

# Vaginal Fluid PH Versus Cervical Length as A Predictor of Preterm Labor in The Second Trimester of Pregnancy

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## ABSTRACT

**Background:** Preterm birth is a major cause of death and a significant cause of long-term loss of human potential amongst survivors all around the world. Complications of preterm birth are the single largest direct cause of neonatal deaths.

**Aim of the work:** is to evaluate and compare the diagnostic value of vaginal pH and cervical length measurement in the second trimester of pregnancy as a preterm labor predictor.

**Patients and methods:** This prospective analytical study was done on a cohort of 100 selected pregnant women who were fulfilled the inclusion criteria in their antenatal visits at Al-Azhar university hospital. Patients coming for routine antenatal care between 18- and 24-weeks gestations were enrolled in the study.

**Results:** The results showed that the minimum cervical length measured was 2.1 (Cm) and the maximum was 4.4 (Cm). The mean cervical length was  $3.71 \pm 0.64$ (Cm). The minimum vaginal pH was 3.5 and the maximum pH was 5.5. The mean vaginal pH was  $4.7 \pm 0.6$ . The statistical analysis found that there is a significant correlation between cervical length and preterm labor. Also, cervical length had better predictive parameters than vaginal pH.

**Conclusion:** This concludes that measuring cervical length by trans vaginal ultrasound has a better predictive value for preterm labor than measuring vaginal pH in the second trimester of pregnancy.

**Keywords:** Vaginal fluid PH; Cervical length; Predictor of preterm labor; Second trimester of pregnancy

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## INTRODUCTION

Early detection of pregnant women at risk of preterm labor (PTL) will help to reduce the occurrence of prematurity-related mortality and morbidity. Incidence of premature birth is approximately 9.6% of all births globally <sup>1</sup>. Current screening tests for the prediction of spontaneous preterm labor can be divided into three general categories: (risk factor assessment, cervical measurement, and biochemical markers); however, it should be emphasized that significant associations with labor may not necessarily translate into clinical predictive utility <sup>2</sup>.

Two topics are related to screening for premature labor; bacterial vaginosis (BV) and cervical insufficiency. Both can be diagnosed using simple, safe, well-accepted, reliable, and reproducible methods; and they are potentially treatable <sup>3</sup>. Bacterial vaginosis is a modification of the vaginal flora characterized by a diminished or absent flora of lactobacilli, which increases the vaginal pH, and a significantly increased colonization of several anaerobic or facultative microorganisms <sup>4</sup>.

An easy, rapid, and inexpensive self-diagnostic test for BV may help to minimize the tendency to self-treat symptomatic BV blindly with antibiotics or treating inappropriately. Assessment of intravaginal pH is a helpful, but

frequently neglected procedure that can be used to evaluate vaginal health <sup>5</sup>.

An alternative method to identify high-risk women is the sonographic measurement of cervical length at 20-24 weeks of gestation, and several small studies have demonstrated that the risk of preterm delivery is inversely related to the length of the cervix <sup>6</sup>. Cervical length measured by trans vaginal ultrasonography has been shown to predict preterm birth in asymptomatic low-risk women as well as in those presenting with threatened preterm labor <sup>7</sup>.

This study aims to evaluate and compare the diagnostic value of vaginal pH and cervical length measurement in the second trimester of pregnancy as a preterm labor predictor.

## PATIENTS AND METHODS

**Study Population and Design:** This prospective analytical study was done on a cohort of 100 selected pregnant women who were fulfilled the inclusion criteria in their antenatal visits at Al-Husein university hospital. Patients were recruited from October 2018 till October 2019. The patients were informed about the study and written consent was taken from each patient.

**Patients:** Patients coming for routine antenatal care between 18- and 24-weeks gestations were enrolled in the study.

Patients were divided into three groups: Group A: with vaginal pH more than 5. The vaginal pH has been measured using pH indicator strips. Group B: with cervical length, less than 30 mm cervical length was determined using trans vaginal ultrasound.

**Sampling and Data Collection:**

*All the studied cases were subjected to the following:*

1-Full history taking. 2-Physical examination: (i) Pulse, blood pressure, temperature, lower limb edema. (ii) Obstetric examination. (iii) Vaginal sterile (dry) speculum examination: The vaginal fluid pH was measured using Ph-indicator strips (MColorpHast, Merck, Germany) after speculum insertion in the lithotomy position. No lubricants will be used to possible interaction with the results. 3-Ultrasonographic examination: (i) A transvaginal ultrasound was done for accurate dating, second-trimester routine scanning. (ii) Cervical length (CL) measurement was done using the transvaginal ultrasound (Toshiba nemio xg).

**Follow up:** All patients were followed up until delivery and gestational age, mode of delivery, and any complications were determined at delivery time.

**Outcome:** (1) To evaluate the diagnostic value of vaginal pH measurement in the second trimester as a preterm labor predictor. (2) To evaluate the diagnostic value of cervical length measurement in the second trimester as a preterm labor predictor.

**Statistical analysis:** Data was entered on the computer using the "Microsoft Office Excel Software" program (2010) for windows, then transferred to the Statistical Package of Social Science Software program, version 21 (SPSS) to be statistically analyzed. Data were summarized using range, mean, and standard deviation for quantitative variables or frequency and percentage for qualitative ones. A comparison between groups was performed

using the Mann Whitney test for quantitative variables while comparison for qualitative variables was performed through Chi-square or Fisher's exact test. Receiver operating characteristics (ROC) analysis was performed to explore the discriminant ability of both cervical length and vaginal PH in predicting preterm labor. P values less than 0.05 were considered statistically significant.

## RESULTS

Preterm Labor			
	Yes (n=11)	No (n=89)	P-value
Age	26.04 ± 5.49	26.56 ± 5.26	0.759 (NS)
Parity	1.44±1.18	1.44±1.13	1.000 (NS)
BMI	27.40 ± 3.06	27.25 ± 3.19	0.883 (NS)

**Table (1):** The relation between patients' mean age, parity, BMI, and preterm labor.

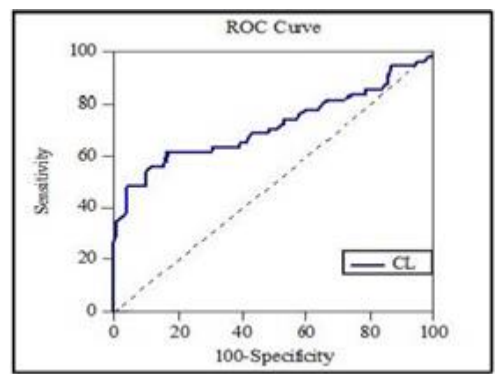
**Patients' Age:** In our cohort, the minimum age was 18 years and the maximum age was 35 years. The mean age was  $26.5 \pm 5.3$  years. The distribution of preterm labor concerning patients' mean age is shown in **(Table 1)**.

**Parity:** In our patients, 73% (n= 73) were multipara while 27 % (n= 27) were primipara. The minimum parity was 0 and the maximum was 6 with a mean parity of  $1.4 \pm 1.1$ . The mean parity for patients who had preterm delivery was  $1.44 \pm 1.18$  while the mean parity for patients who had a term delivery was  $1.44 \pm 1.13$ . The distribution of preterm labor to patients' mean parity is shown in **(Table 1)**.

**Body mass index ("MI):** The range of BMI of our patients is (22-48.7) with mean BM (of  $27.3 \pm 3.2$ ). The distribution of preterm labor with patients' mean BMI is shown in **(Table 1)**.

**Mode of delivery:** We found that 69 (69 %) of our patients have a normal vaginal delivery, while 31 (30%) have a cesarean section. The relation to preterm labor is non-significant (P= 0.756).

The predictive value of the cervical length in PTL:



**Figure (1):** ROC curve for cervical length.

The analysis of the receiver operating characteristic (Roc) curve is used to explore the discriminant ability of cervical length (Cm) to predict preterm labor. **(Figure 1)**

Cervical length (Cm)	Preterm labor				P-value
	Yes (n=11)		No (n=89)		
	N	%	N	%	
≤2.9	7	63.6	15	16.9	FE P=0.002 (SS)
>2.9	4	36.4	74	83.1	

Table (2): Predictive significance of cervical length in preterm labor

The Predictive significance of cervical length in preterm labor with cut-off value ≤ 2.9 Cm is shown in (Table 2).

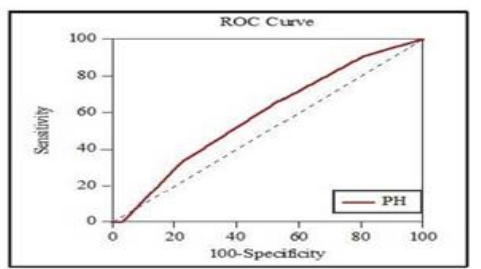


Figure (2): ROC curve for vaginal Ph

The analysis of ROC curve is used to explore the discriminant ability of vaginal pH to predict preterm labor. (Figure 2)

Vag. pH	Preterm labor				P-value
	Yes (n=11)		No (n=89)		
	N	%	N	%	
≤4.5	7	65.5	47	53.0	0.497 (NS)
>4.5	4	34.5	42	47.0	

Table (3): Predictive significance for vaginal pH in preterm labor

The Predictive significance for vaginal pH in preterm labor with cut-off value ≥4.5 is shown in (Table 3). Compares the correlation between mean cervical length and preterm labor (P= <0.001) and the correlation between mean vaginal pH and preterm labor (P= 0.04).

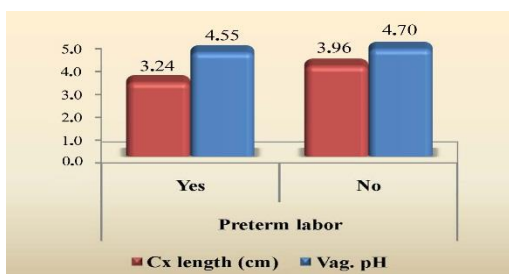


Fig. (3): Mean cervical length and mean vaginal pH concerning preterm labor

This concludes that the cervical length has a better predictive value for preterm labor than vaginal pH in the second trimester of pregnancy with significant value (p= <0.001). (Figure 3)

## DISCUSSION

In our cohort study, we found that the incidence of PTL < 37 weeks was 11/100 (11%). The significant risk factors included the history of preterm labor and the number of previous abortions with p values (0.001) and (0.006) respectively.

Our study determined that the cut-off values for cervical length and vaginal pH are (≤2.9 Cm) and (≥4.5) respectively.

We concluded that the cervical length measurement using vaginal ultrasound has a better predictive value for preterm labor than vaginal pH in the second trimester of pregnancy with significant (p value= <0.001)

This analysis shows that, for the use of cervical length, the sensitivity (61.8%), specificity (83.4%), positive predictive value (PPV) (31.5%), negative predictive value (NPV) (94.6%) and accuracy (81%). This also shows that, for the use of vaginal pH, the sensitivity (65.5%), specificity (47%), positive predictive value (PPV) (13.2%), negative predictive value (NPV) (91.7%) and accuracy (49%).

This is consistent with the study performed by Foroozanfard et al. <sup>1</sup> who conducted a prospective cohort study on 88 singleton pregnant women (18 - 24 weeks of gestation).

Vaginal pH of 5 and above was found in 32/88 women (37%) while cervical length <30mm was found in 8/88 (8.7%). The incidence of PTL < 37 weeks was 17/88 (19.9%). The predictive value of higher vaginal PH was significantly more (31%) than vaginal PH<5 (13%) in predicting PTL. As a result, alkaline vaginal PH significantly increases the odds of preterm Labor (OR=3.06). The study concluded that shortened cervical length is a better predictor of PTL than higher vaginal PH with a positive predictive value of 71% and a negative predictive value of 85%.

Cervical length <30mm nearly 14-fold increases odds of preterm birth (OR=13.9) Following our study, Banicevic et al. <sup>8</sup> studied cervical length measured by TV US and cervicovaginal infection as a predictor of preterm birth risk. This study was conducted as a prospective study of two groups. In the high-risk group, they had 8% of patients with cervical length <15mm, 30% of patients with cervical lengths from 15 to 25m, and 62% of patients with cervical length more than 25mm. In the low-risk group, we had no patients with cervical length bellow 15 mm, 95% of patients had cervical length more than 25mm, and 5% of patients had a cervical length from 15 to 25 mm. A high premature birth incidence of 50% was presented in patients with cervical length below 15mm. In the group of patients with cervical length up to 25mm the premature risk incidence was 10.52±0.05. In the high-risk group of patients with a positive cervical smear finding, regarding the cervical length the percentage was as follows; in the subgroup of 15mm length 88,89±11,87, in subgroup from 15 to 25mm was 62,07±11,43 and the subgroup bigger than 25min, 60.06±8.05.

Many other studies related the cervical length only to preterm labor, such as the study of Barber et al. <sup>9</sup>, that

is consistent with our study, measured cervical length in 2351 women between the 18th and 22nd week of pregnancy. Preterm delivery was categorized as before 37 weeks, before 34 weeks, and before 30 weeks. The study shows that before the 37<sup>th</sup> week, the odds ratios (ORs) of spontaneous delivery for cervical lengths in the 3<sup>rd</sup>, 5<sup>th</sup>, and 10<sup>th</sup> percentiles were, respectively, 25.47 (95% confidence intervals [CI], 15.5- 41.73); 16.98 (95% CI, 11.51-25.05); and 7.55 (95% CI, 5.44- 10.5). Before the 34<sup>th</sup> week, the ORs were 28.7 (95% CI, 14.54-41.73, 20.5 (95% CI, 11.51-25.05); and 10.3 (95% CI, 5.44-10.5). Before the 30<sup>th</sup> week, they were 29.8 (95% CI, 15.54-41.73); 23.1 (95% CI, 11.51-25.05); and 19.1 (95% CI, 7.44-31.5). In predicting premature delivery, the sensitivity, specificity, positive predictive value, and negative predictive value of cervical length were 26%, 98%, 63.6%, and 93.57% for the 3<sup>rd</sup> percentile; 34%, 97%, 51%, and 94% for the 5<sup>th</sup> percentile; and 39%, 92%, 31%, and 94% for the 10<sup>th</sup> percentile.

Following our study, Rashed et al. <sup>10</sup> entailed 294 women with singleton pregnancy; found that 10.8% of the women delivered prematurely. Transvaginal ultrasonographic cervical length measurements of term and preterm deliveries showed a statistically significant difference ( $P < 0.05$ ) but no significant difference was found in trans abdominal measurements ( $P > 0.05$ ). Although transvaginal cervical length measurements showed a statistically significant difference between primiparous and multiparous women ( $P > 0.05$ ), the difference was not significant by the transabdominal route ( $P > 0.05$ ).

Duration of pregnancy and cervical length significantly differed between women with and without funneling ( $p = 0.001$ ). The sensitivity and specificity of screening based on cervical length of 25mm were 55.5% (50.9-60.1%) and 93.6% (91.2-96%) respectively.

Mancuso et al. <sup>11</sup> performed a Secondary analysis of pre-randomization data from a multicenter trial of ultrasound- indicated cerclage. Women with prior spontaneous PTB  $< 34$  weeks underwent initial CL assessment and vaginal fluid collection at 16-21 weeks. Grain stains were scored with Nugent criteria. With serial scans, the shortest CL was observed. 949 women had complete data. In unadjusted regression models, the Nugent score ( $p = 0.003$ ) and vaginal fluid pH ( $p = 0.008$ ) were inversely related to CL. 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; however, all of these effects were null after covariate adjustment.

In contrast to our study, another study conducted by Matijevic et al. <sup>3</sup>, involved 316 low-risk pregnant women. Elevated vaginal pH was found in 4.4% whereas shortened CL was found in 2.8%. The incidence of PTL ( $< 37$  weeks) was 7.2%, and early PTL ( $< 34$  weeks) was 3.4%. They found that elevated vaginal pH is a better predictor of early PTL (LR weighted by prevalence 1.7, 95% CI 1.1-3.1).

In contrast to our study, a study was performed at the Cairo university Obstetrics outpatient clinic by El-Sheikhah et al. <sup>12</sup>; this study concluded that an elevated vaginal pH in early pregnancy was the best predictor of preterm labor. The cervical length was not related to abnormalities in the vaginal flora nor had a relationship with the vaginal pH. Increased

vaginal pH ( $\geq 4.5$ ) among this cohort was 31%; 16.6% of them had normal flora, 43.3% had intermediate flora, and 43.3% had bacterial vaginosis. A statistically significant higher difference was found in the mean vaginal pH in the preterm delivery at 37 weeks or less than in the term delivery at more than 37 weeks ( $P = 0.025$ ). No statistically significant difference was found in the mean cervical length between the group who had a term delivery and the group who had a preterm delivery ( $< 34$ ,  $< 37$  weeks).

In contrast to our study, a prospective cohort study included 580 pregnant women uncomplicated singleton pregnancy between 22 and 24 weeks of gestation was done by Fahnty et al. <sup>13</sup>. They found that the incidence of PTL was 100/500 (20 %). The incidence of PTL had bacterial vaginosis were 52/100 (52%) which is statistically significant. The incidence of PTL in cases with short CL ( $\leq 30$ mm) was 39/100 (39%) while short cervix cases in full-term were 3/400 (0.8%) which is statistically significant. The incidence of PTL were (16%) for cases had BV and short CL while no cases for full-term labor which is statistically significant ( $P < 0.001$ ).

In contrast to our study, another study conducted by Jain et al. <sup>14</sup> as a Case-control study in which pregnant women of gestational age between 28-37 weeks with preterm labor were taken as study group and pregnant women of same gestational age without any signs and symptoms of preterm labor were taken as a control group to compare the incidence of bacterial vaginosis. The result showed that in the study group 33% of women were having bacterial vaginosis compared to 17% in the control group. This result was statistically significant to prove bacterial vaginosis as a significant cause of preterm labor ( $p = 0.0143$  and  $RR = 1.48$ ).

## CONCLUSION

In our prospective cohort study, we came to the following conclusions: The measurement of vaginal pH is not significant for preterm labor prediction. The measurement of cervical length using vaginal ultrasound has better predictive value for preterm labor than the measurement of vaginal pH in the second trimester of pregnancy with ( $P$ -value  $< 0.001$ ) and accuracy (81%). The cut-off value for cervical length is (2.9 Cm) in predicting preterm labor.

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