Prevalence of Urinary Tract Infection in Pregnancies with Premature Uterine Contractions

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ABSTRACT

Objective: This study aimed to determine the prevalence of urinary tract infection (UTI) among pregnant women with premature uterine contractions. Roles of the current practice of routine simultaneous urinalysis and urine culture in these cases were also evaluated.

Materials and Methods: Medical records of pregnant women admitted with premature uterine contractions at Siriraj Hospital between January 2013 and December 2017 were reviewed. Prevalence of UTI in these women was determined. Women were divided into 2 groups based on diagnosis at admission; group 1 included preterm labor/preterm prelabor rupture of membranes (PTL/PPROM), and group 2 was threatened preterm labor (TPL). Evaluations of urinalysis and/or urine culture were performed in these two groups to establish a strategy to reduce unnecessary urine culture.

Results: The prevalence of UTI among 2,286 women with premature uterine contractions was 4.9%. Prevalence of UTI were not different between the two groups of women. A positive urine culture was found in 2.4%. The most common organism identified in both groups of women was *Escherichia coli*. Urinalysis with abnormal cell counts and/or significant presence of bacteria could be used to screen for women in TPL group who should have urine culture with a positive screening rate of 6.5% and 90.9% sensitivity. With this strategy, unnecessary urine culture could be reduced.

Conclusion: The prevalence of UTI among pregnant women admitted with premature uterine contractions was 4.9% and was not different between PTL/PPROM group and TPL group. Urinalysis with abnormal cell counts or significant bacteriuria could be a screening tool to reduce number of urine culture in women with TPL.

Keywords: Asymptomatic bacteriuria; urinalysis; urine culture; premature uterine contractions; pregnancy outcomes (Siriraj Med J 2023; 75: 699-706)

INTRODUCTION

Asymptomatic bacteriuria (ASB) is a significant bacterial infection of the urine without signs or symptoms of urinary infection. It is defined by the presence of one or more species of bacteria identified in the urine culture at a quantitative count of > 10^5 colony-forming units (CFU/ml).[1] Reported prevalence of ASB in pregnancy ranges from 2% to 7%[2] and may be higher in some conditions, such as diabetic pregnancies.[3] If pregnant women with ASB are not treated, up to 30% will develop acute pyelonephritis, which has been associated with low birth weight and preterm birth.[4] Therefore, once detected, active management with antibiotics is recommended.[5] Although early routine screening for and treatment of ASB in pregnancy are recommended in antenatal care guidelines,[6] the benefits and harm of screening and treatment are still questionable in low-risk singleton pregnancies.[7-9] Like most hospitals in Thailand, Siriraj

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Hospital does not perform screening for ASB during the antenatal period due to the low prevalence (2.3%) without a significant difference in prevalence by trimester.[9]

Preterm birth is an important cause of neonatal morbidity and mortality due to the immaturity/prematurity of the newborn various organ systems. Preterm birth rate at Siriraj Hospital was reported to be 9-14%.[10] Preterm birth usually is preceded by regular uterine contractions[11] or membrane rupture. Infection is one of the proposed mechanisms involved in this condition. Urinary tract infections (UTIs), genital tract infections, and periodontal diseases have been reported to be associated with spontaneous preterm labor.[12]

Premature uterine contraction is a common problem in pregnancy. As mentioned, the contractions can precede a preterm birth. On the other hand, the contractions can be a mere false alarm. Generally, regular uterine contractions with a cervical dilatation of ≥ 2 cm and ≥ 80% effacement have a high risk of labor progression, hence the condition is termed preterm labor (PTL). Condition of regular premature uterine contractions with less cervical changes is traditionally termed "threatened preterm labor" (TPL). However, with a subtle or borderline cervical change, it is difficult at the initial assessment to differentiate between early PTL and TPL. Further observation is needed to evaluate cervical progression. Another condition associated with preterm birth is preterm prelabor rupture of membranes (PPROM). It defines spontaneous membrane rupture before 37 completed weeks and before labor onset or cervical changes. With PPROM, risk of infection is increased along with time.

Management of pregnancies with either of the three conditions (PTL, PPROM, TPL) aims to delay delivery usually by tocolytics to avoid or reduce the risk of preterm birth unless/until there is a contraindication to do so. The women are admitted for evaluation and managed accordingly. Pregnancies with advanced PTL or PPROM are more likely than TPL to deliver in the same admission.

Guidelines suggested by the Royal Thai College of Obstetricians and Gynaecologists (RTCOG) for managing preterm labor recommend performing septic work-ups to determine if an infection is the cause of preterm labor. Urine analysis and urine culture are often used to diagnose UTIs, despite the absence of signs and symptoms with midstream urine culture (MUC) being the gold standard.[13] This is due to concern of ASB in these women.

At Siriraj Hospital, urinalysis is performed in women with premature uterine contractions on admission to detect UTI. Urine culture is also carried out simultaneously if feasible. This approach follows the RTCOG guidelines with an idea that UTI is a possible cause of premature uterine contractions or membrane rupture, which in turn may lead to preterm birth. If found, treating UTI may improve the pregnancy outcomes. However, previous studies could not demonstrate clear association between positive midstream urine culture (MUCs) in pregnancies with preterm labor, preterm delivery or pregnancy outcomes.[14] Furthermore, the rates of positive MUCs among women with preterm labor were reported to be 2.3% to 5% and the costs and benefits of performing MUCs were unclear.[9,14-16]

We aimed to determine the rate of UTI diagnosed by urinalysis and/or a positive urine culture in women admitted with premature uterine contractions. We carried out a study similar to the one previously performed in our institution.[15] However, in that study, only urine culture results had been considered. We added urinalysis into the diagnostic process to investigate whether urine culture number could be reduced or not. Furthermore, currently, the urine specimen would be collected by a single urinary catheterization instead of clean voided urine catch to reduce the risk of contamination especially from the vaginal discharge/fluids which often presented in larger amount than normal in cases with premature uterine contractions and/or PPROM. The common organisms involved and the association between the urine culture results and pregnancy outcomes were also evaluated.

MATERIALS AND METHODS

This retrospective study was performed at Siriraj Hospital, a tertiary care and teaching hospital in Bangkok, Thailand. The Institutional Review Board of the Faculty of Medicine Siriraj Hospital approved this study (COA no. Si 320/2018). The medical records of pregnant women admitted between January 2013 and December 2017 with an ICD-10 diagnosis code related to preterm with delivery (O60.1), preterm without delivery or threatened preterm labor (O60.0), and preterm prelabor rupture of membranes (O42.91) were reviewed. They received medications to inhibit labor, and were worked-up to determine the causes of premature uterine contractions. Pregnant women with an underlying renal disease or with a known urinary tract disease or with signs or symptoms of UTI from history taking and/or physical examination were excluded, as were cases with a contraindication for labor inhibition.

An "abnormal urinary analysis suggestive of UTI" was defined as a white blood cell count > 5/high-power field[17] or a red blood cell count > 5/high-power field without contamination and without crystal or casts.[18] As

we excluded women with preexisting urinary tract diseases, we assumed that abnormal urinalysis was associated with UTI. For urine culture, "positive growth" was defined as a bacterial count > 10^5 CFU/ml, whereas lower counts or positive growth of multiple organisms were more likely to be associated with contamination.[1] Since the women with symptoms of UTI had been excluded from the study, a positive growth in urine culture was also considered ASB.

Sample size was calculated based on the findings of Kiatsuda et al[19] that UTI or ASB were presented in 15.5% of women admitted with preterm labor or threatened preterm labor. With alpha of 0.05 and d= 0.015, the sample size needed was 2,237 women.

At the admission, an initial diagnosis was given according to the history taking and vaginal speculum and/or cervical examination as appropriate. Women were divided into two groups according to their diagnosis. As women with TPL were likely to be able to continue pregnancy and PTL/PPROM were likely to deliver in the same admission, they were allocated into either PTL/PPROM or TPL group. Patient characteristics, urinary results, and pregnancy outcomes were recorded on a case record form. Data analyses were performed using PASW Statistics for Windows, version 18 (SPSS Inc., Chicago, IL, USA). Descriptive data are presented as percentages, means, standard deviations (SDs), or medians with interquartile ranges (IQRs). Continuous variables were analyzed using Student's t-test, while categorical variables were examined with Pearson's Chi-square test or Fisher's exact test. A statistically significant difference was defined as a value < 0.05.

RESULTS

A total of 2,286 medical records were reviewed. Of these, simultaneous urinalysis and urine culture were available in 1,805 cases. There were 479 cases who had only urinalysis carried out. The remaining 2 cases had only culture result due to a mistake in specimen handling. As shown in Table 1, the mean maternal age at admission

TABLE 1. Basic characteristics of the study cohort.

Diagnosis at admission	n (%)	PTL/PPROM n (%)	TPL n (%)	*P* value
Total N = 2,286		810 (35.4)	1,476 (64.6)	
Age (years), mean = 29.1, (SD = 7.0)				
< 20	278 (12.2)	116 (14.3)	162 (11.0)	0.07
20 - 34	1,455 (63.6)	503 (62.1)	952 (64.5)	
≥ 35	553 (24.2)	191 (23.6)	362 (24.5)	
Gestational age at admission, mean = 31.3, (SD = 2.6)				
< 28	202 (8.8)	58 (7.2)	144 (9.8)	**< 0.001**
28- 31^{+6}	799 (35.0)	250 (30.9)	549 (37.2)	
32- 37	1,285 (56.2)	502 (62.0)	783 (50.3)	
Gestation				
Primigravida	1,102 (48.2)	392 (48.4)	710 (48.1)	0.89
Multigravida	1,184 (51.8)	418 (51.6)	766 (51.9)	
Parity				
Primipara	1,348 (59.0)	477 (58.9)	871 (59.0)	0.96
Multipara	938 (41.0)	333 (41.1)	605 (41.0)	
Prior preterm birth	156 (6.8)	63 (7.8)	93 (6.3)	0.11
Administration of dexamethasone for fetal lung maturity	2,122 (92.8)	731 (90.2)	1,391 (94.2)	**< 0.001**
complete	2,087 (91.29)	707 (87.28)	1,380 (93.50)	**< 0.001**
Side effects from inhibiting labor	903 (39.5)	264 (32.6)	639 (43.3)	**< 0.001**
Delivery in this admission	1,072 (46.89)	773 (95.43)	299 (20.26)	**< 0.001**

was 29 ± 7 years old and the mean gestational age was 31.3 ± 2.6 weeks. Approximately 60% of the women were primiparous. About 7% of the women had a history of a prior preterm birth. Table 2 shows that abnormal urinalysis suggestive of infection was presented in 94 cases (4.1% of those who had a urinalysis performed) and a positive urine culture was presented in 43 cases (2.4% of those who had urine culture performed). Among these two categories, there were 24 women who had both abnormal urinalysis and a positive urine culture. Therefore, altogether there were 113 women diagnosed with UTI by urinalysis and/or culture, comprising 4.9% of the total cohort.

As mentioned earlier, we divided women into two groups based on the initial diagnosis: PTL/PPROM group and TPL group. Approximately two-thirds of the women were diagnosed with TPL. The patient characteristics are summarized in Table 1. At the end, 20% of women with TPL delivered in the same admission, mostly from progression of labor. Ninety-five percent of women in PTL/PPROM group delivered in this admission. Women in this group who had not delivered were either referred to another hospital or discharged against advice. Length of stay of the total cohort was 8.8 ± 10.8 days, 9.3 ± 9 days and 8.5 ± 11.6 days in the total cohort, PTL/PPROM and TPL groups respectively.

Table 1 also shows that lower gestational age at admission were more prevalent in TPL group. This might be due to uterine contractions at such gestational age was likely to be a false alarm. The lower proportions of dexamethasone administration or side effects from inhibiting labor in the PTL/PPROM group were explained by the discontinuation of medications once the women delivered.

The urinary results of the cohort are presented in detail in Table 2. There were no statistically significant differences between the proportions of abnormal urinalysis (4.3% vs. 4.0%) or positive urine culture (1.7% vs. 2.7%) between PTL/PPROM group and TPL group. The most common organism identified in urine culture in both groups was *Escherichia coli*, presented in 40% and 75% in PTL/PPROM group and TPL group respectively.

TABLE 2. Urinary results of the study cohort.

Test		PTL/PPROM	TPL	
Urinalysis	**N = 2284, n (%)**	**N = 809, n (%)**	**N = 1475, n (%)**	***P* value**
Normal	2,190 (95.9)	774 (95.7)	1,416 (96.0)	0.71
Abnormal	94 (4.1)	35 (4.3)	59 (4.0)	
Mid-stream urine culture	**N = 1,807, n (%)**	**N = 600, n (%)**	**N = 1,207, n (%)**	
No growth	1,730 (95.7)	582 (97.0)	1,148 (95.1)	0.17
< 10^5 cfu/ml or contaminated	34 (1.9)	8 (1.3)	26 (2.2)	
Positive (>10^5 cfu/ml)	43 (2.4)	10 (1.7)	33 (2.7)	
Organisms in positive cultures				0.02
Escherichia coli	29 (67.4)	4 (40.0)	25 (75.8)	
Streptococcus agalactiae (Streptococcus group B)	2 (4.7)	2 (20.0)	0 (0.0)	
Enterococcus spp.	4 (9.3)	2 (20.0)	2 (6.1)	
Enterobacter spp.	2 (4.7)	0 (0.0)	2 (6.1)	
Klebsiella pneumoniae	2 (4.7)	0 (0.0)	2 (6.1)	
Citrobacter koseri	1 (2.3)	1 (10.0)	0 (0.0)	
Proteus mirabilis	2 (4.7)	0 (0.0)	2 (6.1)	
Staphylococcus saprophyticus	1 (2.3)	1 (10.0)	0 (0.0)	

Others various gastrointestinal bacteria were presented randomly in both groups. Remarkably, *Streptococcus agalactiae* (Streptococcus Group B; GBS) was found in 2 cases who were diagnosed with PPROM. Membrane rupture increases risk of urinary ascending infection from a rectovaginal GBS colonization.

Pregnancy outcomes were analyzed according to the urinalysis results in Table 3. Delivery rates in the studied admission were similar between women with abnormal and normal urinalysis and between women with positive and negative culture. Pregnancies with abnormal urinalysis had the gestational age at delivery and newborn birth weight greater than the corresponding values of the normal urinalysis group. This finding was despite the delivery rate and mode of the 2 groups being approximately the same. Unfortunately, when breaking into more details in gestational age or birth weight, there was no clear or consistent pattern to draw conclusion from. Other neonatal outcomes, such as the rates of birth asphyxia and neonatal intensive care unit (NICU) admission, were not significantly different.

Table 4 reveals pregnancy outcomes according to the urine culture results. Similar to urinalysis, delivery rates in the studied admission were similar between the women with a positive and a negative culture. On the other hand, pregnancies with a positive urine culture resulted in newborns with higher rates of extremely low birth weight (< 1,000 g) and NICU admission than cases with a negative urine culture. Even though the mode of delivery of these 2 groups was statistically similar, the cesarean section rate of the positive urine culture group was distinctly higher than that of the MUC-negative group (77.8% vs 52.5%).

From Tables 3 and 4, urine culture appears more meaningful than urinalysis. However, universal urine culture in cases with premature uterine contractions to identify the 2.4% positive rate would be costly. Based on the obtained data, we looked for a strategy to use the urinalysis as a screening tool to reduce the number of urine culture. Considering TPL comprising two-thirds of cases with premature uterine contractions, we concentrated on TPL group. In this group, simultaneous

TABLE 3. Pregnancy outcomes according to urinalysis results.

	Abnormal N = 94, n (%)	Normal N = 2,190, n (%)	*P* value
Delivery in this admission	52 (55.3)	1019 (46.5)	0.09
	N = 52	**N = 1019**	
Gestational age at delivery (weeks), mean (SD) 32.56 (SD = 0.074)	33.52 (2.236)	32.51 (2.418)	**0.003**
< 28	2 (3.8)	46 (4.5)	**0.048**
28- 31^{+6}	4 (7.7)	227 (22.3)	
32- 36^{+6}	46 (88.5)	727 (71.3)	
≥ 37	0 (0.0)	19 (1.9)	
Mode of delivery			
Normal delivery	23 (44.2)	466 (45.7)	0.89
Cesarean section	29 (55.8)	542 (53.2)	
FE/VE	0 (0.0)	5 (0.5)	
Assisted breech	0 (0.0)	6 (0.6)	
Birth weight (grams) 1,942.64 (SD = 566.20)	2,233.85(618.49)	1,927.62 (559.93)	**< 0.001**
< 1,000	2 (3.8)	42 (4.1)	0.002
1,000 - 1499	4 (7.7)	189 (18.5)	
1,500 - 2,499	28 (53.8)	632 (62.0)	
2500 or more	18 (34.6)	156 (15.3)	
Birth asphyxia[a]	3 (5.8)	98 (9.6)	0.35
NICU admission	12 (23.1)	345 (33.9)	0.11

Birth asphyxia[a] : Apgar score at 5 min after birth < 7

TABLE 4. Pregnancy outcomes according to results of urine culture.

N = 1,807	MUC + N = 43, n (%)	MUC - N = 1,764 n (%)	*P* value
Delivery in this admission	18 (41.9)	774 (43.9)	0.79
	N = 18	**N = 774**	
Gestational age at delivery (weeks), mean (SD) 32.56 (SD = 2.42)	31.72 (2.74)	32.28 (2.38)	0.33
< 28	3 (16.7)	39 (5.0)	0.16
28- 31^{+6}	3 (16.7)	187 (24.2)	
32- 36^{+6}	12 (66.7)	535 (69.1)	
≥ 37	0 (0.0)	13 (1.7)	
Mode of delivery			
Normal delivery	4 (22.2)	361 (46.6)	0.21
Cesarean section	14 (77.8)	406 (52.5)	
FE/ VE	0 (0.0)	4 (0.5)	
Breech assisting	0 (0.0)	3 (0.4)	
Birth weight (grams) 1,942.64 (SD = 566.20)	1,671.67 (664.30)	1,895.57 (549.15)	0.09
< 1,000	4 (22.2)	28 (3.6)	**0.001**
1,000 – 1,499	3 (16.7)	158 (20.4)	
1,500 - 2,499	9 (50.0)	481 (62.1)	
2,500 or more	2 (11.1)	107 (13.8)	
Birth asphyxia[a]	4 (22.2)	77 (9.9)	0.89
NICU admission	11 (61.1)	275 (35.5)	**0.03**

Birth asphyxia[a] : Apgar score at 5 min after birth < 7

urinalysis and culture were performed in 1,206 cases, urinalysis only in 269 cases and urine culture only in 1 case. Of the 1,206 cases who had both modalities of urine testing, the urine culture was positive in 33 cases. Within these 33 cases, 19 had an abnormal urinalysis based on WBC or RBC counts in the urine sediment. Thus, "abnormal urinalysis" using these criteria would detect only 57.6% of positive urine culture cases. Another marker from urinalysis was needed to improve sensitivity and the presence of bacteria in the sediment at the time of urinalysis was added into consideration. Urinalysis with abnormal cell count and/or presence of bacteria of ≥ 2+ was considered a positive screening. Urinalysis without significant cell count and significant presence of bacteria was considered negative. With this urinary screening criteria, a positive urine culture could be identified with the performance as shown in Table 5. The urine culture would have been performed in 78 cases (6.5%) with 90.9% sensitivity.

DISCUSSION

The overall prevalence of positive urine culture and abnormal urinalysis among pregnant women with premature uterine contractions was 2.4% and 4.1%, respectively. Considering in combination, UTI was present in 4.9%. The prevalence of abnormal urinalysis and positive urine culture were not significantly different between the PTL/PPROM and TPL groups. The most common organism identified was *Escherichia coli* in both groups. Newborns of women with positive urine culture had higher rates of extremely low birth weight (birth weight < 1,000 g) and admission to the NICU than newborns of women with negative urine culture.

Although ASB screening in early pregnancy is recommended as standard care, its benefits are still controversial. The reported prevalence of ASB among preterm labor or presumptive preterm labor groups has varied between studies.[14-16,20] The current investigation revealed a lower prevalence of positive urine culture

TABLE 5. Urinalysis as a screening tool for urine culture in TPL cases.

	Positive urine culture	Negative urine culture	Total
Positive urinalysis screening	30	48	78
Negative urinalysis screening	3	1,125	1,128
Total	33	1,173	1,206

Sensitivity: 90.9%; Specificity: 95.9%;
Negative predictive value: 99.7%; Positive predictive value: 38.5%
Positive urinalysis screening: Urinalysis with abnormal cell count and/or presence of bacteria of ≥ 2+
Negative urinalysis screening: Urinalysis without significant cell count and significant presence of bacteria (≤ 1+)

(2.4% vs 5%) among pregnant women admitted with premature uterine contractions than an older study at our institute.[15] More recent research at our hospital in 2015 revealed a comparable prevalence among pregnancies in any trimester without premature uterine contraction.[9] The prevalence might have decreased due to different urine collection techniques, which changed from voluntary urination to clean urinary catheterization.

The most common organism for positive urinary culture in the present investigation was *Escherichia coli*, which was similar to the findings of other investigations.[9,15,20,21] The current work also found 2 women with *Streptococcus agalactiae* (Group B *Streptococcus*; GBS), both presented with PPROM which might have increased the risk of urinary infection from the rectovaginal colonization of GBS. Antenatal screening of GBS colonization and the use of an appropriate intrapartum antibiotic prophylaxis should be considered to prevent newborn infections.[22]

This study showed that abnormal urinalysis and positive urine culture were not associated with delivery rate in that particular admission. This evidence agrees with other work in which an MUC was not recommended as a routine laboratory test in pregnancy with preterm labor without clinical indications.[14] However, newborns of pregnancies with positive MUCs were related to poor neonatal outcomes, such as risk of extremely low birth weight and NICU admission.[7,8]

Our study revealed a rather low prevalence of abnormal urinalysis (4.1%) and positive urine culture (2.4%) in pregnancies with premature uterine contractions. We propose a strategy to identify those who need a urine culture in women diagnosed with TPL instead of universal culture. Urinalysis is first performed and the results are used for contemplating urine culture. The cases with abnormal WBC or RBC counts, or cases a bacteria rating of ≥ 2+ should proceed to urine culture, while those with normal cell counts and lower rate of bacteria in the sediment should not. With this strategy, only 6.5% of cases with TPL would need urinary culture with 90.9% sensitivity. This would save cost, time and manpower considerably. The evidence from this study can be used to guide the routine ordering of appropriate laboratory tests.

This study assessed the benefit of simultaneous urinalysis and urine culture in women with premature uterine contractions with a large number of subjects. Moreover, a strategy to reduce number of unnecessary urine culture in TPL cases has been proposed. However, this retrospective study was unable to demonstrate a causal relationship. Besides, selection bias from incomplete screening might have affected the results as urine culture was performed in 79% of the total cohort.

In conclusion, routine urinalysis and urine culture in women admitted with premature uterine contractions did not predict whether the pregnancy could be continued or not. However, adverse neonatal outcomes were more common in pregnancies with positive urine culture. Urinalysis result could be used to identify women with TPL who should have a urine culture to reduce unnecessary culture.

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Conflict of interest

None declared.

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