

## ภาวะความเป็นกรดต่างในช่องคลอดร่วมกับการวัดความยาวปากมดลูก ในการทำนายการคลอดก่อนกำหนด

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### Abstract : Comparison of Vaginal pH with Cervical Length in the Second Trimester for Prediction Preterm Birth

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**Objective :** To find the diagnostic value of combined vaginal pH and cervical length measurement in the second trimester of pregnancy as a preterm birth predictor.

**Materials and Methods :** A descriptive, diagnostic test of 311 singleton pregnant women between 18 and 24 weeks of gestation were measured vaginal pH and cervical length. The cut-off values for vaginal pH and cervical length were defined as 5 and <3 cm. The pH-indicator strips were used for vaginal pH and transvaginal ultrasound was used for cervical length.

**Results :** The incidence of preterm birth was 37 (11.9 %). Alkaline vaginal pH was found 122 women (39.23 %), shorted cervical length was found 61 (19.6 %) and both was found 45 (14.5 %). Low pos predictive value of vaginal pH (9.84) and short cervical length (14.75) was not significantly in predicting PTL. But, High specificity (81.08 %) and NPV (88.2) of short cervical length could use to exclude PTL and combine with both cervical length and vaginal pH have better result than cervical length (86.86) (89.37). Alkaline vaginal pH significantly decreases the odds of preterm labor (OR=0.72) but short cervical length and combine both increases the odds (OR=1.37), (OR=2.21).

**Conclusion :** Low risk population, cervical length measurements more than 3 cm at 18-24 week gestation, preterm birth is low. Vaginal pH alone cannot be a good predictor for preterm birth. When combined these two parameters, negative result can be good sign to preclude spontaneous preterm birth.

**Keywords :** Bacterial vaginosis, cervical length measurement, preterm birth, second trimester

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#### บทคัดย่อ

**วัตถุประสงค์ :** เพื่อศึกษาความแม่นยำของภาวะความเป็นกรดต่างในช่องคลอดร่วมกับการวัดความยาวปากมดลูก ในการทำนายการคลอดก่อนกำหนด

**วัสดุและวิธีการ :** การวิจัยเชิงพรรณนา ในหญิงตั้งครรภ์ 311 คน ที่มาฝากครรภ์ที่อายุครรภ์ระหว่าง 18 ถึง 24 สัปดาห์ ได้รับการตรวจภาวะความเป็นกรดต่างในช่องคลอดร่วมกับการวัดความยาวปากมดลูก โดยใช้ค่า 5 หรือน้อยกว่า แสดงว่าสารคัดหลั่งในช่องคลอดเป็นด่าง และความยาวปากมดลูกที่สั้นกว่า 3 เซนติเมตรในการทำนายการคลอดก่อนกำหนด

**ผลการศึกษา :** อุบัติการณ์การคลอดก่อนอายุครรภ์ 37 สัปดาห์ 37 ราย (11.9 %) สารคัดหลั่งในช่องคลอดเป็นด่าง 122 ราย (39.23 %) ปากมดลูกสั้นกว่า 3 เซนติเมตร 61 ราย (19.6 %) พบภาวะทั้งสองอย่างร่วมกัน 45 ราย (14.5 %) ความจำเพาะและการทำนายในการทำนายว่าทารกจะคลอดครบกำหนด เท่ากับ 81.08 % และ 88.20 % ตามลำดับ อำนาจในการทำนายผลบวกของอุบัติการณ์การคลอดก่อนอายุครรภ์ 37 สัปดาห์ ของภาวะความเป็นด่าง และช่องคลอดสั้นเท่ากับ 9.84 % และ 14.75 % ตามลำดับ เมื่อรวมทั้งสองปัจจัยสามารถทำนายอายุครรภ์ที่คลอดได้ดีขึ้น โดยภาวะความเป็นด่างในช่องคลอด ลดอัตราการคลอดก่อนกำหนดได้ 0.72 เท่า แต่เมื่อรวมกับความยาวปากมดลูก พบว่าเพิ่มอัตราการคลอดก่อนกำหนด 1.37 เท่า

**สรุป :** ในหญิงตั้งครรภ์ที่มีความเสี่ยงต่ำ ภาวะความเป็นด่างในช่องคลอดร่วมกับการวัดความยาวปากมดลูก ไม่สามารถทำนายการคลอดก่อนกำหนดได้

**คำสำคัญ :** ภาวะความเป็นกรดต่างในช่องคลอด, ความยาวปากมดลูก, การทำนายการคลอดก่อนกำหนด



## Introduction

Preterm labor and preterm birth is the important problem in obstetrics. Preterm birth (PTB) has been increasing and now complicates 6-12.5 % of pregnancies<sup>(1)</sup>. Preterm birth is the leading cause of perinatal morbidity and mortality, responsible for 75-90 % of all neonatal deaths not due to congenital malformation<sup>(2)</sup>. Amniotic fluid infection caused by a variety of microorganisms in the genital tract has been the cause of PTB<sup>(3)</sup>. Bacterial vaginosis (BV) is the most common genital tract infection in reproductive age women. One-third of pregnant women have BV<sup>(4,5)</sup>. BV is characterized by a complex change in the vaginal flora with a reduction in lactobacillus, an increase in the vaginal pH, and an overgrowth of other organisms, especially anaerobes. BV increased risk of PTB<sup>(6-9)</sup>. Diagnostic criteria for BV include clinical findings and laboratory tests. Amstel criteria include a grayish-white discharge that smoothly coats the vaginal walls, vaginal pH >4.5, positive whiffamine test, and clue cells on wet mount<sup>(10)</sup>. Vaginal pH alone is also considered diagnostic if >5.11. Vagina pH is 88.3 % sensitive and 58.6 % specific for the diagnosis of BV when using gram stain as the reference method<sup>(11)</sup>.

Ultrasound-based cervical length measurement was developed to identify women who increased risk of preterm birth. The risk of preterm birth was inversely correlated to the length of the cervix as measured by ultrasound. The most widely accepted and used technique is transvaginal ultrasound<sup>(12)</sup>. This study objective is to detect diagnostic value of abnormal vagina pH plus transvaginal cervical length measurement for preterm birth.

## Material and method

The descriptive, diagnostic test was conducted at Bhumibol Adulyadej hospital between

1 July 2016 and 31 July 2017. The study was approved by hospital ethic committee. Inclusion criteria are singleton pregnancy, accurate gestational age (GA) confirmed by LMP or first trimester ultrasonographic examination, gestational age between 18 and 24 week gestation at first diagnostic procedure and plan to delivery at the hospital. Exclusion criteria were pregnant women whose known medical disease, fetal anomaly, history of cervical surgery, recent sexual intercourse or use of products that can affect vaginal pH over the past 24 hours, current vagina bleeding and history of previous preterm birth. After written informed consent, recruited pregnant women were systematic sampling to performed vagina pH and ultrasonographic transvaginal cervical length measurement. Vaginal pH was measured by obstetric physician. The pH-indicator strips were used after speculum insertion in lithotomy position and no lubricants. Our study was correct pH by compare pH-indicator strips with pH color chart. The cut-off point of vaginal pH was 5 in this study population that it seem orange color. Transvaginal ultrasound examination was performed to measure the cervix length after the measurement of vaginal pH. Our study used Philip HD 11 to measure. The patient should empty her bladder prior to the examination. With the real-time image in view, the transducer is gently inserted into the anterior fornix until the cervix is visualized, while avoiding excessive pressure on the anterior cervical lip. The image of the cervix is enlarged to fill at least one-half of the ultrasound screen and oriented so that cephalad is to the left of the screen. The internal os is then located, often just below this edge. The appropriate sagittal long-axis view for measuring cervical length includes the usually V-shaped notch at the internal os, the triangular area of echodensity at the external os, and the endocervical canal, which appears as a faint line of

echodensity or echolucency between the two. It is usually the distance between calipers placed at the notches made by the internal os and external os. Choosing the shortest of three excellent images reduces interobserver variation. The cut-off point of cervical length was 3 cm in this study. Population to increase the validity and reliability of the vaginal pH measurements, same standard tests were used in all clinics and private offices. Vaginal pH and cervical length were collected by obstetric physician to increase the validity and reliability of the measurements.

All of them were followed antenatal care (ANC) until delivery. ANC management and other intervention were followed hospital protocol and blind to test result. All patient data were recorded in data recorded form. Sample size was calculated to detect diagnostic value of cervical length and vagina pH for preterm birth at sensitivity of 80 % with 10 % acceptable error and preterm birth rate 12 %. At least two hundred and ninety two subjects were needed. Statistical analysis was performed by SPSS version 18 (SPSS Inc. USA). Continuous data were described as mean and proportion as percentage. Group comparison was performed by chi square and student t test depend on data type, p value < 0.05 level was considered significant.

## Results

A total of 311 pregnant women were enrolled into the study. Demographic data was showed in table 1. Minimum gestational age at delivery was 32 weeks and maximum were 41. Minimum cervical length and vaginal pH were 2.7 cm and 4.5. Maximum were 6 cm and 7.

The incidence of preterm labor was 37 (11.96 %). Alkaline vaginal pH was found in 122 women (39.23 %), shorted cervical length was found in 61 (19.6 %) and both was found in 45 (14.5 %). (Table 2).

Sensitivity, specificity positive predictive value (PPV) positive likelihood ratio and was showed in table 3. This study present vaginal pH decreased the odds of preterm labor (OR=0.72) but not significant. Short cervical length (<30mm) are increased the odds of preterm labor (OR=1.37) but not significant. Combining of vaginal pH with cervical length had result higher than cervical length (OR=2.21) but not significant. (Table 4).

**Table 1. Number of preterm birth**

	GA < 37	GA ≥ 37	Total
pH ≥ 5	12	110	122
Cervical length < 30 mm	9	52	61
pH ≥ 5 and Cervical length < 30 mm	9	36	45

**Table 2 Demographic data and obstetric characteristic (n=311)**

Characteristics	Mean SD or number (%)
Age (years)	26.8±6.4
BW (kg)	72.5±14.7
Height (m)	1.6±0.1
BMI (kg/)	28.9±5.3
Parity	2+1
GA at 2 <sup>nd</sup> trimester (week)	21±3
GA at delivery (week)	38±2
Birthweight (gm)	3186.5±485.4
Vaginal pH	5.5±0.2
Cervical length	4.1±0.9



**Table 3. Diagnostic accuracy of vaginal pH  $\geq 5$  and cervical length  $<30$ mm as preterm labor predictors**

Variable	Sensitivity %	Specificity %	PPV %	NPV %	+LR
pH $\geq 5$	32.43	59.85	9.84	86.77	1.13
Cervical length $<30$ mm pH $\geq 5$ and	24.32	81.02	14.75	88.8	0.93
Cervical length $<30$ mm	24.32	86.86	20	89.47	0.87
p Value	$<0.001$	$<0.001$	$<0.001$	$<0.001$	$<0.001$

PPV positive predictive value

NPV negative predictive value

LR+ positive likelihood ratio

**Table 4. Odd ratio of vaginal pH5 and cervical length  $<30$ mm as preterm labor predictors**

Variable	Odd ratio (95 %CI)
pH $\geq 5$	0.72 (0.35-1.48)
Cervical length $<30$ mm pH $\geq 5$ and	1.37 (0.61-3.08)
Cervical length $<30$ mm	2.12 (0.97-4.91+)

## Discussion

This study presents a correlation between alkaline vaginal pH and shortened ultrasound cervical length measurement to prediction of preterm labor. In fact, preterm labor in vaginal pH higher than 5 was seen to be less than the vaginal pH below 5 (OR=0.98) but cervical length less than 30 mm almost 1.13-fold increases odds of preterm birth (OR=1.13). Series of studies were combined of vaginal pH, cervical length for evaluated preterm labor and result was little higher than cervical length result (OR=1.76). This study showed that vaginal pH cannot candidate for predicted of preterm labor. When vaginal pH combined with cervical length, they can improve specificity (86.86 %) and NPV (89.47).

Figueroa D et al planned secondary analysis of a randomized cerclage trial in women with prior spontaneous preterm birth 17-33 weeks<sup>(6)</sup>.

Vaginal gram stain and pH were collected at the initial study visit. Conclusion is presence of bacterial vaginosis at 16-21 week does not predict gestational age at birth in women at risk for recurrent preterm birth<sup>(6)</sup>. Melissa S. et al. was secondary analysis of pre-randomization data from a multicenter trial of ultrasound-indicated cerclage. 949 women with prior spontaneous PTB  $<34$  weeks underwent initial CL assessment and vaginal fluid collection by Nugent criteria at 16-21 weeks. Results in women with BV based on Nugent score  $\geq 7$  ( $p=0.04$ ) or pH  $\geq 5$  ( $p=0.016$ ), had significantly lower CL than unaffected women. They concluded that Nugent score, pH, and BV are inversely associated with CL. Both of study support result of this study.

Foroozanfar F et al. performed a prospective cohort 438 singleton pregnancy at 18-24 wk. in their study regarding vaginal pH and cervical length. The cut-off values for vaginal pH and cervical length were defined as 5 and  $<30$  mm. Alkaline vaginal pH was found 162 women (37 %) and shortened cervical length was found in 38 (8.7 %). The incidence of preterm labor weeks was 87 (19.9 %). Odd ratio of vaginal pH and cervical length was 3.06, 13.9. Conclusion is shortened cervical length has better value to predict preterm labor overall<sup>(15)</sup>. Sendag F et al. via a prospective study not only

found that there is a significant correlation between vaginal pH < 5 and increase risk of preterm delivery (that supports this study results), but also found simultaneously, there is a significant correlation between an elevated vaginal pH (> 5.0) and a shortened cervical length ( $r = -0.59$ ,  $p < 0.001$ )<sup>(16)</sup>.

These results differ from this study findings regarding accuracy of vaginal pH and cervical length, since we concluded that vaginal pH was not good to predictor of preterm labor. A possible explanation might be that they used more number and incidence of alkaline of vaginal pH is less than this study. Another reason is difference in population. This inconsistency with this study results may be due to a number of reasons like different methodology and analysis.

As results showed alkaline vaginal pH plus cervical length < 3 cm do not significantly predict preterm birth, but their specificity and NPV was 86.41 % and 89. This finding would reassure obstetrician for the less likelihood of having preterm birth in pregnant women with acid vaginal discharge and longer than 3 cm cervix. Because of performing vaginal pH test is not difficult and not time-consuming, this method is interesting to exclusion preterm birth.

In the next study if we can reduce interference of vaginal pH and collect them with method more precisely than pH-indicator strips then result of that study may difference and more significantly.

The limitation of this study is small number of sample size. Controlling variability for vaginal pH is difficult. Vaginal pH itself may not represent vaginal infection that direct effect on preterm birth. Treatment vaginitis was not presented in this study.

## Conclusion

In conclusion, in low risk population, cervical length measurements more than 3 cm at 18-24-week gestation, preterm birth is low. Vaginal pH alone cannot be a good predictor for preterm birth. When combined these two parameters, negative result can be good sign to preclude spontaneous preterm birth.

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