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Incidence of Asymptomatic Bacteriuria in a Local Pregnant Population

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ABSTRACT

Introduction: *Asymptomatic bacteriuria occurs in 2 to 10% of pregnancies. Clinical guidelines recommend routine antenatal screening of asymptomatic bacteriuria due to its association with increased risk of pyelonephritis, preterm labor and low birth weight. Routine screening of asymptomatic bacteriuria is not practiced in our institution. There is no local study on the prevalence of asymptomatic bacteriuria. This is a pilot study that aims to define the local incidence of asymptomatic bacteriuria and its associated adverse outcomes in our population.*

Methods: *This is a retrospective study in a tertiary obstetrics and gynecology center in Singapore between October 2017 and August 2018. Urine dipstick for albumin, urine microscopy and urine culture with sensitivity were performed. A positive urine culture was defined when more than 10^5 bacteria per milliliters is present in a single voided midstream urine. Outcomes of interest were low birth weight, preterm delivery and admission for pyelonephritis.*

Results: *Fifty patients had antenatal urine studies performed during this period. Asymptomatic bacteriuria was detected in 6% (n = 3). None of these cases had complications of low birth weight, preterm delivery or admission for pyelonephritis. The BMI of patients with asymptomatic bacteriuria was found to be statistically significantly higher than the group without (28.7 ± 1.7 vs 22.9 ± 4.7 kg/m2, p = 0.04). There was no significant difference in outcomes between the group with asymptomatic bacteriuria and the group without.*

Conclusion: *The incidence of asymptomatic bacteriuria is consistent with international data. There were no adverse outcomes detected among these patients.*

Keywords: Asymptomatic bacteriuria, pregnancy, screening, urine culture

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INTRODUCTION

Asymptomatic bacteriuria is defined as the presence of more than 10^5 bacteria per millilitres of freshly voided urine specimen without symptoms of urinary tract infection. [1] This is estimated to occur in 2 to 10% of pregnancies. [2,3] Most clinical guidelines including the US Preventive Services Task Force (USPSTF), The Obstetrician and Gynaecologist (TOG), and The National Institute for Health and Care Excellence (NICE) recommend routine antenatal screening of asymptomatic bacteriuria due to its association with increased risk of pyelonephritis (up to 50%), preterm labor and low birth weight (<2500 grams). [4,5,6] However, these recommendations are based on earlier studies dating back to the period from the 1960s to 1980s. A recent multi-centre prospective cohort study in the Netherlands by Kazemier et al which showed

only 5% of women tested positive for asymptomatic bacteriuria. [7] While there was an increased risk of pyelonephritis in women with untreated asymptomatic bacteriuria, the absolute risk is low at 2.4%. The study was terminated early as the incidence of pyelonephritis was much less than expected. [7] A cost analysis study by Wadland et al concluded that screening of asymptomatic bacteriuria would be justified if the risk of asymptomatic bacteriuria is more than 2% and the risk of pyelonephritis with asymptomatic bacteriuria is more than 13%. [8]

At present, routine antenatal screening for asymptomatic bacteriuria is not practiced in our institution. There is no local study in Singapore to determine the local incidence of asymptomatic bacteriuria. This study aims to determine the local incidence of asymptomatic bacteriuria. This will help obstetricians in Singapore decide if routine screening for asymptomatic bacteriuria in local antenatal patients should be incorporated into routine clinical practice.

METHODS

We performed a retrospective cohort study in KK Women's and Children's Hospital, the largest tertiary obstetrics and gynecology center in Singapore. Urine studies to detect asymptomatic bacteriuria are not routinely performed by all clinicians in the institution. However, some clinicians offer urine screening for asymptomatic bacteriuria to their antenatal patients at booking visits. Antenatal patients with urine studies performed from October 2017 and August 2018 were identified. Patients with lower urinary tract symptoms, known abnormalities of the urinary tract, pre-existing diabetes, recent use of antibiotics within the last two weeks, current immunosuppressive therapy and retroviral disease were excluded.

Urine studies performed include urine dipstick for albumin, urine microscopy and urine culture and sensitivity. Urine microscopy was considered significant when 10 or more white cells per cubic millimeter are present or leukocyte esterase or nitrites are detected. A positive urine culture was defined when more than 10^5 bacteria per milliliters is present in a single voided midstream urine. Patients diagnosed with asymptomatic bacteriuria were treated with empirical antibiotics.

Clinical characteristics studied include maternal race, age, body mass index, gestational age at booking, and gestational age at urine studies. The outcomes of interest were low birth weight (defined as less than 2500 grams), preterm delivery (delivery before 37 weeks without another contributing cause) and admission for pyelonephritis.

RESULTS

During the 10-month period, there were 50 patients who had antenatal urine studies performed for asymptomatic bacteriuria screening identified from the database. 6% (n=3) of these patients had asymptomatic bacteriuria. None of these 50 cases had complications of low birth weight, preterm delivery or admission for pyelonephritis. The characteristics of these patients are described in Table I. There was no significant difference in maternal age, gestational age at urine studies or gestational age at booking visit between the group with asymptomatic bacteriuria and the group without. The average gestational age at booking visit and urine studies of this whole cohort were 12.1 and 12.5 weeks, respectively. However, the body mass index (BMI) of patients with asymptomatic bacteriuria was found to be statistically significantly higher than the group without (28.7 ± 1.7 vs 22.9 ± 4.7 kg/m2, p=0.04).

The three cases of asymptomatic bacteriuria are described in detail in Table II. Two of these cases booked early and had urine studies performed in the first trimester. Cephalexin was used to treat these cases. The last case was however a late booker. Interestingly, no white cells were detected on the urine microscopy in all three cases. The organisms isolated were *Escherichia coli, Enterococcus faecalis and Klebsiella pneumoniae*.

Outcomes of these patients were studied and are described in Table III. Eight patients (16%) were lost to follow up and three (6%) miscarried from the group without asymptomatic bacteriuria. Among the patients with asymptomatic bacteriuria, there

were no admissions for pyelonephritis. All 3 patients delivered at term, with a mean birth weight of 3400g. There was no significant difference in outcomes between the group with asymptomatic bacteriuria and the group without.

DISCUSSION

Asymptomatic bacteriuria is a common condition, found in up to 5% of healthy premenopausal women. [9] The most common organism isolated is Escherichia coli. In healthy individuals, asymptomatic bacteriuria has not been shown to be associated with significant adverse effects and hence, screening and treatment are not recommended. [9,10,3] However, the Infectious Disease Society of America (IDSA) recommends screening and treatment in the following groups of patients: pregnant women, before urological procedures in which mucosal bleeding is anticipated, and women with catheter-acquired bacteriuria that persists 48 hours after removal of indwelling catheter. [3] Mechanical obstruction by the gravid uterus, along with smooth muscle relaxation from the effects of progesterone, result in urinary stasis. This increases the risk of pyelonephritis complicating asymptomatic bacteriuria.

Asymptomatic bacteriuria is estimated to occur in about 2 to 10% of pregnancies. [2,3] This is consistent with the local Singaporean incidence of 6% found in our study. Most clinical guidelines recommend routine antenatal screening for asymptomatic bacteriuria due to the association with increased risk of pyelonephritis (up to 50%), preterm labour and low birth weight (<2500 grams). [4,5,6] However, among the cases of asymptomatic bacteriuria detected in our study, there was no adverse outcome such as those described. This could be attributed to the prompt treatment of asymptomatic bacteriuria with antibiotics in two out of three cases. The remaining case did not receive antibiotics, as this patient was a late booker at 30 weeks and subsequently defaulted follow up until delivery. This is consistent with findings by Kazemier et al in Netherlands. [7] Our lack of observed adverse outcomes may be due to our small study population. However, our study serves as a pilot study for future studies on asymptomatic bacteriuria in Singapore.

Interestingly, the BMI of patients with asymptomatic bacteriuria was found to be significantly higher than the group without. This was statistically significant ($p = 0.04$). A review of current literature revealed mixed opinions with regards to the effect of BMI as a risk factor of asymptomatic bacteriuria or urinary tract infection. Several other retrospective analyses on asymptomatic bacteriuria in pregnancy failed to detect any significant difference in BMI between these two groups of patients. [11,12,13] However, a large observational study in Australia found that women with a BMI ≥ 35 kg/m2 had a significantly higher risk of urinary tract infection compared to those with normal BMI. [14] Asymptomatic bacteriuria was not discussed. Future studies such as a large epidemiological prospective cohort studies may potentially guide us in determining the effect of raised BMI as a risk factor for asymptomatic bacteriuria.

With a larger population, we would be able to determine the true incidence of asymptomatic bacteriuria in the local population and in turn, assess the risk of adverse outcomes. Studies such as randomized controlled trials comparing the effects of screening and treatment of asymptomatic bacteriuria could also guide our decision on whether this should be incorporated into management of our local antenatal population. However, many might question the need for screening especially in terms of its cost-effectiveness. As our study found that the risk of asymptomatic bacteriuria is 6% with risk of pyelonephritis lower than 13%, further cost analysis studies need to be performed for this population. It is likely based on Wadland et al's study that screening for asymptomatic bacteriuria is not cost effective in our population. [8]

Other possible adjuncts to the much more costly urine culture include the urine dipstick and urine microscopy. However, among all the cases with asymptomatic bacteriuria in our study, their urine microscopy test was negative for white blood cells. The value of urine dipstick as an alternative to urine culture was compared in a

recent cross-sectional study in Iran. The nitrite test had a high specificity of 100% but a low sensitivity of 37%; while the leucocyte esterase test had a high sensitivity of 100% but a low specificity of 65%. [15] In Taiwan, antenatal urine screening is routinely performed using urinalysis as part of the National Health Insurance program. In a retrospective analysis by Lai et al, asymptomatic pyuria was associated with preterm delivery, low birth weight and lower APGAR score. [13] However, an important weakness pointed out by the authors was that there was no information on whether these patients had any lower genital tract infection. [13] Lower genital tract infections such as bacterial vaginosis are well established to be associated with preterm birth [16], and this could have resulted in the pyuria as well. Likewise, a review article on eight studies comparing the use of rapid urine screening alone or in combination against urine culture concluded that no test is a sufficiently accurate alternative to urine culture. [17] Urine culture remains the gold standard for detection of asymptomatic bacteriuria. [2,5]

Our study was limited by its small sample size which was insufficiently powered to determine the incidence of complications in patients with asymptomatic bacteriuria. A larger study population is necessary to determine the true incidence of asymptomatic bacteriuria and neonatal outcomes. Moreover, the diagnosis of asymptomatic bacteriuria in our study was based on a single urine culture. Up to 80% of women have true bacteriuria after a single urine culture. The diagnostic accuracy increases to 95% after 2 consecutive cultures positive for the same organism. [2,3,18] However, this is unlikely to be feasible in our clinical practice due to the cost of urine cultures and difficulty in patients' compliance with repeated visits. Nevertheless, this is the first local study on the incidence of asymptomatic bacteriuria in our antenatal population. It encourages further studies and discussions onto whether urine screening for asymptomatic bacteriuria in pregnancy should be performed, if at all. If the risk of adverse outcomes is truly low, then perhaps it is justified to continue our current practice of not screening for asymptomatic bacteriuria in pregnancy. In addition, the subjects in our study were culturally and socioeconomically diverse, which is representative of the larger population in this multiracial country.

To date, the screening of asymptomatic bacteriuria is controversial. Rather, the fundamental question lies in whether asymptomatic bacteriuria does in fact need to be treated. A systematic review by Angelescu et al concluded that the reduction in incidence of pyelonephritis in women who received treatment with antibiotics was based on data collected more than 50 years ago, whereas recent statistics reveal that there is actually no significant difference. [1] Kazemier et al found no significant difference in the proportion of women who developed pyelonephritis, preterm birth (less than 34 weeks) or both between asymptomatic bacteriuria-positive women who were untreated or received placebo and asymptomatic bacteriuria-negative women. [7]

CONCLUSION

The incidence of asymptomatic bacteriuria in our study is 6%, consistent with international data. However, there was no adverse outcome among these patients. Larger adequately powered studies are needed to provide more information on the true incidence and guide recommendations on the role of routine screening for asymptomatic bacteriuria in our antenatal population. Randomized controlled trials evaluating the benefits and risks of screening of asymptomatic bacteriuria will also be useful in guiding future local practice.

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Table I. Characteristics of Patients with and without Asymptomatic Bacteriuria

Characteristics	Asymptomatic Bacteriuria $n = 3$ (Mean ± SD)	No Asymptomatic Bacteriuria $n = 47$ (Mean ± SD)	*P*
Age (years)	29.7 ± 6.5	29.2 ± 4.3	0.851
Gestational age at urine studies (weeks)	15.4 ± 12.9	12.3 ± 6.2	0.721
Gestational age at booking visit (weeks)	14.4 ± 13.6	11.9 ± 6.3	0.787
BMI (kg/m^2)	28.7 ± 1.7	22.9 ± 4.7	**0.04**
Race			
Chinese	1 (33.3%)	21 (44.7%)	
Malay	1 (33.3%)	14 (29.8%)	
Indian	1 (33.3%)	3 (6.4%)	
Others	0	9 (19.1%)	

Table II. Cases of Asymptomatic Bacteriuria

Case	Age (years)	Gravida/Para	GA at booking (weeks)	GA at urine studies (weeks)	BMI (kg/m^2)	White Cell Count on Urine Microscopy/ mm^3	Epithelial Cell on Urine Microscopy/ mm^3	Organism on urine culture ($>10^5$ count)	Treatment	GA at delivery (weeks)	Birth Weight (g)
1	23	G1P0	7.0	10.0	27.0	0	2	*E. coli*	Cephalexin	39.3	3092
2	30	G2P1	30.1	30.1	28.6	0	0	*E. faecalis*	Nil	38.7	3410
3	36	G3P1	6.0	6.0	30.5	0	2	*K. pneumoniae*	Cephalexin	37.9	3698

(GA: Gestational age, BMI: Body Mass Index)

* Cephalexin dose: 500mg three times per day for 5 days

Table III. Observed outcomes in patients with and without asymptomatic bacteriuria

Outcome	Asymptomatic Bacteriuria $n = 3$ (Mean ± SD)	No Asymptomatic Bacteriuria $n = 36$ (Mean ± SD)	*P*
Pyelonephritis	0	0	
Gestation age at delivery (weeks)	38.6 ± 0.7	37.6 ± 4.7	0.714
Birth Weight (g)	3400.0 ± 303.1	3065.4 ± 324.1	0.093

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