: 27.04.2017

Cite this article as: Aktün LH, Karaca N, Akpak YK. Asymptomatic Bacteriuria in Pregnancy: Prevalence, Antibiotic Susceptibility, and Related Demographic Factors. Bezmialem Science 2018; 6(3): 163-7.

©Copyright 2019 by the Bezmialem Vakıf University
Bezmialem Science published by Galenos Publishing House.

pyelonephritis in the following weeks of pregnancy. Otherwise, the development rate of these clinical pictures is around 1% (5). Maternal infective status can progress to sepsis and respiratory distress. Fetal complications are undesirable clinical pictures such as premature rupture of membranes, premature birth, low-birth-weight infant and intrauterine growth retardation (IUGR) (6,7).

Biological variations and geographic localization have been thought to be the factors affecting the prevalence (5). In this prospective study, our aim is to determine the prevalence of ABU, the most common microorganism and the antibiotic susceptibility of microorganisms in pregnant women admitting to the obstetrics and gynecology clinic in our region.

Methods

Our study was carried out with 980 pregnant women who had an antenatal visit before the 20th gestational week between January 2014 and July 2016 and whose informed consents were obtained. The patients with symptoms of urinary tract infection, suprapubic pain, painful urination, frequent urination, urinary incontinence, and vaginal discharge and malodor symptoms, the patients who actively use antibiotics or have used any in the last month, the patients with a medical history of kidney disease and kidney stones, and the pregnant women with gestational diabetes were excluded from the study. Medium-flow urine samples were taken from 749 pregnant patients remaining after exclusion, and culture test was performed within 2 hours, in addition to routine antenatal tests. The culture of microorganisms in urine was done on CLED (Cystine Lactose Electrolyte Deficient) medium/MacConkey agar and blood agar using standard loop (semiquantitative method). Culture results were read 24 hours after aerobic incubation at 37°C. The samples were incubated again in a another 24 hours before a negative result. Detecting a single organism at an amount of >10⁵ organism/mL in the results was accepted as bacteriuria. The pathogens were isolated and standard antibiotic sensitivity testing was performed with *E. coli* ATCC 25922 and *S. aureus* ATCC 25923. Multiple organisms were considered as contamination and the tests were repeated. The pregnant with bacteriuria were treated for 7 days with sensitive antibiotics known to be safe in pregnancy.

Statistical analysis

Descriptive and analytical statistics were made for all patient records using IBM SPSS 21.0 (IBM Statistical Package for the Social Sciences Corp.; Armonk, NY, USA). Descriptive statistics were shown by indicating the mean±standard deviation and minimum-maximum values for the continuous measurement variables, and the numerical variables were shown as the number of cases and percentage (%). Student t test was used to determine whether there was a statistically significant difference between the groups in terms of the normally distributed continuous measurement variables, and the significance of difference in terms of the non-normally distributed continuous measurement variables was assessed with Mann-Whitney U test.

Results

The demographic characteristics of 749 pregnant women screened for asymptomatic bacteriuria are summarized in Table 1. No statistically significant difference was observed in both groups in terms of age, gravida, parity and sexual activity. Hemoglobin levels were found to be higher in the ABU patient group, although not statistically significant (Table 1).

ABU was detected in 53 (7.1%) of 749 pregnant women included in the study. *E. coli* was the most commonly isolated microorganism in 36 (69%) of the 53 pregnant women diagnosed with ABU (Table 2).

The most frequently isolated microorganism *E. coli* was found to be sensitive to phosphomycin at a rate of 99.3% and to cefuroxime, which is the most frequently used antibiotic in pregnancy, at a rate of 85%. *Klebsiella pneumoniae* (*K. pneumoniae*), the second most frequently isolated microorganism, was found to be sensitive to phosphomycin at a rate of 86% and to cefepime and ceftriaxone at a rate of 100%. *Enterococcus* sp., the third most frequently isolated gram positive microorganism, was found to be sensitive to ampicillin and phosphomycin at a rate of 100% (Table 3, 4).

Table 1: Summary of demographic data in pregnant women screened for ABU

Characteristics	Group 1 (n=53) ABU	Group 2 (n=696) ABU Negative	P
Patient age (years)	26,7±4,4	25,4±4,9	>0,05
Parity (number)	0,84 (0-5)	0,89 (0-5)	>0,05
Gravida (number)	1,95 (0-4)	2,0 (0-4)	>0,05
Hgb (g/dL)	12,9±1,2	10,9±2,1	>0,05
Latest Sexual activity (weeks)	3	3	>0,05

Mean ± SD (minimum-maximum), ABU: asymptomatic bacteriuria

Table 2: Distribution of isolated microorganisms in pregnant women diagnosed with ABU

Microorganism	n (%)
<i>Escherichia coli</i>	37 (69)
<i>Klebsiella pneumoniae</i>	8 (15)
<i>Enterococcus species</i>	4 (8)
<i>Proteus</i> spp.	1 (2)
<i>Staphylococcus aureus</i>	1 (2)
<i>Enterobacter species</i>	1 (2)
Total	53 (100)

Table 4: Antimicrobial sensitivity of isolated g(+) microorganisms

Microorganism	Antibiotic sensitivity (%)						
	Am	Phos	Pen G	Sxt	Clin	Eryt	Fm
<i>Enterococcus species</i>	100	100	100	NS	100	NS	NS
<i>Staphylococcus aureus</i>	NS	NS	0	NS	100	100	100
<i>Staphylococcus saprophyticus</i>	0	NS	0	100	100	NS	NS

Am: Ampicillin, Phos: phosphomycine, pen G: penicillin G, SXT: co-trimoxazole, Clin: clindamycin, Eryt: erythromycin, Fm: Nitrofurantoin, NS: not studied

Table 3: Antimicrobial sensitivity of isolated g (-) microorganisms

Microorganism	Antibiotic sensitivity (%)							
	Phos	Cefu	Cf	Cef	Ceft	Am	Amo/clav	Fm
<i>Escherichia coli</i>	99,3	85	86	90	91	54	63	93,2
<i>Klebsiella pneumoniae</i>	86	83	92	100	100	54	81	34
<i>Proteus spp.</i>	100	100	100	100	100	52	100	100
<i>Enterobacter species</i>	100	100	0	100	100	0	0	100

Phos: phosphomycine, Cefu: Cefuroxime, Cf: Cefazolin, Cef: Cefepime, Ceft: Ceftriaxone, Am: Ampicillin, Amo/clav: Amoxicillin /clavulanic acid, Fm: Nitrofurantoin

Discussion

In this prospectively designed study; we found the prevalence of ABU as 7.1%, the most common microorganism as *Escherichia coli* and the antibiotic to which it was most sensitive as phosphomycine in our pregnant population.

There is still no clear world-wide consensus on screening ABU in pregnant women. According to the results of a review in 2016, there was no randomized controlled trial evaluating the benefits and harms of ABU screening (2). However, the US Preventative Task Force certainly recommends screening for ABU between the 12th and 16th weeks of gestation (8). In general, this screening is found appropriate in terms of cost effectiveness when compared to complications. While the average cost for ABU was 2.20 dollars per patient, the cost for preterm birth or IUGR was found to be 40-46 dollars per case (9).

The rate of ABU was found to be 8.5% in a large-scale publication from the ABU prevalence studies performed in pregnant women in our country (4). This rate was 7.1% in our study. In the meta-analysis studies from Iran, the average rate was found as 13% (10). Urinary tract infection is observed frequently in countries with low socioeconomic status where antenatal care is not sufficient, such as African countries [14.6% (Tanzania), 11.6% (Ethiopia)] (11, 12). However, sociodemographic features were observed not to contribute to these infections in the studies performed in this region. In our study, no significant data could be found in terms of the contribution of demographic data to ABU or its being an associated risk factor (11,13).

In our country, microorganisms with similar priorities were observed in the world. In our study, *E. coli* was the first most common with a rate of 69% and *K. pneumoniae* was the second most common with a rate of 15%. Similarly; in another study

in which approximately 2000 patients were screened in our country, *E. coli* was in the first place with a rate of 76.6% and *K. pneumoniae* was in the second place with a rate of 14.6% (4). While *Escherichia coli* was the most commonly found microorganism with 37.6% in a study conducted in North India, *Enterococcus spp.* was the second most commonly observed microorganism with 21.1% (14). While the detection rate of *E. coli* was 42.4% in another study, the second most common microorganism was *Staphylococcus aureus* 39.3% (13). One of the causes for this microorganism to be the most common bacteria in bacteriuria is the fact that the increase in the concentration of estrogen in urine due to physiological changes during pregnancy plays a role in increasing the pathogenicity of *E. coli*.

If ABU is treated during pregnancy, the incidence of pyelonephritis, which may develop in the future, is reduced by 75% and the incidence of subsequent urinary tract infection is reduced by 80-90% (8). For this reason, whether symptomatic or not, bacteriuria should be treated during pregnancy (1). Antimicrobial therapy should be chosen properly for maternal and fetal safety. Due to the physiological changes in pregnant women, the dose of the selected antidiotics should be adjusted. As the rate of renal filtration increases in pregnant women, urine concentration decreases. Antibiotics with high urinary concentration and low serum concentrations are preferred (2). First of all, no treatment modality has any proven superiority according to the results of compilation and meta-analyses. Therefore, it is recommended that the clinician decides according to the price, accessibility and best side effect profile (8). In the literature, ampicillin/ amoxicillin, nitrofurantoin and oral cephalosporins are the first recommended drugs according to relatively favorable cure rates, safety and high concentrations in urine (8). As also found in our study, there was a high resistance to ampicillin and amoxicillin. Since oral cephalosporins are long treatment regimens, they can

cause continuation problems for patients (16). Nitrofurantoin has been used in pregnancy for many years. Moreover, there are obstetricians who use it as a daily dose. A one-day treatment regimen was compared with a seven-day treatment protocol in a randomized controlled trial that investigated this condition, and long-term treatment was found to be more effective (17). However; although nitrofurantoin is effective, it causes maternal hemolytic anemia in glucose 6 phosphate dehydrogenase enzyme deficiency. In addition; when the safety scale of other antimicrobial agents is examined, it should be kept in mind that tetracycline may cause fetal malformation and maternal acute liver failure, chloramphenicol may cause fetal toxicity, fluoroquinolones may cause fetal cartilage malformations and renal toxicity, and aminoglycosides may cause both maternal and fetal nephrotoxicity and ototoxicity (6,8).

When evaluated in terms of the antibiotic sensitivity tests and safety profile, the most preferred antimicrobial agent is phosphomycine (4,16). The antimicrobial agents in the FDA-approved category B (no evidence indicating risk in humans) for the treatment of lower urinary tract infections and asymptomatic bacteriuria without specific dose adjustment during pregnancy are penicillins, oral cephalosporins and phosphomycine tromethamine. The most important factor in suggesting and preferring this group is that they inhibit the synthesis of the cell wall, which does not exist in humans and exists only in the structure of bacteria (18,19). Although phosphomycine trometamol, which was first obtained from *Streptomyces* cultures in Spain in 1969 and was formerly called as phosphonomycine, has been used in the treatment of various infections for many years, it is one of the rare antibacterial agents in which the incidence of resistance remains extremely low in *Escherichia coli* strains (20). It has been distinguished from other agents with high sensitivity rates in our study, as well. In addition, it is emphasized with respect to antibiotics to be used in treatment algorithms that the antibiotics with a resistance ratio reaching 20% in the community should not be used in empirical treatment any longer (21).

One of the most important limitations of our study is that we examined the reproduction in urine culture only once. The study may be more meaningful in groups of pregnant women with ABU who have been diagnosed with the reproduction of the same microorganism in at least 2 consecutive cultures. In addition, the absence of maternal and fetal outcomes is another limitation for making interpretation.

Conclusion

ABU is a condition with high prevalence in pregnancy. Because it is also a clinical picture that presents a risk in terms of miscarriage and premature birth, it is advisable to be screened. The most appropriate screening period may be the beginning of the second trimester in order to minimize these risks. Although it is recommended to perform twice, its diagnosis can be made with at least one culture test of the medium-flow urine (22). Phosphomycine may be preferred because of its high sensitivity rate, ease of use and safety.

Ethics

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul Medipol University (10.03.2017).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions

Concept - L.H.A.; Design - L.H.A., N.K.; Supervision - N.K., Y.K.A.; Resources - L.H.A., N.K.; Materials -

L.H.A., N.K.; Data Collection and/or Processing - L.H.A.; Analysis and/or Interpretation - L.H.A., N.K., Y.K.A.; Literature Search -Y.K.A.; Writing Manuscript - Y.K.A., L.H.A.; Critical Review - N.K.

Conflict of Interest: Authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

- Macejko AM, Schaeffer AJ. Asymptomatic Bacteriuria and Symptomatic Urinary Tract Infections During Pregnancy. *Urol Clin North Am* 2007; 34: 35-42.
- Angelescu K, Nussbaumer-Streit B, Sieben W, Scheibler F, Gartlehner G. Benefits and harms of screening for and treatment of asymptomatic bacteriuria in pregnancy: a systematic review. *BMC Pregnancy Childbirth* 2016; 16: 336.
- Delzell JE, Lefevre ML. Urinary tract infections during pregnancy. *Am Fam Physician* 2000; 61: 713-21.
- Celen S, Oruç AS, Karayalçın R, Saygan S, Unlü S, Polat B, et al. Asymptomatic bacteriuria and antibacterialsusceptibility patterns in an obstetric population. *ISRN Obstet Gynecol* 2011; 2011: 721872.
- Haider G, Zehra N, Munir AA, Haider A. Risk factors of urinary tract infection in pregnancy. *J Pak Med Assoc* 2010; 60: 213-6.
- Christensen B. Which antibiotics are appropriate for treating bacteriuria in pregnancy? *J Antimicrob Chemother* 2000; 46: 29-34.
- Uncu Y, Uncu G, Esmer A, Bilgel N. Should asymptomatic bacteriuria be screened in pregnancy? *Clin Exp Obstet Gynecol* 2002; 29: 281-5.
- Guinto VT, De Guia B, Festin MR, Dowswell T. Different antibiotic regimens for treating asymptomatic bacteriuria in pregnancy. *Cochrane Database Syst Rev* 2010: CD007855.
- Rouse DJ. Potential cost-effectiveness of nutrition interventions to prevent adverse pregnancy outcomes in the developing world. *J Nutr* 2003; 133: 1640-4.
- Ghafari M, Baigi V, Cheraghi Z, Doosti-Irani A. The Prevalence of Asymptomatic Bacteriuria in Iranian Pregnant Women: A Systematic Review and Meta-Analysis. *PLoS One* 2016; 11: e0158031.
- Masinde A, Gumodoka B, Kilonzo A, Mshana SE. Prevalence of urinary tract infection among pregnant women at Bugando Medical Centre, Mwanza, Tanzania. *Tanzan J Health Res* 2009; 11: 154-9.

12. Assefa A, Asrat D, Woldeamanuel Y, Hiwot Y, Abdella A, Melesse T. Bacterial profile and drug susceptibility pattern of urinary tract infection in pregnant women at Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia. *Ethiop Med J* 2008; 46: 227-35.
13. Hamdan HZ, Ziad AH, Ali SK, Adam I. Epidemiology of urinary tract infections and antibiotics sensitivity among pregnant women at Khartoum North Hospital. *Ann Clin Microbiol Antimicrob* 2011; 10: 2.
14. Jain V, Das V, Agarwal A, Pandey A. Asymptomatic bacteriuria & obstetric outcome following treatment in early versus late pregnancy in north Indian women. *Indian J Med Res* 2013; 137: 753-8.
15. Enayat K, Fariba F, Bahram N. Asymptomatic bacteriuria among pregnant women referred to outpatient clinics in Sanandaj, Iran. *Int Braz J Urol* 2008; 34: 699-707.
16. Lumbiganon P, Laopaiboon M, Thinkhamrop J. Screening and treating asymptomatic bacteriuria in pregnancy. *Curr Opin Obstet Gynecol* 2010; 22: 95-9.
17. Lumbiganon P, Villar J, Laopaiboon M, Widmer M, Thinkhamrop J, Carroli G, et al. One-day compared with 7-day nitrofurantoin for asymptomatic bacteriuria in pregnancy: a randomized controlled trial. *Obstet Gynecol* 2009; 113: 339-45.
18. Taşbakan MI, Pullukcu H, Yamazhan T, Arda B, Ulusoy S. Comparison of in-vitro activity of fosfomycin and other antibacterials in *Escherichia coli* strains isolated from community acquired urinary tract infections. *ANKEM* 2004; 18: 216-9.
19. Lecomte F, Allaert FA. The single-dose treatment of cystitis with fosfomycin trometamol (Monuril™): an analysis of 15 controlled trials on 2048 patients. *Med Malad Infect* 1996; 26: 338-43.
20. Schito GC. Why fosfomycin trometamol as first line therapy for uncomplicated UTI? *Int J Antimicrob Agents* 2003; 22(Suppl 2): 79-83.
21. Warren JW. Practice guidelines for the treatment of uncomplicated cystitis. *Curr Urol Rep* 2001; 2: 326-9.
22. Schnarr J, Smaill F. Asymptomatic bacteriuria and symptomatic urinary tract infections in pregnancy. *Eur J Clin Invest* 2008; 38(Suppl 2): 50-7.