The Prevalence of Asymptomatic Bacteriuria in Pregnant Hong Kong Women

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Objectives: To determine the prevalence, causating agents, and associated factors of asymptomatic bacteriuria in Hong Kong pregnant women.
Methods: This was a 6-month prospective cross-sectional epidemiological study carried out in a Hong Kong public hospital from 2 December 2011 to 2 June 2012. Pregnant women, who were Hong Kong residents, attending their first antenatal visit without symptoms of urinary tract infection and able to give written consents were recruited. A mid-stream urine sample was collected from each recruited subject and sent for microscopy and culture to the Department of Microbiology, Queen Elizabeth Hospital, Hong Kong.
Results: Of a total of 1537 urine samples, 87% were collected in the first trimester. On culture of all the samples, 8.3% (95% confidence interval [CI], 6.9-9.7%) were found to yield borderline growth (10^{4-5} colony-forming unit [CFU]/ml), and 2.0% (95% CI, 1.4-2.9%) yielded significant growth ($>10^5$ CFU/ml). For borderline growth, *Staphylococcus* species constituted the most common isolate (42%), followed by *Streptococcus* species (24%). While for patients with significant growth, the most common isolates were *Escherichia coli* (33%), followed by *Streptococcus agalactiae* (21%). Neither age, parity, gestation, education level, or recent sexual activity were definitively associated with asymptomatic bacteriuria.
Conclusion: Among local pregnant women, asymptomatic bacteriuria is common during the first trimester. For patients with significant growth, the common isolates were *Escherichia coli* and *Streptococcus agalactiae*, both of which are associated with potential risks in pregnancy.
Hong Kong J Gynaecol Obstet Midwifery 2013; 13(1):40-4

Keywords: Bacteriuria; Escherichia coli*; Mass screening; Pregnancy;* Streptococcus agalactiae

Introduction

Asymptomatic bacteriuria (ASB) is generally defined as the presence of significant bacteriuria without symptoms of an acute urinary tract infection (UTI). Such ASB is the most common bacterial infection considered to require medical treatment during pregnancy[1].

According to the literature, the prevalence of ASB in pregnancy is 2 to 11%[2]. Associated factors include a history of recurrent UTI, diabetes, anatomical abnormalities of the urinary tract[3], low socioeconomic status[4], and lower levels of education[5]. Multiparity and third trimester of pregnancy are also associated with a higher frequency of bacteriuria[6].

A relationship between ASB in pregnancy with symptomatic UTI and adverse pregnancy outcomes was first suggested by Kass[7] in 1959. He based this inference following his placebo-controlled trial, which showed that treatment of bacteriuric pregnant women prevented pyelonephritis and appeared to avoid up to 20% of preterm deliveries. Whalley[8] showed that symptomatic UTI occurred in 30% of patients, if ASB was untreated as compared with 1.8% in non-bacteriuric controls. A Cochrane review indicated that antibiotic treatment for ASB in pregnancy was effective in reducing the risk of pyelonephritis (risk ratio [RR]=0.23; 95% confidence interval [CI], 0.13-0.41) and low birth weight (RR=0.66; 95% CI, 0.49-0.89), but no difference in preterm delivery rate was evident[9].

Screening and aggressively treating pregnant women with ASB appears to significantly decrease the annual incidence of pyelonephritis during pregnancy and hence also the incidence of preterm births[9]. According to the *Clinical guideline on Antenatal Care* by the National Collaborating Centre for Women's and Children's Health

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in the United Kingdom, "women should be offered routine screening for asymptomatic bacteriuria by midstream urine culture early in pregnancy"[10]. The guideline also stated that "Identification and treatment of asymptomatic bacteriuria reduces the risk of pyelonephritis". However, in the *Guidelines on Antenatal Care* published by The Hong Kong College of Obstetricians and Gynaecologists in 2008[11], routine screening for ASB was considered controversial, because there were no local data to support or refute such routine screening.

In the absence of local data to date, the current study set out to determine the prevalence of ASB in pregnancy, its causative agents and associated factors in the Hong Kong population. The information gained might therefore help to determine whether screening for ASB should be included in the course of routine antenatal care in our locality.

Methods

Study Population

This 6-month (2 December 2011 to 2 June 2012) prospective cross-sectional epidemiological study was carried out in the Department of Obstetrics and Gynaecology at Queen Elizabeth Hospital (QEH), Hong Kong. Ethical approval was obtained from the Research Ethics Committee (Kowloon Central/Kowloon East) of the Hospital Authority. The targeted pregnant women (who were Hong Kong residents) attended the antenatal clinic at QEH for their first antenatal visit. Attendees without symptoms of acute UTI were interviewed, and those who gave informed consent were enrolled into the study. Information about their age, education level, parity, gestation, history of UTI or renal tract disease, and any sexual intercourse the day before they attended the clinic were recorded.

The following patients were excluded from this study: those who refused or were unable to give written consent, those with a history of UTI in the recent 6 months, those with a history of renal disease (e.g. renal stone, abnormal renal function, urinary tract anatomical abnormalities), those with a history of recurrent UTI (i.e. 3 or more episodes a year), and patients taking any long-term antibiotic treatment for a medical condition.

Patients were considered as having ASB if their midstream urine (MSU) samples yielded no white cells on microscopy but borderline (10^{4-5} colony-forming unit [CFU]/ml) or significant ($>10^5$ CFU/ml) growth on culture. These criteria differed from most studies, which defined ASB as $>10^5$ CFU/ml growth on culture without white cells on microscopy. This study also looked at the prevalence of patients with MSUs showing borderline (10^{4-5} CFU/ml) growth on culture to compare with rates in previous studies[12,13]. The latter studies showed that even culture counts of $<10^5$ CFU/ml may cause lower or upper UTIs in immunocompromised and special patient groups (e.g. those having long-term catheters). Even being pregnant may be considered to be a relatively immunocompromised state, for which reason it is important to investigate the prevalence and outcome of treating patients having ASB with culture counts of 10^{4-5} CFU/ml.

This is particularly important for pregnant women who have asymptomatic group B streptococcal (GBS) bacteriuria. Anderson et al[14] showed that there was evidence of a rank correlation between GBS colony counts and the grade of chorioamnionitis (p=0.02). Thus, whereas the treatment of women with colony counts of $>10^5$ CFU/ml is a generally accepted and recommended strategy, it is also important to consider treatment for GBS bacteriuria at lower colony counts.

Collection and Analysis of Sample

A well-labelled sterile universal boric acid container was given to each participant to collect about 20 ml of an MSU. Each participant was advised to clean the perineum before collection of the sample. The specimen was transported to the Department of Microbiology, QEH for processing on the day of collection. If the culture result showed mixed growth suggestive of contamination or organisms with 10^{3-4} CFU/ml or less, a repeat MSU was requested from the patient. The laboratory (no. 14238) processing these samples was accredited by the National Association of Testing Authorities, Australia (NATA)/ Royal College of Pathologists of Australasia.

This particular study was based on previous research[15], which showed that in non-pregnant asymptomatic patients with an identified pathogen (specifically *Escherichia 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 UTI in pregnancy.

If there were white cells seen evident on microscopy with a culture growing of $>10^5$ CFU/ml in the MSU, the patient was deemed to have a UTI and treated with a course of antibiotics depending on culture and sensitivity results. These patients were instructed to provide a repeat MSU for culture and sensitivity 1 week after their antibiotic treatment.

Statistical Analysis

The sample size calculation was based on the assumption that the prevalence of ASB in the local population is around 10% and was chosen so that the 95% CI for the proportion would have a total width of 10% (±5% on either side). It was assumed that around 50% of the subjects who were recruited might default follow-up and not send the MSU for investigation. Therefore, it was planned to recruit 1000 to 1200 subjects for this study. The annual delivery rate in the Department of Obstetrics and Gynaecology at QEH was around 6000. Thus, recruitment for around 1200 subjects was expected to take around 3 to 6 months. All the data obtained were analysed using the Statistical Package for the Social Sciences (Windows version 15.0; SPSS Inc, Chicago [IL], US).

Results

In all, 1537 urine samples were collected and analysed for bacteriuria using microscopy, culture, and sensitivity testing. A total of 127 samples (8.3%; 95% CI, 6.9-9.7%) yielded borderline growth (10^{4-5} CFU/ml) and 31 samples (2.0%; 95% CI, 1.4-2.9%) yielded significant growth (>10^5 CFU/ml) on culture. The point prevalence of significant and borderline ASB among pregnant women seen in our study population was 10.3% (95% CI, 8.8-11.9%).

Table 1 shows the socio-demographic characteristics of the pregnant patients with and without ASB in our study. Their mean ages were 32 (standard deviation [SD], 5; range, 19-44) years and 32 (SD, 5; range, 17-45) years for patients with and without ASB, respectively. No statistical significance was observed between the mean ages of the groups (p=0.835). There was no particular trend in ASB within patients, with respect to differences in parity (p=0.540) or gestation (p=0.652). Moreover, there was no significant association between ASB in pregnancy and education levels (p=0.099) or recent sexual activity (p=0.798).

A total of 158 samples yielded borderline (10^{4-5} CFU/ml) or significant (>10^5 CFU/ml) growth on culture, among which 141 yielded one organism and 17 yielded two organisms. No specimen yielded more than two organisms. Thus, these 158 MSU samples yielded a total of 175 organisms. Table 2 shows the frequency of isolates in this study. Among MSUs with borderline growth (culture count of 10^{4-5} CFU/ml), over 40% were *Staphylococcus* species and over 20% were *Streptococcus* species. For MSU samples with a significant culture count (>10^5 CFU/ml), 33% were *E. coli* and 21% were *Streptococcus agalactiae*.

Table 1. Socio-demographic characteristics of pregnant patients in a public hospital with and without asymptomatic bacteriuria (ASB)*

Characteristic	No. (%) of subjects		p Value†
	With ASB	Without ASB	
Age-group (years)			0.835
<16	0 (0)	0 (0)	
16-20	1 (7.7)	12 (92.3)	
21-25	13 (9.8)	119 (90.2)	
26-30	45 (9.2)	442 (90.8)	
31-35	66 (11.0)	536 (89.0)	
36-40	27 (10.2)	237 (89.8)	
>40	6 (15.4)	33 (84.6)	
Parity			0.540
0	91 (9.7)	852 (90.3)	
1	58 (12.0)	424 (88.0)	
2	7 (7.6)	85 (92.4)	
3	2 (11.8)	15 (88.2)	
4	0 (0)	3 (100)	
Gestation (weeks)			0.652
$4\text{-}11^{+6}$	142 (10.5)	1204 (89.5)	
$12\text{-}27^{+6}$	15 (8.4)	164 (91.6)	
≥28	1 (8.3)	11 (91.7)	
Education level			0.099
Primary	1 (5.3)	18 (94.7)	
Secondary	66 (8.8)	688 (91.2)	
Tertiary	91 (11.9)	673 (88.1)	
Sexual activity			0.798
With coitus	55 (10.6)	466 (89.4)	
Without coitus	103 (10.1)	913 (89.9)	

* ASB was defined as a midstream urine yielding borderline (10^{4-5} CFU/ml) or significant growth (>10^5 CFU/ml) on culture

† Pearson Chi-square tests

Discussion

In this study, the point prevalence of significant and borderline ASB (i.e. with culture count of >10^4 CFU/ml) in pregnancy was 10.3%. The highest prevalence rate (15%) was found among subjects aged 40 years or above, which was similar to the findings of Turpin et al[16], whose highest rate of 13% was reported in the age-group of 35 to 39 years.

In contrast to previous studies[17-19] showing that the occurrence of bacteriuria during pregnancy increases with later trimesters, in multiparity and with sexual activity, we did not find any significant association with these parameters. This may have been because the majority (87%)

Table 2. Frequency of isolates in patients with asymptomatic bacteriuria, with borderline (10^{4-5} CFU/ml) or severe (>10^5 CFU/ml) growth on culture

Isolates	No. (%) of isolates*	
	Culture count >10^5 CFU/ml (n=33)	Culture count of 10^{4-5} CFU/ml (n=142)
Staphylococcus species	0 (0)	59 (42)
Streptococcus species	0 (0)	34 (24)
Enterococcus species	1 (3)	15 (11)
Escherichia coli	11 (33)	1 (1)
Streptococcus agalactiae	7 (21)	2 (1)
Coliform organisms	1 (3)	8 (6)
Coagulase-negative *Staphylococcus*	2 (6)	6 (4)
Candida species	0 (0)	5 (4)
Candida albicans	0 (0)	4 (3)
Gram-negative bacilli	0 (0)	4 (3)
Klebsiella species	2 (6)	1 (1)
Staphylococcus aureus	1 (3)	2 (1)
Lactobacillus species	2 (6)	1 (1)
Alpha-haemolytic *Streptococcus*	2 (6)	0 (0)
Non-haemolytic *Streptococcus*	2 (6)	0 (0)
Acinetobacter species	1 (3)	0 (0)
Beta haemolytic *Streptococcus*	1 (3)	0 (0)
Total	**33**	**142**

* 141 Samples yielded one organism and 17 samples yielded two organisms on culture, which makes a total of 175 isolates yielded in 158 samples

of our samples were collected during the first trimester and only 0.8% were collected in the third trimester. Repeat MSU screening at later trimesters may help to better investigate possible associations with gestation and ASB.

The close association between ASB and low socioeconomic status has been documented in previous studies[16,20,21], but no such association was noted by us.

This was the first study of its kind to be performed in local Hong Kong population. Differences from what was described in previous literature can be attributed to a multitude of factors[22-24]. They include geographical variation, ethnicity, and study settings (primary care, community-based, or in hospitals). Moreover, variations could also have been due to differences in screening tests (urine dipstick [sensitivity, 8.18-50.0%], microscopy [sensitivity, 25%], culture [different cut-off of bacterial counts, e.g. 4.7% in Canada[2] and 8.1% in Turkey[25] for culture count >10^5 CFU/ml]). Notably, the prevalence of ASB in a study from Nigeria was 21%, using >10^3 CFU/ml as a significant level of bacteriuria[6].

For the borderline growth (culture count of 10^{4-5} CFU/ml) group, in this study the *Staphylococcus* species accounted for the most commonly encountered (42%), followed by the *Streptococcus* species (24%). Their presence may have been due to contamination from skin flora. While for ASB patients with significant growth (culture count >10^5 CFU/ml), the most common isolates were *E. coli* (33%), which was consistent with a previous study in Turkey[25]. In pregnancy, *E. coli* bacteriuria is important because certain specific uropathogenic strains of *E. coli* produce toxins and adhesins, and pili or fimbriae that allow adherence to uroepithelial cells and interfere with urinary lavage of bacteria. These are known to be associated with invasive infections and pyelonephritis in pregnancy[26].

This study also shows that the point prevalence of ASB with significant and borderline growth of *S. agalactiae* was 0.6% in the local population. Of 1537 patients, seven and two patients had significant and borderline growth, respectively. Its isolation from the urine in pregnancy reflects heavy vaginal colonisation. For these patients, intrapartum antibiotics should be given to prevent early-onset neonatal GBS disease. In which case, routine GBS screening at 35 to 37 weeks gestation could be omitted.

Further studies should nevertheless be carried out to compare the sensitivity of GBS colonisation using MSU screening with routine screening based on vaginal/rectal swabs at 35 to 37 weeks of gestation.

This study did not investigate the outcome of patients with ASB as compared with the controls, for which further studies are necessary and the impact of treating ASB should also be explored. Another limitation of this study was that repeat screening was not done in later trimesters. A previous study[25] showed that women with no bacteriuria in their initial examination in the first trimester nevertheless developed bacteriuria in later trimesters, for which reasons further studies to investigate this phenomenon are needed. Conceivably, repeat screening in the second and third trimesters might help to improve outcomes.

ASB is the major risk factor for developing symptomatic UTI during pregnancy and may be associated with adverse effects such as pyelonephritis and preterm birth. Although no definite associated factors were found in this study, most asymptomatic UTIs develop in women with bacteriuria early in pregnancy. Hence, screening for ASB and subsequent treatment appears indicated (preferably during the first trimester and at the first antenatal visit). Repeat screening for ASB should also be considered in the second and third trimester.

In conclusion, the point prevalence of borderline and significant ASB during the first trimester in a local Hong Kong population was 10.3%, with an 8.3% yield for borderline growth (10^{4-5} CFU/ml) and a 2.0% yield for significant growth (>10^5 CFU/ml). For borderline growth, *Staphylococcus* species were the most common isolates (42%), followed by *Streptococcus* species (24%). While for patients with significant growth, the most common isolates were *E. coli* (33%), followed by *S. agalactiae* (21%). Age, parity, gestation, education level, and recent sexual activity were not definitively associated with ASB in this Hong Kong population in our locality.

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