DOI: 10.1111/j.1365-2362.2008.02009.x

REVIEW ARTICLE

Asymptomatic bacteriuria and symptomatic urinary tract infections in pregnancy

J. Schnarr and F. Smaill

Faculty of Health Sciences, McMaster University, Hamilton, Canada

ABSTRACT

Symptomatic and asymptomatic bacteriuria is common in pregnant women. A history of previous urinary tract infections and low socioeconomic status are risk factors for bacteriuria in pregnancy. *Escherichia coli* is the most common aetiologic agent in both symptomatic and asymptomatic infection and quantitative culture is the gold standard for diagnosis. Treatment of asymptomatic bacteriuria has been shown to reduce the rate of pyelonephritis in pregnancy and therefore screening for and treatment of asymptomatic bacteriuria has become a standard of obstetrical care. Antibiotic treatment of asymptomatic bacteriuria is associated with a decrease in the incidence of low birth weight, but the methodological quality of the studies limits the strength of the conclusions that can be drawn. Debate exists in the literature as to whether treated pyelonephritis is associated with adverse fetal outcomes. There is no clear consensus in the literature on antibiotic choice or duration of therapy for infection. With increasing antibiotic resistance, consideration of local resistance rates is necessary when choosing therapy.

Keywords Asymptomatic, bacteriuria, infection, pregnancy, pyelonephritis, urinary.

Eur J Clin Invest 2008; 38 (S2): 50–57

Introduction

Although the incidence of bacteriuria in pregnant women is similar to that in non-pregnant women, the incidence of acute pyelonephritis in pregnant women with bacteriuria is significantly increased [1]. Pregnancy is a unique state with anatomic and physiologic urinary tract changes. While asymptomatic bacteriuria in non-pregnant women is generally benign, pregnant women with bacteriuria have an increased susceptibility to pyelonephritis [2]. The renal pelvis and ureters begin to dilate as early as the eighth week of pregnancy [3] and the bladder itself is displaced superiorly and anteriorly. Mechanical compression from the enlarging uterus is the principle cause of hydroureter and hydronephrosis, but smooth muscle relaxation induced by progesterone may also play a role. Smooth muscle relaxation results in decreased peristalsis of the ureters, increased bladder capacity and urinary stasis. Differences in urine pH and osmolality and pregnancy-induced glycosuria and aminoaciduria may facilitate bacterial growth [4].

Urinary tract infections in pregnancy are classified as either asymptomatic or symptomatic. Asymptomatic bacteriuria is defined as the presence of significant bacteriuria without the symptoms of an acute urinary tract infection. Symptomatic urinary tract infections are divided into lower tract (acute cystitis) or upper tract (acute pyelonephritis) infections. Cystitis is defined as significant bacteriuria with associated bladder mucosal invasion, whereas pyelonephritis is defined as significant bacteriuria with associated inflammation of the renal parenchyma, calices and pelvis [5].

Screening for and treatment of asymptomatic bacteriuria in pregnancy has become a standard of obstetric care and most antenatal guidelines include routine screening for asymptomatic bacteriuria [6–11]. Despite universal guidelines recommending screening and treatment of asymptomatic bacteriuria in pregnancy, there is an ongoing debate in the literature regarding the role of asymptomatic bacteriuria in perinatal outcomes. Similarly, controversy exists as to whether antibiotic treated pyelonephritis leads to adverse pregnancy outcomes. Although there have been many articles published on the subject, very little new evidence to address these issues has accumulated since the mid-1970s. This review, based on a critical assessment of the relevant literature, will focus on the clinical significance, diagnosis and management of both asymptomatic and symptomatic urinary tract infections in pregnancy.

Epidemiology

Urinary tract infections represent the most common bacterial infection in pregnancy. Asymptomatic bacteriuria occurs in 2–10% of all pregnancies [1]. The prevalence has remained constant and most of the recent observational studies, including those from

developing countries, report similar rates [12–18]. There is a paucity of literature on cystitis in pregnancy and an accurate prevalence is difficult to obtain. In a prospective examination of 9734 pregnant women, 7·4% of them were diagnosed as having a urinary tract infection: 5·1% with asymptomatic bacteriuria, 1·3% with acute cystitis and 1% with acute pyelonephritis [19]. The prevalence of pyelonephritis during pregnancy ranges from 0·5 to 2% [18,20–23] but was reported to be as high as 4·9% in indigenous communities in Australia [24]. Many studies have reported that pyelonephritis is more common during the second half of pregnancy [18,20,21]. This is thought to be a result of the increasing mechanical compression of the enlarging uterus. One retrospective chart review of 24 000 patients reported only 7% of cases of pyelonephritis in the first trimester, 67% in the second and third trimesters, 8% intrapartum and 19% in the postpartum period [20].

The prevalence of bacteriuria in pregnancy is closely related to socioeconomic status [1]. Turck *et al*. reported the prevalence of significant bacteriuria determined by a single catheterized urine at delivery to be 2% in non-indigent pregnant women of middle socioeconomic status compared to 6·5% of indigent patients [25].

Other factors that have shown an association with bacteriuria include a history of recurrent urinary tract infections, diabetes and anatomical abnormalities of the urinary tract [26]. The effects of other host factors, such as race, sickle cell disease, age and parity on the prevalence of bacteriuria are less clear and there is controversy in the literature [18,27–31].

A retrospective study applied logistic regression modelling to data from all prenatal care recipients who delivered during 1990–93 in selected North Carolina counties (N = 8037) [28]. The two strongest predictors of bacteriuria at prenatal care initiation were an antepartum urinary tract infection prior to prenatal care initiation [for whites, adjusted prevalence odds ratio (POR) 2·5, 95% confidence interval (CI) 0·6–9·8; for blacks, POR 8·8, 95% CI 3·8–20·3] and a pre-pregnancy history of urinary tract infection (POR 2·1, 95% CI 1·4–3·2). A similar study in the same population to identify predictors of symptomatic urinary tract infection after 20 weeks gestation also concluded the strongest predictor of pyelonephritis was prior antenatal urinary tract infections (adjusted incidence odds ratio 5·3, 95% CI 2·6–11·0) [29].

One of the biggest risk factors for symptomatic infection is asymptomatic bacteriuria. If asymptomatic bacteriuria is left untreated 30% of mothers develop acute pyelonephritis compared with 1·8% of non-bacteriuric controls [1].

Some authors suggest that screening and testing algorithms should be designed incorporating identified risk factors, including a history of previous urinary tract infections, in order to lower overall costs while improving maternal and infant outcomes [28,32]. To date, no algorithm has been prospectively evaluated.

Microbiology

The aetiologic agents associated with bacteriuria are similar in pregnant and non-pregnant women. The relatively short female urethra is frequently colonized with organisms from the gastrointestinal tract. *Escherichia coli* is the most common pathogen associated with both symptomatic and asymptomatic bacteriuria, representing 70–80% of isolates [18,19,21,33,34] but was found to be greater than 90% in one study [35]. Other organisms include other gram negative bacteria and Group B streptococcus.

Specific virulence determinants in uropathogenic strains of *E. coli* are associated with invasive infection and pyelonephritis in pregnancy. These include toxins and adhesions, pili or fimbriae that allow adherence to uroepithelial cells and prevent bacteria from urinary lavage, allowing for multiplication and tissue invasion [36]. The frequencies of virulence associated determinants are lower in *E. coli* associated with asymptomatic bacteriuria compared with pyelonephritis. Only 22% of strains of *E.coli* isolated from women with asymptomatic bacteriuria had the capacity to adhere to uroepithelial cells compared with 75% in the group of women who developed acute pyelonephritis. Adherence is the single marker most frequently associated with progression to pyelonephritis [22]. Although proposed as a means to identify a group of women at risk of invasive infection, screening for these virulent strains is still only a theoretical possibility.

Group B streptococcus (*Streptococcus agalactiae*) isolated from the urine in pregnancy has been reported to be associated with preterm rupture of the membranes, premature delivery and early onset neonatal sepsis. One small randomized trial comparing treatment of group B streptococcal bacteriuria with penicillin versus placebo found a reduction in preterm rupture of membranes and preterm delivery with treatment. In this study women were included if any colony count of group B streptococcus was isolated from the urine, suggesting that lower values than usually reported for asymptomatic bacteriuria [10^5 colony forming units (cfu)/mL] are probably important for this organism [37]. Due to the assumed heavy vaginal colonization, women with group B streptococcal bacteriuria in pregnancy should receive appropriate treatment at the time of diagnosis as well as intrapartum prophylaxis to prevent neonatal infection [38].

Anaerobic organisms and other fastidious microorganisms have been identified in the urine of a large percentage of pregnant women but the significance of these organisms isolated from the urine and perinatal outcomes is unknown [39]. At present, there is no evidence to routinely examine the urine for these organisms.

Diagnosis

Acute cystitis presents with clinical signs and symptoms of urgency, frequency, dysuria, pyuria and haematuria without evidence of systemic illness. The symptoms of frequency, urgency

and nocturia, however, are not specific for an infectious process and are commonly described by pregnant women in the absence of a urinary tract infection [40]. A study of 400 pregnant women reported urinary frequency at some stage of pregnancy in 81% of women [41]. Several studies have confirmed that urinary symptoms occur early in pregnancy and persist throughout the pregnancy [42–44].

Signs and symptoms of pyelonephritis in pregnancy are similar to those in non-pregnant women and include fever, costovertebral angle tenderness, flank pain, nausea and vomiting. In a retrospective study of 656 pregnant women, chills accompanying back pain were the presenting complaint in 82% of women. Almost all women had tenderness to percussion at the costovertebral angle [20].

A key aspect in the diagnosis of both symptomatic and asymptomatic urinary tract infections is differentiating contamination from true bacteriuria. The original criterion for diagnosing asymptomatic bacteriuria was $> 10^5$ cfu/mL of a single uropathogen on two consecutive clean catch samples, with a 95% probability that the woman has true bacteriuria. The detection of $> 10^5$ cfu/mL in a single voided midstream urine is accepted as a more practical and adequate alternative, although there is only an 80% probability the woman has true bacteriuria [45]. In non-pregnant symptomatic patients with an identified pathogen, specifically *E. coli* or *Staphylococcus saprophyticus*, a colony count of $\geq 10^2$–10^3 cfu/mL may indicate infection, but this cut-off has not been evaluated for symptomatic urinary tract infections in pregnancy [46].

Although urine cultures are expensive, require laboratory expertise and take 24–48 h for results to become available, quantitative culture remains the gold standard for diagnosis of urinary tract infection in pregnancy as the performance of rapid urine screening tests in pregnancy is poor [17,47,48]. A systematic review of eight prospective studies comparing the accuracy of any one or a combination of rapid urine screening tests with quantitative urine culture in asymptomatic pregnant patients has been reported [49]. The author concluded that the available evidence does not support the use of any screening test for asymptomatic bacteriuria among pregnant women and that no test is accurate enough to be an alternative to urine culture.

A recently reported meta-analysis of the accuracy of the urine dipstick to rule out a urine infection also included studies of pregnant women [50]. Ten studies in pregnancy were included in the subgroup analyses of accuracy of nitrites on urine dipsticks. The authors concluded that in pregnant women the accuracy of nitrites was high (diagnostic odds ratio = 165) and that a negative test for both leukocyte esterase and nitrites could rule out infection in pregnant women. Positive results, however, required confirmation. In this study women with both symptomatic and asymptomatic bacteriuria were included in the analysis.

To date there has been no prospective evaluation of a diagnostic strategy that rules out infection with a negative dipstick for nitrite and leukocyte esterase and performs culture on urine specimens that screen positive for nitrites or leukocyte esterase to confirm bacteriuria.

There is no consistent recommendation for specimen collection. A clean voided specimen with cleansing of the perineum and urethra is standard [1]. However, a study of 100 adolescent pregnant women found perineal cleansing before midstream urine did not decrease bacterial contamination of the urine cultures [51]. There is in fact little evidence to support the additional cost of collecting a clean-catch urine specimen for screening.

Screening for asymptomatic bacteriuria

There is no consensus in the literature as to the optimal timing and screening frequency for asymptomatic bacteriuria. A prospective study of 3254 pregnant women from Sweden examined the risk of acquisition of bacteriuria during pregnancy [52]. The risk of acquiring bacteriuria during pregnancy increased from 0·8% in the 12th gestational week to 1·93% at the end of pregnancy. The authors concluded the risk of acquisition was the highest between the 9th and 17th week and that the 16th gestational week was the optimal time for screening because treatment at that time would provide the greatest number of bacteriuria-free gestational weeks. In this study, a single urine specimen obtained between 12 and 16 weeks gestation identified 80% of women who ultimately had asymptomatic bacteriuria.

Although the majority of guidelines recommend a single urine culture at the first prenatal visit, two more recent prospective studies have concluded that urine should be cultured in each trimester of pregnancy to improve the detection rate of asymptomatic bacteriuria [12,16]. There has been no prospective evaluation of repeated testing during pregnancy.

Using a decision analysis, screening for and treatment of asymptomatic bacteriuria to prevent pyelonephritis has been shown to be cost effective over a wide range of estimates, although the cost benefit is diminished if the rate of asymptomatic bacteriuria is less than 2% [53,54]. These two studies evaluated a single urine culture/dipstick test. There has been no cost analysis of repeated testing in pregnancy.

Significance of bacteriuria in pregnancy

Kass *et al*. published the first randomized placebo controlled trial showing that treatment of bacteriuric pregnant women prevented pyelonephritis and avoided up to 20% of preterm deliveries [45]. Many studies followed and, combining data from more than 20 of those early descriptive studies in the 1960s, Whalley reported that symptomatic urinary tract infections occurred in 30% of patients if asymptomatic bacteriuria was untreated compared with 1·8% of non bacteriuric controls [1].

A recent meta-analysis of 11 randomized or quasi-randomized controlled trials of antibiotic versus no treatment for pregnant women with asymptomatic bacteriuria found that treatment substantially decreased the risk of pyelonephritis [Relative risk (RR) 0·23; 95% CI 0·13–0·41] [55]. Although the methodological quality of the included studies was weak, the results were highly consistent among trials and the reduction in the incidence of pyelonephritis was dramatic. Overall the number needed to treat to prevent one episode of pyelonephritis was seven (95% CI 6–8).

Epidemiological evidence also supports the relationship between the treatment of asymptomatic bacteriuria and the prevention of pyelonephritis. A prospective longitudinal study from 2000 to 2001 reported an incidence of hospitalization for acute pyelonephritis in pregnancy of 1·4%. This is less than the 3–4% rate reported in the early 1970s before screening for asymptomatic bacteriuria became routine [21].

Although there is good evidence that screening for and treatment of asymptomatic bacteriuria will decrease the incidence of pyelonephritis, the relationship between asymptomatic bacteriuria, low birth weight and preterm delivery is controversial. It is hypothesized that the mechanism of preterm labour is associated with microorganism production of phospholipase A2 and subsequent prostaglandin activation [56,57].

A meta-analysis of 17 cohort studies showed that untreated asymptomatic bacteriuria during pregnancy significantly increased the rates of low birth weight and preterm delivery, although the possibility of confounding variables limit the strength of these conclusions [58]. In contrast, the Cardiff Birth Survey, which prospectively studied 25 844 births, reported that asymptomatic bacteriuria, adjusted for demographic and social factors was not associated with preterm delivery [Odds Ratio (OR) 1·2; 95% CI 0·9–1·5] [59]. The same database, when categorized into medically indicated or spontaneous preterm births, reported a significant association between bacteriuria and medically indicated preterm birth (OR 2·03; 95% CI 1·5–2·8), but not for spontaneous preterm births (OR 1·07; CI 0·78–1·46) [60]. The authors concluded from this finding that if subclinical urinary tract infections did not progress to pyelonephritis or other renal disease, it is not associated with preterm birth.

The Cochrane Review of antibiotic treatment for asymptomatic bacteriuria in pregnancy included nine randomized or quasi-randomized controlled trials that reported the outcome of low birth weight ($n = 7$) or prematurity ($n = 3$) [55]. Antibiotic treatment was associated with a reduction in the incidence of low birth weight (RR 0·66; 95% CI 0·49–0·89) but there was no evidence of a reduction in preterm delivery (RR 0·37; 95% CI 0·10–1·36). Poor methodological quality of the studies included limits the strength of the conclusions from this meta-analysis. In the 1960s, when the majority of the original literature on asymptomatic bacteriuria was published, the standard definition of prematurity was a birth weight < 2500 g. While preterm deliveries are associated with low birth weight, some low birth weight infants are small for gestational age as a consequence of intrauterine growth retardation, for which there are many aetiologies.

Pyelonephritis in pregnancy has been associated with many perinatal complications including bacteraemia, respiratory insufficiency, anaemia, renal disease, hypertension, preterm labour and low birth weight [20,21,33,61,62]. Reports from the pre-antibiotic era are often cited in support of an association between acute pyelonephritis and premature delivery [33]. Inadequate description of the methods used in these early studies makes any evaluation of the evidence impossible and limits any conclusions that can be drawn. There is continuing controversy in the literature as to whether antibiotic treated pyelonephritis leads to adverse fetal outcomes and, in contrast to asymptomatic bacteriuria, no systematic review has examined the association between treatment of pyelonephritis and perinatal outcomes [18,21,33,63,64].

A recent longitudinal study examined the maternal complications of treated pyelonephritis in pregnancy [21]. Reported complications included anaemia (23%), septicaemia (17%), transient renal dysfunction (2%) and pulmonary insufficiency (7%). The number of preterm births < 37 weeks and birth weight < 2500 g were 5% and 7%, respectively. The rates of preterm births and birth weight < 2500 g were no different from the rest of the general obstetric population during the study period.

Treatment

There is no clear consensus in the literature on either the duration of therapy or the choice of antibiotic, and as a result practice is more likely guided by national patterns of practice and local resistance patterns than by evidence from clinical trials.

While short course therapy of asymptomatic bacteriuria has become accepted practice, the optimal duration of treatment is unknown. A Cochrane review of 10 studies and over 568 women comparing single dose treatment with 4 to 7 day treatment found the 'no cure rate' for asymptomatic bacteriuria higher for 1 day treatment than for 7 day treatment (RR 1·25, 95% CI 0·93–1·67), although the difference was not statistically significant [65]. The World Health Organization is currently conducting a large randomized controlled trial to address optimal duration of treatment in asymptomatic bacteriuria.

There has been no systematic review of which antibiotic is best for the treatment of asymptomatic bacteriuria. The antibiotic chosen should have a good maternal and fetal safety profile, excellent efficacy and low resistance rates in a given population. Although many review articles suggest antibiotic regimens for both symptomatic and asymptomatic bacteriuria in pregnancy, increasing antibiotic resistance complicates empirical regimens

Table 1 Common antibiotics for asymptomatic and symptomatic lower urinary tract infections

Common antibiotics for asymptomatic and symptomatic lower urinary tract infections	Advantages and disadvantages
Ampicillin	Advantages: No β-lactam antibiotic is known to be teratogenic [66]
	Disadvantages: High resistance rates limit its use as a single agent. Resistance to ampicillin in *E. coli* in European countries and Canada averaged 29·8%, but was as high as 53·9% in Spain [75]. Malaysia and Tanzania reported rates of resistance of *E. coli* to ampicillin of 48% and 17%, respectively [76,77]. Pharmacokinetic changes of pregnancy decrease plasma concentrations of β-lactams by up to 50% [78].
Cephalexin	Advantages: No evidence of teratogenicity [79]
	Disadvantages: Penicillins and cephalosporins are sometimes associated with allergic and at times anaphylactic reactions. Cephalexin is not active against *Enterococcus* spp. [66].
Nitrofurantoin	Advantages: Nitrofurantoin in all trimesters of pregnancy appears safe. One meta-analysis of four trials reported a non significant pooled odds ratio of any fetal malformation with nitrofurantoin of 1·29 (95% CI 0·25–6·57), although the number and quality of the studies included are limited [80]. There is a low level of resistance to nitrofurantoin among uropathogens with NCCLS data from 2000 reporting only a rate of 1% [81].
	Disadvantages: Nitrofurantoin only achieves therapeutic levels in the urine, so it cannot be used to treat pyelonephritis. Nitrofurantoin is not active against *Proteus* spp. It may cause haemolytic anaemia in patients who have glucose-6-phosphate dehydrogenase deficiency [78].
Trimethoprim-Sulfamethoxazole	Disadvantages: Based on observational and case-control data there have been concerns raised over the use of trimethoprim-sulfamethoxazole in the first trimester due to an association with neural tube and other birth defects. The evidence in the literature is however, mixed. In theory, sulfonamides should also be avoided after 32 weeks gestation because of their associated toxicity in newborns. Sulfonamides could displace bilirubin from albumin-binding sites and could cause severe jaundice leading to kernicterus. Practical evidence of this risk, however, is sparse. Acute haemolytic anaemia is another complication that could occur in newborns with glucose-6-phosphate dehydrogenase deficiency [82]. Overall rates of resistance of *E. coli* to trimethoprim-sulfamethoxazole among urinary tract isolates across the US was 16·8% but was as high as 33·3% in some states [83].

and needs to be taken into consideration for the population in question. Fluoroquinolones have been shown to impair cartilage development in animal studies. Although this adverse effect has not been described in humans, quinolones should be avoided in pregnancy. Tetracycline is not an appropriate agent to use in pregnancy because it leads to discoloration of deciduous teeth if given after 5 months gestation [66]. Table 1 reviews common antibiotics for asymptomatic and symptomatic lower urinary tract infections.

Few studies exist comparing the efficacy of different antibacterial regimens in pyelonephritis. A systematic review including nine trials with 997 pregnant women was undertaken to determine which treatment is most effective in symptomatic urinary tract infections in pregnancy [67]. The included trials compared different antibiotic classes, regimens, routes and inpatient versus outpatient treatment. As expected, because of the small sample size of all the included trials, there were no significant differences among the different antibiotic regimens regarding cure rates, recurrent infection, incidence of preterm delivery, admission to neonatal intensive care unit, need for antibiotic change and incidence of prolonged pyrexia. All regimens achieved high cure rates, and adverse events were reported in only a few women. The authors concluded because of the lack of good quality primary data and appropriate sample size, and therefore power, it is not possible to draw reliable conclusions on what is the best class, route or regimen of antibiotics to treat symptomatic urinary tract infections during pregnancy.

For pyelonephritis (after 24 weeks gestation) most authors suggest that intravenous antimicrobial therapy should be initiated empirically and continued until the patient has been afebrile for 48 hours. Conversion to oral antibiotics to complete a course lasting 10–14 days should occur before hospital discharge [68–70]. A recent meta-analysis of 14 studies examining the route of administration of antibiotics for symptomatic severe urinary tract infections that included one study with pregnant women concluded the mode of administration does not determine therapeutic success [71]. There is interest in investigating the possibility of outpatient treatment of pyelonephritis in pregnancy as a cost saving measure. If careful selection of appropriate patients is undertaken, the results of the existing trials encourage the ambulatory treatment of acute pyelonephritis in pregnancy up until 24 weeks gestation [72–74].

Common therapeutic regimens include ampicillin plus gentamicin or a cephalosporin. Ampicillin as a single agent has fallen out of favour due to high resistance rates [75–77]. The advantage of using an aminoglycoside is that high renal parenchymal concentrations are obtained but there is a theoretical risk of ototoxicity and nephrotoxicity in the fetus because the drug crosses the placenta. No congenital anomalies, ototoxicity or nephrotoxicity after *in utero* exposure to gentamicin have been reported [66].

Summary

Symptomatic and asymptomatic bacteriuria is commonly encountered in pregnant women. Previous urinary tract infections and low socioeconomic status are risk factors for bacteriuria in pregnancy. Untreated asymptomatic bacteriuria is a risk factor for pyelonephritis in pregnancy. *E. coli* is the most common aetiologic agent in asymptomatic and symptomatic bacteriuria of pregnancy and quantitative culture remains the gold standard for diagnosis. No conclusion about the association between asymptomatic bacteriuria and adverse pregnancy outcomes can be made from the available literature. The strength of the association between treatment of asymptomatic bacteriuria and acute pyelonephritis will preclude any further investigation of the effects of untreated asymptomatic bacteriuria on pregnancy outcomes. Acute pyelonephritis has associated maternal complications, but debate exists in the literature as to whether treated pyelonephritis is associated with adverse fetal outcomes. There is no clear consensus in the literature on either the duration of therapy or the choice of antibiotic for bacteriuria in pregnancy. Increasing antibiotic resistance complicates empirical regimens and local resistance rates need to be taken into consideration when deciding on therapy.

Conflict of interest

The authors have declared that there are no conflicts of interest.

Address

Department of Obstetrics and Gynecology (J. Schnarr), Department of Pathology and Molecular Medicine (F. Smaill), Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada.
Correspondence to: Fiona Smaill, Department of Pathology and Molecular Medicine, Faculty of Health Sciences, McMaster University, Room 2N16, McMaster University Medical Centre, 1200 Main Street West, Hamilton, Ontario, Canada L8N 3Z5.
Tel.: 1-905-521-2100 Ext. 76332; fax: 1-905-521-5099;
e-mail: smaill@mcmaster.ca

Received 17 January 2008; accepted 09 July 2008

References

1 Whalley P. Bacteriuria of pregnancy. *Am J Obstet Gynecol* 1967;**97**:723–38.
2 Dafnis E, Sabatini S. The effect of pregnancy on renal function: physiology and pathophysiology. *Am J Med Sci* 1992;**303**:184–205.
3 Fried AM. Hydronephrosis of pregnancy: ultrasonographic study and classification of asymptomatic women. *Am J Obstet Gynecol* 1979;**135**:1066–70.
4 Jeyabalan A, Lain KY. Anatomic and functional changes of the upper urinary tract during pregnancy. *Urol Clin North Am* 2007;**34**:1–6.
5 Connolly A, Thorp JM Jr. Urinary tract infections in pregnancy. *Urol Clin North Am* 1999;**26**:779–87.
6 National Collaborating Centre for Women's and Children's Health. Clinical Guidelines 6. Antenatal Care. Routine care for the healthy pregnant woman. London: National Institute for Clinical Excellence;2003.
7 US Preventative Services Task Force. Screening for asymptomatic bacteriuria: U.S. Preventative Services Task Force reaffirmation recommendation statement. *Ann Intern Med* 2008;**149**:43–43.
8 Nicolle LE. Screening for asymptomatic bacteriuria in pregnancy. In: *Canadian Guide to Clinical and Preventative Health Care*. Ottawa: Health Canada;1994.pp. 100–6.
9 Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis* 2005;**40**:643–54.
10 Naber KG, Bergman B, Bishop MC, Bjerklund-Johansen TE, Botto H, Lobel B *et al*. EAU guidelines for the management of urinary and male genital tract infections. Urinary Tract Infection (UTI) Working Group of the Health Care Office (HCO) of the European Association of Urology (EAU). *Eur Urol* 2001;**40**:576–88.
11 Scottish Intercollegiate Guidelines Network. Management of suspected bacterial urinary tract infection in adults. A national clinical guideline. Edinburgh: Scottish Intercollegiate Guidelines Network; July 2006.
12 Tugrul S, Oral O, Kumru P, Kose D, Alkan A, Yildirim G. Evaluation and importance of asymptomatic bacteriuria in pregnancy. *Clin Exp Obstet Gynecol* 2005;**32**:237–40.
13 Fatima N, Ishrat S. Frequency and risk factors of asymptomatic bacteriuria during pregnancy. *J Coll Physicians Surg Pak* 2006;**16**:273–5.
14 Bandyopadhyay S, Thakur JS, Ray P, Kumar R. High prevalence

of bacteriuria in pregnancy and its screening methods in north India. *J Indian Med Assoc* 2005;**103** (259–62):66.
15 Abdullah AA, Al-Moslih MI. Prevalence of asymptomatic bacteriuria in pregnant women in Sharjah, United Arab Emirates. *East Med Health J* 2005;**11**:1045–52.
16 McIsaac W, Carroll JC, Biringer A, Bernstein P, Lyons E, Low DE *et al*. Screening for asymptomatic bacteriuria in pregnancy. *J Obstet Gynaecol Can* 2005;**27**:20–4.
17 McNair RD, MacDonald SR, Dooley SL, Peterson LR. Evaluation of the centrifuged and Gram-stained smear, urinalysis, and reagent strip testing to detect asymptomatic bacteriuria in obstetric patients. *Am J Obstet Gynecol* 2000;**182**:1076–9.
18 Sharma P, Thapa L. Acute pyelonephritis in pregnancy: a retrospective study. *Aust N Z J Obstet Gynaecol* 2007;**47**:313–5.
19 Harris RE, Gilstrap LC 3rd. Cystitis during pregnancy: a distinct clinical entity. *Obstet Gynecol* 1981;**57**:578–80.
20 Gilstrap LC 3rd, Cunningham FG, Whalley PJ. Acute pyelonephritis in pregnancy: an anterospective study. *Obstet Gynecol* 1981;**57**:409–13.
21 Hill JB, Sheffield JS, McIntire DD, Wendel GD Jr. Acute pyelonephritis in pregnancy. *Obstet Gynecol* 2005;**105**:18–23.
22 Stenqvist K, Sandberg T, Lidin-Janson G, Orskov F, Orskov I, Svanborg-Eden C. Virulence factors of Escherichia coli in urinary isolates from pregnant women. *J Infect Dis* 1987;**156**:870–7.
23 Kincaid-Smith P. Bacteriuria and urinary infection in pregnancy. *Clin Obstet Gynecol* 1968;**11**:533–49.
24 Bookallil M, Chalmers E, Andrew B. Challenges in preventing pyelonephritis in pregnant women in Indigenous communities. *Rural Remote Health* 2005;**5**:395.
25 Turck M, Goffe BS, Petersdorf RG. Bacteriuria of pregnancy. Relation to socioeconomic factors. *N Engl J Med* 1962;**266**:857–60.
26 Golan A, Wexler S, Amit A, Gordon D, David MP. Asymptomatic bacteriuria in normal and high-risk pregnancy. *Eur J Obstet Gynecol Reprod Biol* 1989;**33**:101–8.
27 Savage WE, Hajj SN, Kass EH. Demographic and prognostic characteristics of bacteriuria in pregnancy. *Medicine (Baltimore)* 1967;**46**:385–407.
28 Pastore LM, Savitz DA, Thorp JM Jr. Predictors of urinary tract infection at the first prenatal visit. *Epidemiology* 1999;**10**:282–7.
29 Pastore LM, Savitz DA, Thorp JM Jr, Koch GG, Hertz-Picciotto I, Irwin DE. Predictors of symptomatic urinary tract infection after 20 weeks' gestation. *J Perinatol* 1999;**19**:488–93.
30 Baill IC, Witter FR. Sickle trait and its association with birthweight and urinary tract infections in pregnancy. *Int J Gynaecol Obstet* 1990;**33**:19–21.
31 Thurman AR, Steed LL, Hulsey T, Soper DE. Bacteriuria in pregnant women with sickle cell trait. *Am J Obstet Gynecol* 2006;**194**:1366–70.
32 Chng PK, Hall MH. Antenatal prediction of urinary tract infection in pregnancy. *Br J Obstet Gynaecol* 1982;**89**:8–11.
33 Gilstrap LC, Leveno KJ, Cunningham FG, Whalley PJ, Roark ML. Renal infection and pregnancy outcome. *Am J Obstet Gynecol* 1981;**141**:709–16.
34 McFadyen IR, Eykyn SJ, Gardner NH, Vanier TM, Bennett AE, Mayo ME *et al*. Bacteriuria in pregnancy. *J Obstet Gynaecol Br Commonw* 1973;**80**:385–405.
35 Dixon HG, Brant HA. The significance of bacteriuria in pregnancy. *Lancet* 1967;**1**:19–20.
36 Eisenstein BI, Jones GW. The spectrum of infections and pathogenic mechanisms of Escherichia coli. *Adv Intern Med* 1988;**33**:231–52.
37 Thomsen AC, Morup L, Hansen KB. Antibiotic elimination of group-B streptococci in urine in prevention of preterm labour. *Lancet* 1987;**1**:591–3.
38 Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. *MMWR Recomm Rep* 2002;**51**:1–22.
39 Gilbert GL, Garland SM, Fairley KF, McDowall DM. Bacteriuria due to ureaplasmas and other fastidious organisms during pregnancy: prevalence and significance. *Pediatr Infect Dis* 1986;**5**:S239–43.
40 FitzGerald MP, Graziano S. Anatomic and functional changes of the lower urinary tract during pregnancy. *Urol Clin North Am* 2007;**34**:7–12.
41 Francis WJ. Disturbances of bladder function in relation to pregnancy. *J Obstet Gynaecol Br Emp* 1960;**67**:353–66.
42 Stanton SL, Kerr-Wilson R, Harris VG. The incidence of urological symptoms in normal pregnancy. *Br J Obstet Gynaecol* 1980;**87**:897–900.
43 Aslan D, Aslan G, Yamazhan M, Ispahi C, Tinar S. Voiding symptoms in pregnancy: an assessment with international prostate symptom score. *Gynecol Obstet Invest* 2003;**55**:46–9.
44 Cutner A, Cardozo LD, Benness CJ. Assessment of urinary symptoms in early pregnancy. *Br J Obstet Gynaecol* 1991;**98**:1283–6.
45 Kass EH. The role of asymptomatic bacteriuria in the pathogenesis of pyelonephritis. In: Quinn EL, Kass EH, editors. *Biology of Pyelonephritis*. Boston: Little, Brown and Co;1960.pp. 399–412.
46 Stamm WE, Counts GW, Running KR, Fihn S, Turck M, Holmes KK. Diagnosis of coliform infection in acutely dysuric women. *N Engl J Med* 1982;**307**:463–8.
47 Bachman JW, Heise RH, Naessens JM, Timmerman MG. A study of various tests to detect asymptomatic urinary tract infections in an obstetric population. *JAMA* 1993;**270**:1971–4.
48 Tincello DG, Richmond DH. Evaluation of reagent strips in detecting asymptomatic bacteriuria in early pregnancy: prospective case series. *BMJ* 1998;**316**:435–7.
49 Garingalo-Molina FD. Asymptomatic bacteriuria among pregnant women; Overview of diagnostic approaches. *Phil J Microbial Infect Dis* 2000;**29**:177–86.
50 Deville WL, Yzermans JC, van Duijn NP, Bezemer PD, van der Windt DA, Bouter LM. The urine dipstick test useful to rule out infections. A meta-analysis of the accuracy. *BMC Urol* 2004;**4**:4.
51 Schlager TA, Smith DE, Donowitz LG. Perineal cleansing does not reduce contamination of urine samples from pregnant adolescents. *Pediatr Infect Dis J* 1995;**14**:909–11.
52 Stenqvist K, Dahlen-Nilsson I, Lidin-Janson G, Lincoln K, Oden A, Rignell S *et al*. Bacteriuria in pregnancy. Frequency and risk of acquisition. *Am J Epidemiol* 1989;**129**:372–9.
53 Wadland WC, Plante DA. Screening for asymptomatic bacteriuria in pregnancy. A decision and cost analysis. *J Fam Pract* 1989;**29**:372–6.
54 Rouse DJ, Andrews WW, Goldenberg RL, Owen J. Screening and treatment of asymptomatic bacteriuria of pregnancy to prevent pyelonephritis: a cost-effectiveness and cost-benefit analysis. *Obstet Gynecol* 1995;**86**:119–23.
55 Smaill F, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. *Cochrane Database Syst Rev* 2007: CD000490.
56 Gomez R, Romero R, Edwin SS, David C. Pathogenesis of preterm labor and preterm premature rupture of membranes associated with intraamniotic infection. *Infect Dis Clin North Am* 1997;**11**:135–76.
57 Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. *N Engl J Med* 2000;**342**:1500–7.

58 Romero R, Oyarzun E, Mazor M, Sirtori M, Hobbins JC, Bracken M. Meta-analysis of the relationship between asymptomatic bacteriuria and preterm delivery/low birth weight. *Obstet Gynecol* 1989;**73**:576–82.

59 Meis PJ, Michielutte R, Peters TJ, Wells HB, Sands RE, Coles EC *et al*. Factors associated with preterm birth in Cardiff, Wales. I. Univariable and multivariable analysis. *Am J Obstet Gynecol* 1995;**173**:590–6.

60 Meis PJ, Michielutte R, Peters TJ, Wells HB, Sands RE, Coles EC *et al*. Factors associated with preterm birth in Cardiff, Wales. II. Indicated and spontaneous preterm birth. *Am J Obstet Gynecol* 1995;**173**:597–602.

61 Cunningham FG, Lucas MJ, Hankins GD. Pulmonary injury complicating antepartum pyelonephritis. *Am J Obstet Gynecol* 1987;**156**:797–807.

62 Cox SM, Shelburne P, Mason R, Guss S, Cunningham FG. Mechanisms of hemolysis and anemia associated with acute antepartum pyelonephritis. *Am J Obstet Gynecol* 1991;**164**:587–90.

63 McGrady GA, Daling JR, Peterson DR. Maternal urinary tract infection and adverse fetal outcomes. *Am J Epidemiol* 1985;**121**:377–81.

64 Cunningham FG, Morris GB, Mickal A. Acute pyelonephritis of pregnancy: a clinical review. *Obstet Gynecol* 1973;**42**:112–7.

65 Villar J, Lydon-Rochelle MT, Gulmezoglu AM, Roganti A. Duration of treatment for asymptomatic bacteriuria during pregnancy. *Cochrane Database Syst Rev* 2000: CD000491.

66 Dashe JS, Gilstrap LC 3rd. Antibiotic use in pregnancy. *Obstet Gynecol Clin North Am* 1997;**24**:617–29.

67 Vazquez JC, Villar J. Treatments for symptomatic urinary tract infections during pregnancy. *Cochrane Database Syst Rev* 2003: CD002256.

68 Le J, Briggs GG, McKeown A, Bustillo G. Urinary tract infections during pregnancy. *Ann Pharmacother* 2004;**38**:1692–701.

69 MacLean AB. Urinary tract infection in pregnancy. *Int J Antimicrob Agents* 2001;**17**:273–6; discussion 6–7.

70 Delzell JE Jr, Lefevre ML. Urinary tract infections during pregnancy. *Am Fam Physician* 2000;**61**:713–21.

71 Pohl A. Modes of administration of antibiotics for symptomatic severe urinary tract infections. *Cochrane Database Syst Rev* 2007: CD003237.

72 Wing DA. Pyelonephritis in pregnancy: treatment options for optimal outcomes. *Drugs* 2001;**61**:2087–96.

73 Millar LK, Wing DA, Paul RH, Grimes DA. Outpatient treatment of pyelonephritis in pregnancy: a randomized controlled trial. *Obstet Gynecol* 1995;**86**:560–4.

74 Wing DA, Hendershott CM, Debuque L, Millar LK. Outpatient treatment of acute pyelonephritis in pregnancy after 24 weeks. *Obstet Gynecol* 1999;**94**:683–8.

75 Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. *J Antimicrob Chemother* 2003;**51**:69–76.

76 Mohammad M, Mahdy ZA, Omar J, Maan N, Jamil MA. Laboratory aspects of asymptomatic bacteriuria in pregnancy. *Southeast Asian J Trop Med Public Health* 2002;**33**:575–80.

77 Blomberg B, Olsen BE, Hinderaker SG, Langeland N, Gasheka P, Jureen R *et al*. Antimicrobial resistance in urinary bacterial isolates from pregnant women in rural Tanzania: implications for public health. *Scand J Infect Dis* 2005;**37**:262–8.

78 Christensen B. Which antibiotics are appropriate for treating bacteriuria in pregnancy? *J Antimicrob Chemother* 2000;**46** (Suppl. A):29–34.

79 Einarson A, Shuhaiber S, Koren G. Effects of antibacterials on the unborn child: what is known and how should this influence prescribing. *Paediatr Drugs* 2001;**3**:803–16.

80 Ben David S, Einarson T, Ben David Y, Nulman I, Pastuszak A, Koren G. The safety of nitrofurantoin during the first trimester of pregnancy: meta-analysis. *Fundam Clin Pharmacol* 1995;**9**:503–7.

81 Sahm DF, Thornsberry C, Mayfield DC, Jones ME, Karlowsky JA. Multidrug-resistant urinary tract isolates of Escherichia coli: prevalence and patient demographics in the United States in 2000. *Antimicrob Agents Chemother* 2001;**45**:1402–6.

82 Sivojelezova A, Einarson A, Shuhaiber S, Koren G. Trimethoprim-sulfonamide combination therapy in early pregnancy. *Can Fam Physician* 2003;**49**:1085–6.

83 Karlowsky JA, Jones ME, Thornsberry C, Critchley I, Kelly LJ, Sahm DF. Prevalence of antimicrobial resistance among urinary tract pathogens isolated from female outpatients across the US in 1999. *Int J Antimicrob Agents* 2001;**18**:121–7.