Review article

Asymptomatic bacteriuria in pregnancy

R Sivalingarajah[a] **, B Balasingham**[b] **, J C Camilas**[c]

Abstract

Asymptomatic bacteriuria (ASB) is diagnosed by the presence of a 10*5 colony-forming units (CFU) in the urine without any urinary symptoms. It commonly occurs in pregnancy with the incidence ranging from 2-10%. It poses a risk of progressing into pyelonephritis in pregnancy. Adverse fetal outcomes include preterm labor, neonatal sepsis, intrauterine growth restriction (IUGR) and neonatal death. Anatomical and physiological changes during pregnancy make pregnant women more vulnerable to ASB and subsequently symptomatic UTI. *E coli* is the commonest organism involved in ASB, followed by *Klebsilla* and *Enterobactericiae*. Evidence suggests that importance of routine screening for ASB in early pregnancy to avoid adverse fetomaternal outcomes. Reduced adverse outcomes were noted with prompt antibiotic treatment for ASB compared to untreated pregnant women with ASB. Urine culture remains as the gold standard method to diagnose ASB in pregnancy. Using urine culture as a routine screening method in Sri Lanka is limited due to financial restrictions.

Key words: asymptomatic bacteriuria, urinary tract infection, screening, pregnancy

Introduction

Urinary tract infection (UTI) occurs in all age groups and it is the commonest infection during pregnancy[1]. Specific groups of people are more vulnerable to UTI such as pregnant women and immune compromised patients[1-3]. In pregnancy, UTI could present in three ways as asymptomatic bacteria, acute cystitis or pyelonephritis. Asymptomatic bacteriuria (ASB) is defined as the presence of a 10*5 colony-forming units (CFU) in the urine without symptoms such as frequency, dysuria and loin pain[1-3]. However, it is not specific to pregnancy as non-pregnant women and adults also have a 5% incidence of ASB[4].

Pregnant women have a high risk of symptomatic UTI and complications despite having no difference in prevalence compared with non-pregnant women. In untreated pregnant women with ASB, 20-40% patients will develop pyelonephritis with negative fetomaternal outcomes[5-8]. Sepsis, acute respiratory distress syndrome and hematological abnormalities are the life

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[a] *Senior Lecturer, Department of Obstetrics and Gynaecology, University of Jaffna, Sri Lanka.*

[b] *Senior Lecturer, Department of Surgery, University of Jaffna, Sri Lanka.*

[c] *Medical Officer, Teaching Hospital Jaffna, Sri Lanka.*

Correspondence: RS, e-mail: sivalingarajahraguraman@gmail.com

https://orcid.org/0000-0001-7157-3680

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threatening consequences of complicated UTI[9,10] in maternal wellbeing. Preterm delivery, low birth weight (LBW), intrauterine growth retardation, spontaneous abortion, neonatal sepsis and perinatal mortality are the adverse consequences in fetal health. Developmental delay and mental retardation are also reported in babies with perinatal complications resulting from ASB.

Screening for ASB in first trimester of pregnancy is recommended and routinely practiced in many countries given the significant prevalence. Urinalysis test is used to screen pregnant women in Sri Lanka. Urine culture is selectively used for further evaluation on patients who are found to have bacteriuria or pyuria in urinalysis. Early diagnosis and intervening at the right time by starting antibiotics would strongly prevent maternal-fetal complications[11-13].

Methods

Studies regarding ASB in pregnancy were searched from EMBASE, PubMed, Google Scholar and LILACS electronic databases. These include prospective and retrospective cohorts, systemic reviews and meta-analysis, randomized controlled trials and guidelines from recommended professional bodies. Titles and abstracts were screened for the inclusion criteria. Of the articles that met inclusion criteria, key articles were reviewed by reading full texts. Narrative synthesis was performed by investigators after a critical appraisal of the literature. Each investigator has an equal contribution.

Epidemiology

The prevalence of ASB ranges from 2 to 10%. It changes with maternal age, educational status, gestational age and population. In Sri Lanka, ASB prevalence was reported at 3.6% in 2012[6]. Since then, no other studies were carried out to evaluate the prevalence and impact of ASB in pregnancy in Sri Lanka. There was a study done by Akerele et al, yielded the prevalence of ASB as high as 86.6% [24]. Given the high incidence of ASB in pregancncy evidenced by many studies, antibiotic treatment is warranted to avoid unfavorable fetomaternal outcomes.

Risk factors and pathophysiology

Usually, the urinary tract is sterile. ASB occurs if organisms gain access to ascending urethra and actively proliferate. Short urethra, easy contamination from fecal flora due to anovaginal proximity and absence of antibacterial prostatic secretions make women more vulnerable to UTIs than males. Extreme ages of the mother, poor socioeconomic status, low educational status, poor perineal hygiene, multiparty and maternal diseases such as diabetes or sickle cell disease are risk factors specific for UTI in pregnancy [16,17].

Past history of UTI, sexual activity, urethral instrumentation, and anatomical abnormalities of urinary tract are also considered as general risk factors for UTI[15]. The immune system is subjected in favor of the embryo's implantation and development during pregnancy, leading to a reduction in maternal immunity[16]. Physiological and anatomical changes involves the entire urinary tract during pregnancy. These changes increase the risk of UTI. Mild enlargement of kidney occurs in pregnancy and it leads to subsequent rise in glomerular filtration and urinary clearance.

Also, volume and capacity of bladder is increased and detrusor tone is reduced. 90% of pregnant women develop ureteric dilatation and reduced peristalsis due to the combined effect of progestogenic relaxation of ureteric smooth muscle and pressure effect from gravid uterus[5]. The left ureter is spared from this effect due to protection from the sigmoid colon and upper rectum[17]. Obstruction to bladder outflow occurs due to gravid uterus causing stasis of urine. Physiological and anatomical changes in pregnancy play an indispensable role in the entry and multiplications of microorganisms. Therefore, increased urinary stasis, compromised ureteric valves and vesicoureteral reflux predispose to UTI in pregnancy[20]. Though these risk factors are established for UTI, considering these as risk for ASB remain controversial.

Complications

Untreated asymptomatic bacteriuria was associated with adverse maternal and fetal outcomes[19]. Maternal adverse outcomes are symptomatic cystitis (up to 30%), pyelonephritis (up to 50%) and sepsis[19]. Adverse fetal outcomes are preterm labor, delivery, prematurity, low birth weight and increased perinatal mortality[20,21]. In addition, there are increased maternal risks for preeclampsia, anemia, chorioamnionitis and postpartum endometritis[17,21,22]. Also fetal growth restriction, stillbirth, perinatal mortality, mental retardation and developmental delay are the other risks associated with ASB[18,23].

Organisms

Organisms are colonized in the urinary tract and periurethral areas cause ASB in pregnancy. As reported by previous studies, colonizers may vary depending on the host defenses and status. The most common organisms causing ASB are *Escherichia coli, Klebsilla, Proteus, Streptococcus faecalis, Candida albicans, Staphylococcus epidermidis* and *Pseudomonas aeruginosa*. In most studies, *Escherichia coli* remains the commonest organism (60-80%), while *Klebsilla* is the second most commonest[23-25]. Group B hemolytic streptococci are less frequently isolated from vaginal swabs but, it remains clinically significant[27]. Vaginal colonization with group B streptococci is strongly associated with preterm rupture of membranes, labor and delivery and is a proven cause of neonatal sepsis. However, treatment of urinary group B streptococcal infection reduces these complications[27].

Screening methods

Several professional bodies recommend screening for ASB in various gestational periods[32]. Commonly using screening methods in pregnancy are urinalysis, urine dipstick test and urine culture. Urine culture remains the gold standard for diagnosing ASB. However, it has limitations as high cost, the need for a laboratory, and long duration to yield results. On the other hand, urine dipstick tests are easy, rapid, and cost-effective. Urinalysis and urine dipstick lacks sensitivity (86%) and can result in false-negative values[32]. However, both can be used as an initial screening method to identify vulnerable patients. Subsequently, urine culture is done selectively in patients. Other urine-based screening tests include the interleukin-8 test, rapid enzymatic test, chromogenic limulus amoebocyte lysate assay, semi-automated urine screen. Dip-slide quantitative kit. These are not recommended as screening tools for ASB in pregnancy[29].

Treatment

Prompt use of antibiotics for ASB in pregnancy is warranted for favorable fetomaternal outcomes and reduction of perinatal complications. Robust evidence recommend that appropriate antibiotic treatment schedules are directed by urine culture and sensitivity testing are continued for at least seven days[32,33]. Several studies have tested shorter treatment courses and even single-dose regime to improve patient compliance and reduce side effects with adequate treatment efficiency[29,30]. Successful treatment is confirmed by follow up negative urine cultures. Several studies have demonstrated that the choice of antibiotics depends on the sensitivity of the causative organisms[13].

However, amoxicillin and cephalosporins remain sensitive to uropathogens and safe to be used in pregnancy[31]. Cephalexin 500 mg three times per day is effective against most organisms[11,29,31]. Nitrofurantoin 100 mg thrice daily and trimethoprim 200 mg twice a day are other safe alternatives. Using Nitrofurantoin in the last few weeks of pregnancy carries a theoretical risk of neonatal hemolytic anemia and trimethoprim should be avoided in the first trimester due to its anti-folate action[29].

Studies regarding ASB

Author	Results and conclusion
Akerele et al (2011) n=500	*Results* – ASB was found in 86.6% of pregnant women. *Staphylococcus aureus* (29.8%), *Escherichia coli* (29.1%), and *Klebsilla pneumonia* (21.5%) were the most isolated pathogens. *Conclusion* – Rational therapy of ASB in pregnant women may prevent associated risks such as pyelonephritis and preeclampsia.
Anayet et al (2007) n=1800	*Results* – ASB prevalence 12% among pregnant women in rural area of Bangladesh. *E.coli* was the common causative organism. *Conclusion* – Pregnant women with ASB were more prone to develop symptomatic bacteriuria and hypertensive disorders during pregnancy and preterm delivery.

(Continued)

Annie et al (2013) n=107	*Results* – Prevalence of ASB in our study was 13.2%. The significant isolates were *Klebsilla pneumonia* and *E.coli*. Most common risk factor was previous history of urinary tract infection. *Conclusion* – Screening of pregnant women for ASB at the first prenatal checkup helps to analyze the associated factors and prevents its effects on pregnancy.
Chandel et al (2012) n=463	*Results* – Significant bacteriuria was present in 7.34% of cases. The most common etiological agent was *E. coli*, followed by other gram-positive and gram-negative organisms. *Conclusion* – ASB is a common occurrence which should be diagnosed and treated in early pregnancy, due to its adverse effects on pregnancy.
Girish Babu et al (2011) n=1000	*Results* – ASB incidence was 10%. *E Coli* was the most predominant organism, followed by *Klebsilla pneumonia.* *Conclusion* – Asymptomatic bacteriuria is not uncommon among antenatal patients in the population studied. Routine urine cultural tests should be carried out on all antenatal patients to identify any unsuspecting infection.
Jenifer Perera et al (2012) n=250	*Results* – Prevalence of ASB was 3.6%. 67% of the etiological agents belonged to the coliform group, and the balance of 33% were staphylococci. All isolates were sensitive to nitrofurantoin. *Conclusion* – It is recommended to screen pregnant mothers early in their pregnancy and treat those with significant bacteriuria as this could significantly minimize adverse maternal and fetal outcomes.
Paul et al (2010) n=1228	*Results* – Prevalence of ASB was 45.3%. *Escherichia coli* was the most predominant organism, followed by *Staphylococcus aureus*. *Conclusion* – ASB is not uncommon among antenatal patients in the population studied. Routine urine culture should be carried out on all antenatal patients to identify any unsuspecting infection.
Siti et al (2013) n=170	*Results* – Prevalence of ASB in the study was 4.1%. The organisms isolated were *Klebsilla species* (2.94%) and *Escherichia coli* (1.18%). These bacteria were both sensitive to amoxicillin, vancomycin, tetracycline and erythromycin. *Conclusion* – Brunei has a similar prevalence of asymptomatic bacteriuria to other Southeast Asian countries.
Vaishali et al (2011) n=371	*Results* – ASB was found in 17 per cent of pregnant women till 20 weeks and in 16% between 32 to 34 weeks gestation. *Conclusion* – Early detection and treatment of ASB during pregnancy prevents complications like PET, IUGR, PTL, PPROM and LBW. Therefore, screening and treatment of ASB may be incorporated as routine antenatal care for safe motherhood and a healthy newborn.

Conclusion

Pregnant women have a serious risk of developing pyelonephritis due to ASB compared with non-pregnant women. Apart from the common risk factors for UTI, physiological and anatomical changes in the urinary tract play a pivotal role in increasing UTI incidence in pregnancy. Urine culture is a preferred screening tool over urine dipstick test and UFR to identify ASB precisely. Untreated ASB and UTI in pregnancy have adverse maternal and fetal outcomes. Evidence has suggested that routine screening for ASB in early pregnancy with prompt use of appropriate antibiotics reduces unfavorable maternal and fetal complications. Due to the heterogeneity of available evidences on ASB, multiple center studies are needed involving large sample size in Sri Lankan population.

Conflicts of interest

None.

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