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OBSTETRICS

Asymptomatic Bacteriuria in Thai Pregnant Women with Preterm Delivery: Prevalence, Pathogens and Pregnancy Outcomes

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ABSTRACT

Objectives: The primary aim was to determine the prevalence of asymptomatic bacteriuria (ASB) in Thai pregnant women with a preterm delivery. The secondary aims were to identify common causative organisms and their antibiotic susceptibilities, and to compare the pregnancy outcomes between ASB-positive and ASB-negative patients.

Materials and Methods: The medical records of low-risk pregnant women with a preterm delivery at Siriraj Hospital from January 2014 to May 2020 were reviewed. Patient characteristics, urine culture results, and pregnancy outcome data were recorded. ASB-positive was defined as the growth of at least 10^5 colony-forming units per milliliter (cfu/ml) isolated from a midstream, clean-catch urine specimen.

Results: A total of 826 eligible women were included. The prevalence of ASB was 3% (25/826). The predominant organism was Escherichia coli (E. coli) (48%). All E. coli were susceptible to nitrofurantoin and only 25% were susceptible to ampicillin. No significant adverse outcomes were detected in the ASB-positive group.

Conclusion: The prevalence of ASB in Thai pregnant women with a preterm delivery was low. Antibiotic treatment should be based on the common organisms and local antibiotic susceptibility patterns.

Keywords: asymptomatic bacteriuria, preterm delivery, pregnancy outcome.

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ความชุกและเชื้อก่อโรคของภาวะการมีเชื้อแบคทีเรียในปัสสาวะแบบไม่มีอาการและผลการตั้งครรภ์ในสตรีไทยที่มีการคลอดก่อนกำหนด

วศินี สุขเฉลิมชัย, นลัท สมภักดี, ภัทรวลัย ตลึงจิตร, พรพิมล เรืองวุฒิเลิศ, บูรยา พัฒนจินดากุล

บทคัดย่อ

วัตถุประสงค์: *วัตถุประสงค์หลัก คือ เพื่อหาความชุกของภาวะการมีเชื้อแบคทีเรียในปัสสาวะแบบไม่มีอาการ (asymptomatic bacteriuria; ASB) ในสตรีไทยที่มีการคลอดก่อนกำหนด วัตถุประสงค์รอง คือ เพื่อหาชนิดของเชื้อก่อโรคและแบบแผนของความไวต่อยาปฏิชีวนะ และเปรียบเทียบผลการตั้งครรภ์ระหว่างกลุ่มที่มีและไม่มีภาวะ ASB*

วัสดุและวิธีการ: *ทำการศึกษาย้อนหลังในสตรีไทยที่มีความเสี่ยงต่ำ และมีการคลอดก่อนกำหนดระหว่าง มกราคม พ.ศ. 2557 ถึง พฤษภาคม พ.ศ. 2563 โดยเก็บข้อมูลพื้นฐาน ผลการเพาะเชื้อจากปัสสาวะ และผลการตั้งครรภ์ ภาวะ ASB วินิจฉัยเมื่อตรวจพบเชื้อแบคทีเรียในปริมาณตั้งแต่ 10^5 colony-forming units (cfu)/mL ขึ้นไปจากการเก็บปัสสาวะเพื่อเพาะเชื้อด้วยวิธี clean-catch midstream urine*

ผลการศึกษา: *ความชุกของภาวะ ASB ในสตรีไทยที่มีการคลอดก่อนกำหนดเท่ากับร้อยละ 3 (25 จาก 826 ราย) โดยเชื้อก่อโรคที่เป็นสาเหตุหลัก คือ Escherichia coli (ร้อยละ 48) ซึ่งทุกรายมีความไวต่อยา nitrofurantoin และมีเพียงร้อยละ 25 ที่มีความไวต่อยา ampicillin เมื่อเปรียบเทียบผลการตั้งครรภ์ไม่พบว่ากลุ่มที่มีภาวะ ASB มีผลการตั้งครรภ์ที่ไม่พึงประสงค์มากกว่ากลุ่มที่ไม่มีภาวะ ASB อย่างมีนัยสำคัญ*

สรุป: *ความชุกของภาวะ ASB ในสตรีไทยที่มีการคลอดก่อนกำหนดค่อนข้างต่ำ การให้การรักษาด้วยยาปฏิชีวนะควรพิจารณาถึงเชื้อก่อโรคที่พบได้บ่อย รวมถึงแบบแผนของความไวต่อยาปฏิชีวนะ*

คำสำคัญ: *ภาวะการมีเชื้อแบคทีเรียในปัสสาวะแบบไม่มีอาการ, การคลอดก่อนกำหนด, ผลการตั้งครรภ์*

Introduction

Asymptomatic bacteriuria (ASB) is the presence of a significant number of bacteria in a urine specimen collected properly from a person without symptoms of urinary tract infection (UTI), such as dysuria, frequent voiding, and incomplete voiding[1-3]. Significant bacteriuria is defined as the growth of at least 10^5 colony-forming units per milliliter (cfu/ml) isolated from a voided midstream, clean-catch urine specimen. Various causative organisms have been identified with the most commonly reported isolate being Escherichia coli (E. coli). Other organisms include gram-negative bacteria, such as Klebsiella pneumoniae (K. pneumoniae), Proteus mirabilis (P. mirabilis), and group B streptococci[1, 4-5]. ASB is common in pregnant women and, if left untreated, could lead to acute pyelonephritis in up to 25%-50% of cases[5, 6]. In addition, ASB has been associated with several adverse outcomes such as hypertensive disorder, low birth weight, preterm delivery, and increased fetal mortality[6-9]. However, the relationship between ASB and preterm delivery remains controversial[10].

International organizations including the American Academy of Pediatrics (AAP), the American College of Obstetricians and Gynecologists (ACOG), the National Institute for Health and Care Excellence (NICE), the World Health Organization (WHO), and the US Preventive Services Task Force, recommend screening for bacteriuria at the first prenatal visit. A positive urine culture result should be promptly treated[11-15]. In Thailand, ASB screening in pregnant women is still not routinely and widely practiced[16]. However, at Siriraj Hospital, urinalysis and urine culture are carried out in pregnant women who present with preterm labor and antibiotic treatment is provided if there is evidence of UTI, such as pyuria or significant bacteriuria.

Depending on the population sampled, the reported prevalence of ASB varies from 2% to 12%[6, 9, 17]. In 2018, Kamel et al[18] reported a 5% prevalence of ASB in Egyptian pregnant women with preterm labor. The prevalence of ASB in Thai pregnant women has been reported to be approximately 10%[16, 19]. However, data on the prevalence of ASB in Thai pregnant women with a preterm delivery has not been published. Common organisms and antibiotic susceptibility patterns vary across populations and over time, requiring ongoing surveillance to inform medical practice.

Therefore, this study was conducted to determine the prevalence of ASB in Thai pregnant women with a preterm delivery. The secondary objectives were to evaluate the common causative organisms and their antibiotic susceptibilities, and to compare pregnancy outcomes between the ASB-positive and ASB-negative patients.

Materials and Methods

Study design and participants

This retrospective study was conducted after the approval of Siriraj Institutional Review Board (COA no. Si381/2020). The medical records of low-risk, Thai pregnant women who had a spontaneous, preterm delivery at the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand from January 2014 to May 2020 were reviewed. Data were collected on patient characteristics, complete blood count, urine culture on admission, and pregnancy outcomes.

Urine culture was performed on a midstream, clean-catch specimen. Significant bacteriuria, defined as the growth of at least 10^5 colony-forming units per milliliter (cfu/ml) isolated, was designated ASB-positive whereas ASB-negative denoted insignificant bacteriuria (less than 10^5 cfu/ml isolated), or no growth. Maternal outcomes included gestational age at delivery, gestational diabetes mellitus, pregnancy-induced hypertension, postpartum hemorrhage, chorioamnionitis, maternal sepsis, postpartum endometritis, and wound complication. Neonatal outcomes included birth weight, intraventricular hemorrhage, retinopathy of prematurity, respiratory distress syndrome, apnea of prematurity, necrotizing enterocolitis, hyperbilirubinemia, neonatal sepsis, ventilator requirement, duration of hospital stay, and admission to the neonatal intensive care unit.

The subjects were pregnant women aged 18 years or older with an uncomplicated singleton pregnancy who had a spontaneous preterm delivery at 24 to 36 weeks' gestation. Gestational age determination

was based on the last menstrual period with a confirmed ultrasound examination during the first or second trimester. Patients with urinary symptoms at the time of specimen collection, a history of a renal disease or any abnormality of the genitourinary tract that impairs voiding, and those with medical or obstetric complications were excluded.

Sample size calculation and statistical analysis

Sample size calculation was based on the primary objective. A study in 2018 by Kamel et al[18] reported the prevalence of ASB in patients with preterm labor to be 5%. Based on a prevalence of 5% and a confidence level of 0.95 with an allowable error of 0.015, the sample size was calculated to be 811 women.

All data analyses were performed using PASW Statistics version 18.0 for Windows (SPSS, Inc., Chicago, IL, USA). Descriptive data are presented as number and percentage, mean ± standard deviation, or median and range (P25-P75), as appropriate. Chi-square or Fisher's exact test was used to compare qualitative characteristics between groups. Student's t-test or Mann-Whitney U test was used to compare continuous data between groups. A p value of less than 0.05 was considered statistically significant.

Results

Eight-hundred and twenty-six women with a mean maternal age of 29.8 ± 6.2 years were enrolled. The mean gestational age at delivery was 33.6 ± 2.4 weeks. Twenty-five (3%) women had significant bacteriuria. Baseline demographic and clinical characteristics were comparable between the ASB-positive and ASB-negative groups (Table 1).

Table 1. Comparison of demographic and clinical characteristics (n = 826, unless otherwise specified).

Characteristics	Reported values*		
	ASB-positive n = 25	ASB-negative n = 801	p value
Age (years)			0.134[a]
18-34	16 (64%)	616 (76.9%)	
≥ 35	9 (36%)	185 (23.1%)	
Gravidity			0.572[a]
1	9 (36%)	398 (49.7%)	
2	11 (44%)	264 (33%)	
3	3 (12%)	92 (11.5%)	
≥ 4	2 (8%)	47 (5.9%)	
Pre-pregnancy body mass index (kg/m^2)	26.4 ± 4.9	25.8 ± 4.5	0.492[b]
Hemoglobin on admission (g/dl) (n = 813)**			0.716[a]
< 11	6 (24%)	215 (27.3%)	
≥ 11	19 (76%)	573 (72.7%)	
Income (Baht/month)			0.782[a]
< 10,000	3 (12%)	54 (6.7%)	
10,000-20,000	5 (20%)	170 (21.2%)	
20,001-30,000	5 (20%)	188 (23.5%)	
30,001-40,000	5 (20%)	118 (14.7%)	
40,001-50,000	3 (12%)	75 (9.4%)	
> 50,000	4 (16%)	196 (24.5%)	
Education (n = 823)***			0.099[a]
Low education (≤ primary school)	17 (68%)	409 (51.3%)	
High education (≥ secondary school)	8 (32%)	389 (48.7%)	
Gestational age at urine collection (weeks)			0.676[c]
< 28	2 (8%)	52 (6.5%)	
≥ 28	23 (92%)	749 (93.5%)	

* Data are reported as number and percentage or mean ± standard deviation. ** Results were available from only 788 women in ASB-negative group. *** Results were available from only 798 women in ASB-negative group. [a] Chi- quare test, [b] t-test, [c] Fisher's exact test. ASB: asymptomatic bacteriuria, g/dl: gram per deciliter, kg/m^2: kilogram per square meter

Among the ASB-positive women, E. coli was the most common causative organism (48%), followed by Enterococcus faecalis (E. faecalis) (16%), and K. pneumoniae (8%). Antibiotic susceptibility patterns of the common organisms are shown in Table 2. All E. coli were susceptible to nitrofurantoin, imipenem, meropenem, piperacillin/tazobactam, amikacin, and cefepime. Ninety-two percent were susceptible to ceftriaxone, 83% were susceptible to amoxicillin/clavulanate, and 25% were susceptible to ampicillin. E. faecalis, the second most common isolate, was 100% susceptible to ampicillin, gentamicin, penicillin, and vancomycin. Seventy-five percent were susceptible to fosfomycin and 25% were susceptible to ciprofloxacin.

All 826 pregnancies resulted in live births. Maternal outcomes for ASB-positive and ASB-negative patients are shown in Table 3. No significant differences in adverse maternal outcomes were detected. Ten newborns (one from the ASB-positive group and nine from the ASB-negative group) were referred to other hospitals after delivery and so only one available outcome, neonatal birth weight was included.

Table 2. Antibiotic susceptibility pattern of common isolated organisms.

Antibiotics	Reported values*		
	E. coli (n = 12)	E. faecalis (n = 4)	K. pneumoniae (n = 2)
Ampicillin	3 (25%)	4 (100%)	ND
Amoxicillin/clavulanate	10 (83%)	ND	2 (100%)
Amikacin	12 (100%)	ND	2 (100%)
Cefepime	12 (100%)	ND	2 (100%)
Ceftriaxone	11 (92%)	ND	2 (100%)
Ciprofloxacin	10 (83%)	1 (25%)	2 (100%)
Cefuroxime	11 (92%)	ND	ND
Gentamicin	8 (67%)	4 (100%)	2 (100%)
Fosfomycin	ND	3 (75%)	ND
Imipenem	12 (100%)	ND	2 (100%)
Meropenem	12 (100%)	ND	2 (100%)
Norfloxacin	4 (33%)	ND	ND
Nitrofurantoin	12 (100%)	ND	ND
Piperacillin/tazobactam	12 (100%)	ND	2 (100%)
Penicillin	ND	4 (100%)	ND
Trimethoprim/sulfamethoxazole	5 (42%)	ND	2 (100%)
Vancomycin	ND	4 (100%)	1 (50%)

* Data are reported as number and percentage. ND: not done

Table 3. Comparison of maternal outcomes among the 2 study groups. (n = 826)

	Reported values*		
	ASB-positive (n = 25)	ASB-negative (n = 801)	p value
Gestational age at delivery (weeks)			0.651[a]
< 34	10 (40%)	357 (44.6%)	
≥ 34	15 (60%)	444 (55.4%)	
Gestational diabetes mellitus	7 (28%)	120 (15%)	0.089[b]
Pregnancy-induced hypertension	3 (12%)	71 (8.9%)	0.484[b]
Postpartum hemorrhage	4 (16%)	55 (6.9%)	0.096[b]
Chorioamnionitis	2 (8%)	44 (5.5%)	0.645[b]
Maternal sepsis	0 (0%)	4 (0.5%)	1.000[b]
Postpartum endometritis	0 (0%)	6 (0.7%)	1.000[b]
Wound infection/dehiscence	1 (4%)	13 (1.6%)	0.352[b]

* Data are reported as number and percentage. [a] Chi-square test, [b] Fisher's exact test. ASB: asymptomatic bacteriuria

All other outcomes of interest were obtainable from the remaining 816 newborns (24 ASB-positive and 792 ASB-negative). Neonatal outcomes in the ASB-positive and ASB-negative groups are compared in Table 4. No significant differences in adverse neonatal outcomes were detected.

Table 4. Comparison of neonatal outcomes among the 2 study groups (n = 816, unless otherwise specified).

	Reported values*		
	ASB-positive (n = 24)	**ASB-negative (n = 792)**	**p value**
Neonatal birth weight (grams) (n = 826)**	2216.4 ± 636	2123.6 ± 538.5	0.399[a]
Intraventricular hemorrhage	2 (8.3%)	43 (5.4%)	0.386[b]
Retinopathy of prematurity	1 (4.2%)	14 (1.8%)	0.363[b]
Respiratory distress syndrome	8 (33.3%)	286 (36.1%)	0.833[b]
Apnea of prematurity	1 (4.2%)	144 (18.2%)	0.101[b]
Necrotizing enterocolitis	0 (0%)	37 (4.7%)	0.621[b]
Hyperbilirubinemia	18 (75%)	602 (76%)	1.000[c]
Neonatal sepsis	6 (25%)	111 (14%)	0.138[b]
Ventilator requirement			0.873[c]
CPAP	4 (16.7%)	159 (20.1%)	
Endotracheal tube	3 (12.5%)	89 (11.2%)	
Median hospital stay (days)	10.5 (5-19)	8 (5-24)	0.867[d]
Admission to NICU			
Admission	7 (29.2%)	190 (24%)	0.559[c]
Median stay (days) (n = 197)	13 (2-33)	8 (3-22)	0.725[d]

* Data are reported as number and percentage, mean ± standard deviation, or median (P25-P75)
** Results were from 25 ASB-positive cases and 801 ASB-negative cases
[a] T-test, [b] Fisher's exact test, [c] Chi-square test, [d] Mann-Whitney U test
ASB: asymptomatic bacteriuria, NICU: neonatal intensive care unit

Discussion

ASB has been associated with adverse perinatal outcomes that can be prevented by screening and treatment. Previous studies in several countries have reported a prevalence among pregnant women of 2% to 12%[6, 9, 17]. The prevalence of ASB in Thai pregnant women across all trimesters was reported to be approximately 10%[16, 19]. However, we measured a 3% prevalence of ASB in women with a preterm delivery, closer to the 5% prevalence in Egypt reported by Kamel et al[18]. The different result we observed may be explained by the fact that we included only pregnant women who had a preterm delivery from a single hospital setting, and differences in the socio-economic status, social behaviors, and education of the studied population might contribute to the outcome[16, 19-20]. In this study, E. coli was found to be the most common causative organism (48%), followed by E. faecalis (16%), and K. pneumonia (8%). These results were similar to other studies that also reported E. coli as the most common isolate[6, 9, 21]. Diverse antibiotic susceptibility patterns are observed across geographical areas due to the use of different antibiotics. Therefore, antibiotic treatment should be based on the common organisms and local antibiotic susceptibility patterns.Our study has some important strengths. First, this is the first survey of ASB prevalence, causative organisms and antibiotic susceptibility patterns, and outcomes in Thai pregnant women with a preterm delivery. Second, our sample size was large and sufficient to test the main objective of prevalence. Our study also has some limitations. The number of patients in the ASB-positive group was small, due to an unexpectedly low prevalence rate. Therefore, a larger study is warranted to evaluate between-group outcome comparisons. Moreover, due to the retrospective study design, there were some potential confounding factors that could affect the adverse pregnancy outcomes such as differences in intrapartum management and route of delivery.

Conclusion

In summary, the prevalence of ASB in Thai pregnant women with preterm delivery was low. E. coli was the dominant causative organism and was very susceptible to nitrofurantoin. We recommend nitrofurantoin for ASB in pregnant women due to its high susceptibility and safety.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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