Prevalence of Positive Culture of Genitourinary Tract Microorganisms in Pregnant Women with Presumptive Preterm Labor

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Background: *Cultures of genitourinary tract microorganisms have been included in routine evaluation for all pregnant women who present with presumptive preterm labor. However, some studies found that this assessment is costly and adds little value.*

Objective: *To determine the proportion of pregnant women with presumptive preterm labor who had positive culture of genitourinary tract microorganisms and to determine the relationship of positive genitourinary infection and pregnancy outcomes.*

Material and Method: *This retrospective cohort study was performed at Department of Obstetrics and Gynecology, Faculty of Medicine, Siriraj Hospital, Mahidol University. Medical records of pregnant women with presumptive preterm labor who were admitted in non-private labor room between January 2003 and December 2008 were reviewed. Characteristics, results of vaginal swab culture and urine culture, and clinical outcomes were analyzed and reported.*

Results: *The prevalence of positive culture of genitourinary tract microorganisms in presumptive preterm labor-women (total n = 704) was 24.3% (95% CI = 21.3-27.6), 22.1% (95% CI = 19.1-25.4) of vaginal swab culture and 5.3% (95% CI = 3.8-7.2) of urine culture. However, only 9.8% were pathologic organisms. There were no statistically significant differences in characteristics and rate of preterm labor between women with a positive and a negative culture. Moreover, there were no statistically significant differences in characteristics and preterm birth outcomes between women in both groups.*

Conclusion: *There were no clinical significances of positivity of pathologic bacteria from genitourinary tract as a predictor of preterm delivery and its outcomes. Although the prevalence is quite high, the value of these screenings is still questionable.*

Keywords: *Presumptive preterm labor, Vaginal swab culture, Urine culture*

J Med Assoc Thai 2013; 96 (9): 1111-8
Full text. e-Journal: *http://jmat.mat.or.th*

Preterm births account for 75% of perinatal mortality and more than half the long-term morbidity[1]. Although most preterm babies survive, they are at increased risk of neurodevelopmental impairments, and of respiratory and gastrointestinal complications[1,2]. In spite of advances in obstetric care, the rate of prematurity has not decreased over the past 40 years. In the United States, the preterm birth rate is approximately 11%, whereas higher incidence rates of the preterm delivery were found in developing countries[1].

Spontaneous preterm labor is responsible for more than half of preterm births[3]. Although there are many factors associated with preterm birth after spontaneous preterm labor, the etiology in most cases is not clear. Identification of the risk factors in the spontaneous preterm labor may assist in screening and taking care of pregnant women at risk more properly[1]. There is an increasing body of evidence linking urinary tract infection[4], intrauterine infection[5], and vaginal infection[1,6,7] with increased risk for spontaneous preterm birth. A prompt diagnosis and treatment can significantly delay delivery, increase birth weight, and improve neonatal outcome[8-10].

Since 2002, in addition to history taking, physical examinations, and evaluate gestational age and other risk factors of preterm birth, urinary analysis, vaginal swab and evaluation of urine cultures have been included in routine evaluation for all pregnant women who present with presumptive preterm labor and thus are admitted in Department of Obstetrics and Gynecology, Siriraj Hospital according to the

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departmental management guidelines for preterm labor[11]. Moreover, another recent study found that there is no correlation between positive culture of genitourinary tract and preterm birth[12].

As aforementioned, further studies are needed to better define the link between various maternal microbial colonization and spontaneous preterm birth, with the possibility establishing new screening and treatment recommendations. The aims of this study are to determine the prevalence of positive culture of genitourinary tract in pregnant women coming with presumptive preterm labor and to determine the relationship of positive culture and pregnancy outcomes.

Material and Method

This retrospective cohort study was performed at the Department of Obstetrics and Gynecology, Faculty of Medicine, Siriraj Hospital, Mahidol University, following the ethics principle of declaration of Helsinki, and was approved by the Siriraj Institutional Review Board. Medical records of all pregnant women who came with presumptive preterm labor and were hospitalized between January 2003 and December 2008 were reviewed. Since 2003, a clinical practice guideline (CPG) for preterm labor has been developed and implemented at our institute. All pregnant women with presumptive preterm labor were admitted to the labor room. Clean catch urine was collected for culture before pelvic examination. During the initial pelvic examination, a speculum was introduced into the vagina. If there were some evidences regarding the status of the membranes, testing for rupture of membranes was performed with nitrazine paper, the presence or absence of pooling was noted and microscopic slide evaluation was done to detect ferning. If rupture of membranes was not evident by the presence of at least two of these findings, collection for vaginal swab culture was then performed before digital examination of cervix for dilatation and effacement. All culture specimens were sent to the hospital's microbiology laboratory. Cultures that grew more than 100,000 colonies of mixed bacteria (at least 3 species) were considered to represent contamination and not included in the analysis[11].

Presumptive preterm labor was defined as the regular uterine contractions occurring at a frequency of four in 20 minutes or eight in 60 minutes (or at an interval of <8 min) in pregnant women with a gestational age between 28^{+0} and 36^{+6} weeks. The management according to CPG included bed rest and hydration without tocolytics or steroids[13] and close observation for clinical signs and symptoms established for preterm labor. If uterine contractions spontaneously ceased for more than 24 hours, a false preterm labor was diagnosed and the patient was discharged. If clinical signs and symptoms met or progressed to meet the preterm labor criteria following criteria documented by the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists[14], preterm labor was diagnosed and the patients who were less than 34 weeks of gestation were treated by tocolytics, steroids, and antibiotics. The only steroid used in Department of Obstetrics and Gynecology, Siriraj Hospital was dexamethasone 5 mg i.m. every 12 hours for four doses[14]. Tocolytic drugs included terbutaline or magnesium sulfate[15-17]. Success of treatment in patients with preterm labor was defined as arrest of labor and no delivery within 48 hours. After successful cessation of uterine contractions and discontinuation of tocolytics for at least 24 hours, these women were discharged with an instruction to restrict physical activity without either maintenance of tocolytics[18], or repeated courses of steroids[17].

Patients who had preterm delivery at the first admission were classified as preterm delivery group (PT) while those who were discharged were classified as discharged undelivered group (DU). Patients were excluded with the following conditions, (a) vaginal swab culture and urine culture were not performed, (b) they were pregnant with multifetal gestations, (c) no antenatal care, (d) uncertain pregnancy date, (e) ultrasonographic evidence of fetal death or lethal congenital anomalies, (f) placenta previa or placental abruption, (g) any contraindication for tocolytics, (h) maternal medical complications, or (i) preterm premature rupture of membranes.

The results of these cultures were reviewed for the final report, and the charts of patients were reviewed to evaluate the diagnosis and outcomes. The sample size was based on our 100-case pilot finding of a 26% prevalence rate of positive culture of genitourinary tract microorganisms in presumptive preterm labor-women. With confidence level at 95% and margin of error at 5%, at least 604 presumptive preterm labor-women were required. Data were analyzed using SPSS version 13 (SPSS, Chicago, IL, USA) and were expressed as mean ± standard deviation (SD) or number (%). Student's t-test was used to compare continuous data. The rank sum test was applied when distributional assumptions were

suspect. Pearson X^2-test or Fisher's exact test was used to compare categorical data. Statistically significant differences were defined as p less than 0.05.

Results

Nine thousand two hundred seventy four pregnant women were admitted to the labor room due to presumptive preterm labor between 2003 and 2008. Vaginal swab culture and/or urine culture were performed in 1,224 women. Five hundred twenty women were excluded because of preterm premature rupture of membranes (n = 265), no antenatal care (n = 103), maternal medical complications (n = 72), multi fetal gestations (n = 53), placenta previa or placental abruption (n = 24) and, anomaly fetus (n = 3). Finally, 704 women were recruited for analysis. Out of 704 women, 219 (31.1%) were the PT group whereas the rest, 485 (68.9%) were in the DU group.

Out of 704 women, 171 (24.3%, 95% CI = 21.3%-27.6%) had positive vaginal swab culture and/or urine culture. The most common organism was fungus. However, only 9.8% of the identified organisms were pathogenic. Concerning pathogenic organisms, *Staphylococcus aureus* (*S. aureus*) and *Escherichia coli* (*E. coli*) were the most common pathologic organisms identified from vaginal discharge and urine, respectively (Table 1). Interestingly, there were no statistically significant differences of all baseline characteristics and rate of preterm delivery (27.5% vs. 27.8%, p = 0.943) between women with a positive and a negative culture (Table 2).

In addition, there was no statistically significant difference in proportion either of positive vaginal swab culture or positive urine culture between women in PT group and DU group (7.7% vs. 5.8%, p = 0.361; 5.2% vs. 4.9%, p = 0.865) (Table 3). Moreover, no statistically significant differences were found in terms of baseline characteristics and pregnancy outcomes of women with preterm birth between women with a positive and a negative culture (Table 4).

Discussion

It is generally accepted that a birth occurring between 20 and 37 weeks' gestation is defined as preterm birth. However, in Thailand and many developing countries, any termination of pregnancy at less than 28 complete weeks' gestational age is defined as abortion; therefore, the gestational age of preterm labor in this CPG is confined between 28 complete weeks and 36^{+6} weeks.

The pathogenesis of preterm labor is not well understood, and it is often not clear whether it represents early idiopathic activation of normal labor process or results from a pathologic mechanism[6]. Upper genital tract infection is one of many factors that are associated with preterm birth[7]. A previous study found that clinical chorioamnionitis complicated 1-5% of term pregnancy, while it complicated nearly 25% of preterm delivery. However, investigation in this regard was not recommended in our CPG due to difficult detection with conventional culture techniques.

In general, it appears that spontaneous preterm deliveries occur much more commonly in women with vaginal infection. The most common pathway that enables microorganisms to gain access to the amniotic cavity is ascending from the vagina and cervix[1,6]. The present study found that there was 6.3% prevalence of

Table 1. Prevalence of positive culture of genitourinary tract in women with presumptive preterm labor

Types of organisms	Vaginal swab culture; n = 648, n (%)	Urine culture; n = 683, n (%)	Vaginal swab and/or urine culture; n = 704, n (%)
Pathologic organisms			
Escherichia coli	6 (0.9)	16 (2.3)	20 (2.8)
Klebsiella pneumoniae	1 (0.2)	2 (0.3)	3 (0.4)
Methicillin sensitivity *Staphylococcus aureus*	28 (4.3)	6 (0.9)	31 (4.4)
Group B streptococcus	4 (0.6)	0	4 (0.6)
Enterobacteriacae	2 (0.3)	10 (1.5)	11 (1.6)
Total pathologic organisms	41 (6.3)	34 (5.0)	69 (9.8)
Non-pathologic organisms			
Lactobacillous	14 (2.2)	0	14 (2.0)
Diptheroides	6 (0.9)	0	6 (0.9)
Yeast	82 (12.7)	2 (0.3)	82 (11.6)
Total non-pathologic organisms	102 (15.7)	2 (0.3)	102 (14.5)
Total	143 (22.1)	36 (5.3)	171 (24.3)

Table 2. Comparison of characteristics in pregnant women with presumptive preterm labor between positive and negative culture

Characteristics	Culture		p-value
	Positive (n = 171) mean ± SD or n (%)	Negative (n = 533) mean ± SD or n (%)	
Age (year)	25.80±6.4	25.2±6.4	0.285
Gestational age (week)	33.10±2.1	33.2±2.0	0.699
Body weight (kilogram)	61.70±10.7	61.6±11.2	0.954
Height (centimeter)	156.10±5.5	156.2±5.8	0.961
Gravida	1.84±0.99	1.83±0.97	0.987
Nullipara	98 (57.3)	312 (58.5)	0.777
Abortion	34 (19.9)	118 (22.1)	0.533
Dexamethasone use	70 (40.9)	253 (47.5)	0.131
Receiving 4 doses of dexamethasone	60/70 (85.7)	200/253 (79.1)	0.286
Tocolytic use	82 (48.0)	280 (52.5)	0.297
Uterine contractions at admission			
Interval of contraction (minute)	3.95±1.51	4.18±1.55	0.254
Duration of contraction (second)	37.43±8.15	38.59±17.08	0.575
Severity of contraction (score 1-3)	1.25±0.44	1.32±0.47	0.276
Cervical status at admission			
Cervical dilatation, median (IQR)	1 (0, 2)	1 (0, 2)	0.446
Cervical effacement, median (IQR)	0 (0, 50)	0 (0, 50)	0.060
Station of presenting part of fetus	2.19±0.80	2.18±1.41	0.971
Rate of preterm delivery	47 (27.5)	148 (27.8)	0.943

Data are mean ± standard deviation, median (IQR) or n (%)
IQR = interquartile range

Table 3. The proportion of positive pathologic bacteria between preterm delivery and discharged undelivered group

Positive culture	Group		p-value
	Preterm delivery n/N (%)	Discharged undelivery n/N (%)	
Positive pathologic bacteria of vaginal swab culture	15/196 (7.7)	26/452 (5.8)	0.361
Positive pathologic bacteria of urine culture	11/212 (5.2)	23/471 (4.9)	0.865
Positive pathologic bacteria of vaginal swab culture and/or urine culture	26/219 (11.9)	44/485 (9.1)	0.250

positive pathologic bacteria identified form vaginal discharge in women with presumptive preterm labor. However, there were comparable proportions of positive culture for pathological bacteria between women with preterm delivery and women who were discharged undelivered (Table 3). The authors classified *Lactobacillous* and *Diptheroides* as non-pathologic organisms, presumed to reflect contamination of the specimen with vaginal flora. Interestingly, 12.7% of positive culture in this study was yeast. This is comparable with results from a large multicenter study involving more than 2,500 pregnant women that found monilia in 20% of patients at 24 to 28 weeks gestation and this was not associated with preterm birth. It was also classified as non-pathologic organisms in the present study.

Based on the best available data there is a relative risk for preterm birth of 2 to 5, with 2 in untreated pregnant women with *Neisseria gonorrhoeae* (*N. gonorrhoeae*) (prevalence 1%), and *Chlamydia trachomatis* (*C. trachomatis*) (prevalence 5%), respectively[7]. These organisms were identified by

Table 4. Comparison of characteristics and outcomes in pregnant women with preterm birth between a positive and a negative culture

Characteristics and outcomes	Pathologic bacteria		p-value
	Positive (n = 26) mean ± SD or n (%)	Negative (n = 193) mean ± SD or n (%)	
Age (year)	25.51±6.25	25.46±6.90	0.974
Gestational age (week)	34.04±1.37	33.70±1.70	0.356
Body weight (kilogram)	58.11±11.50	61.02±12.79	0.510
Height (centimeter)	153.00±5.12	156.03±5.20	0.095
Gravida	2.00±1.23	1.81±0.93	0.357
Nullipara	14 (53.80)	117 (60.6)	0.508
Abortion	6 (23.10)	38 (19.7)	0.686
Uterine contractions at admission			
Interval of contraction (minute)	3.54±1.36	3.92±1.40	0.191
Duration of contraction (second)	38.85±7.91	42.49±27.63	0.505
Severity of contraction (score 1-3)	1.46±0.47	1.38±0.52	0.559
Cervical status at admission			
Cervical dilatation, median (IQR)	2 (0, 3)	2.50 (1, 3)	0.288
Cervical effacement, median (IQR)	75 (0, 80)	80 (25, 100)	0.082
Station of presenting part of fetus	2.19±0.80	2.18±1.41	0.826
Dexamethasone use	12 (44.7)	107 (53.4)	0.372
Rate of 4 doses of dexamethasone (n = 100)	9/21 (34.6)	59/79 (30.6)	0.676
Tocolytic use	9 (60.0)	94 (57.2)	0.831
Antibiotic use	16 (61.5)	144 (74.6)	0.158
Fetal birth weight (gram)	2,310.40±321.20	2,193.70±364.80	0.129
APGAR score at 1st minute	8.62±1.99	8.27±1.69	0.344
APGAR score at 5th minute	9.42±1.86	9.62±0.81	0.587
Need for resuscitation	10 (38.0)	84 (43.5)	0.624
Length of hospital stay (day)	4.33±1.9	6.48±9.1	0.233
NICU admission	1 (3.8)	12 (6.7)	0.486

Data are mean ± standard deviation, median (IQR) or n (%)
IQR = interquartile range

DNA amplification test. However, DNA amplification techniques for identification of these organisms were not recommended in our CPG due to the limitation in resources. No *N. gonorrhoeae* and *C. trachomatis* were identified in our study. In addition to different backgrounds, different technique of identification is another factor for these conflict results.

There are numerous studies showing an association between the presence of bacterial vaginosis (BV) and preterm delivery[19,20]. However, the diagnosis of BV is generally performed by using the Amsel's criteria. Traditional score of Gram's stain of vaginal smears using the Nugent system also aids in the identification of BV[21,22]. This requires expensive equipment and well-trained or experienced personnel. Therefore, it is not readily available in labor and delivery suites. Our recent study in which BV blue, a more convenient but more expensive test, was used for diagnosis of BV, found no association between the presence of bacterial vaginosis (BV) and preterm delivery (22% in BV group vs. 17.7% in non-BV group), although a quarter of pregnant women with preterm labor had positive test for BV(23). With limited resources, currently we do not use any investigation to diagnose BV in women with presumptive preterm labor in our CPG.

Concerning urine culture, it is generally recognized that asymptomatic bacteriuria occurs in

3 to 10% of pregnancies[24]. A prevalence of 5% of bacteriuria was found in the present study. Although there is a strong suggestion of relationship between asymptomatic bacteriuria and preterm labor[4], and many institutions have incorporated the practice of obtaining a urine culture as a part of routine workup of patients with presumptive preterm labor, interestingly, there was no statistically significant difference in proportion of positive urine culture between pregnant women in PT group and DU group in our study.

Exposure to infection is associated not only with preterm birth but also with several of the complications of prematurity[5]. However, the authors found no statistically significant differences of all baseline characteristics and pregnancy outcomes of women with preterm birth between women who had a positive and a negative culture for pathological bacteria. In addition, there were comparable administration rates of steroid and tocolytics and antibiotics between the two groups (44.7% vs. 53.4%, p = 0.372; 60% vs. 57.2%, p = 0.831; 61.5% vs. 74.6%, p = 0.158, respectively). Genitourinary infection in pregnancy may be a primary causative role in a fraction of the cases of preterm birth and may interact adversely with a variety of maternal and fetal factors.

The authors' study has limitations that should be acknowledged. It was a retrospective study. Symptoms of genitourinary tract infection were not recorded so no sensitivity and specificity calculations could be performed regarding symptoms and their ability to predict a positive culture. No investigation was used for diagnosis of BV and no DNA amplification tests were used for *N. gonorrhoeae* and *C. trachomatis* in this study. The authors conclude that positivity of pathologic bacteria from genitourinary tract infection is not a clinically significant association of preterm delivery and its outcomes.

Conclusion

There were no clinical significantly associated with positive pathologic bacteria from genitourinary tract and preterm delivery and its outcomes. Although this prevalence is quite high, the value of these screenings is still questionable.

What is already known in this topic?

There is an increasing body of evidence linking urinary tract infection[4], intrauterine infection[5], and vaginal infection[1,6,7] with increased risk for spontaneous preterm birth. A prompt diagnosis and treatment can significantly delay delivery, increase birth weight, and improve neonatal outcome[8-10]. However, a particular study has found that the use of urine cultures in the assessment of preterm labor is costly and adds little value to obtaining a diagnosis in this group of patients[11]. Moreover, another recent study found that there is no correlation between positive culture of genitourinary tract and preterm birth[12].

What this study adds?

The authors found that there were no clinical significances of positivity of pathologic bacteria from genitourinary tract as a predictor of preterm delivery and its outcomes.

Potential conflicts of interest

None.

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ความชุกของการตรวจพบการติดเชื้อจุลชีพจากการเพาะเชื้อในทางเดินปัสสาวะและอวัยวะสืบพันธุ์ในกลุ่มสตรีตั้งครรภ์ที่ได้รับการสันนิษฐานว่ามีภาวะเจ็บครรภ์คลอดก่อนกำหนด

อัมพัน เฉลิมโชคเจริญกิจ, สุขุมาล โพธิ์ทอง, พรพิมล เรืองวุฒิเลิศ, มานพชัย ธรรมคันโธ

ภูมิหลัง: *การเพาะเชื้อเพื่อตรวจหาการติดเชื้อจุลชีพของทางเดินปัสสาวะและอวัยวะสืบพันธุ์ ได้ถูกรวมอยู่ในแนวทางการประเมินกลุ่มสตรีตั้งครรภ์ที่ได้รับการสันนิษฐานว่ามีภาวะเจ็บครรภ์คลอดก่อนกำหนด อย่างไรก็ตามมีบางการศึกษาพบว่าการประเมินดังกล่าวนี้สิ้นเปลืองค่าใช้จ่ายและได้ประโยชน์น้อย*

วัสดุและวิธีการ: *การศึกษาชนิดนี้เป็นการศึกษาแบบ retrospective cohort ได้ทำการทบทวนเวชระเบียนของสตรีตั้งครรภ์ที่ได้รับการสันนิษฐานว่ามีภาวะเจ็บครรภ์คลอดก่อนกำหนด ที่เข้ารับการรักษาในห้องคลอดสามัญ โรงพยาบาลศิริราช ระหว่างเดือนมกราคม พ.ศ. 2546 ถึง เดือนธันวาคม พ.ศ. 2551 ลักษณะพื้นฐานของผู้ป่วย ผลของการตรวจเพาะเชื้อจากทางเดินปัสสาวะและอวัยวะสืบพันธุ์ ตลอดจนผลลัพธ์ของภาวะเจ็บครรภ์คลอดก่อนกำหนดที่เกิดขึ้นจะถูกนำมาวิเคราะห์และรายงานผล*

ผลการศึกษา: *จากสตรีตั้งครรภ์ที่ได้รับการสันนิษฐานว่ามีภาวะเจ็บครรภ์คลอดก่อนกำหนดจำนวน 704 คน พบความชุกของการตรวจพบเชื้อจุลชีพ จากการเพาะเชื้อในทางเดินปัสสาวะและอวัยวะสืบพันธุ์ ร้อยละ 24.3 โดยพบความชุกของของการตรวจพบเชื้อจุลชีพจากการเพาะเชื้อจากช่องคลอด ร้อยละ 22 และความชุกของการตรวจพบเชื้อจุลชีพจากการเพาะเชื้อจากปัสสาวะ ร้อยละ 5.3 มีเพียงร้อยละ 9.8 ที่เป็นเชื้อจุลชีพก่อโรค อย่างไรก็ตามไม่พบว่ามีความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างลักษณะพื้นฐานของผู้ป่วย อัตราการคลอดก่อนกำหนดระหว่างกลุ่มผู้ป่วยที่มีผลการเพาะเชื้อเป็นบวกและเป็นลบ นอกจากนี้ยังไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างผลของการคลอดก่อนกำหนดในระหว่างกลุ่มสตรีที่มีผลการเพาะเชื้อเป็นบวกและเป็นลบเช่นกัน*

สรุป: *ไม่มีนัยสำคัญทางคลินิกของการตรวจพบเชื้อจุลชีพก่อโรค จากการเพาะเชื้อทางเดินปัสสาวะและอวัยวะสืบพันธุ์ที่จะใช้เป็นตัวทำนายอัตราการคลอดก่อนกำหนด ตลอดจนผลของการคลอดก่อนกำหนดที่เกิดขึ้น แม้จะพบว่ามีความชุกการตรวจพบเชื้อจุลชีพค่อนข้างสูงก็ตาม แต่ประโยชน์ของการตรวจคัดกรองนี้ยังไม่ได้ข้อสรุป*