Vaginal fluid pH, cervicovaginitis and cervical length in pregnancy

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Summary

Aim: The purpose of this prospective study was to determine the possible association among vaginal fluid pH, cervicovaginitis and cervical length in singleton pregnancies at 16-22 weeks of gestation. *Methods:*A total of 240 asymptomatic singleton pregnancies at 16-22 weeks of gestation were included to the study. Vaginal fluid pH was determined using pH paper in a sterile speculum examination, and cervical length was examined by transvaginal ultrasonographic measurement. Vaginitis was diagnosed by pH determination and wet mount smear; cervicitis was diagnosed by cervical examination. Patients were followed to delivery and hospital records were reviewed to extract obstetric information. Preterm delivery was defined as delivery at or prior to 36 weeks of gestation. Abnormal pH was defined as a pH of > 5.0. Patients with cervicovaginitis (n = 72) were compared with those without any trace of infection (n = 60). *Results:* The mean gestational age was 20.3 ± 1.4. We found an significant association among cervicovaginitis, cervical length and vaginal pH. There was a significant correlation between an elevated vaginal pH (> 5.0) and a shortened cervical length (r = -0.59, $p < 0.001$). Vaginal fluid pH > 5.0 was associated with increased risk of preterm delivery (OR 4.3, 95% CI 2.0, 9.3; $p = 0.001$) as well as delivering an infant of less than 2,500 g (OR 4.0, 95% CI 1.4, 11.0; $p = 0.009$). *Conclusions:* Elevated vaginal fluid pH in women at 16-22 weeks of gestation seems to be associated with a decreased cervical length and increased risk of preterm delivery.

Key words: Vaginal fluid pH; Cervical length; Preterm birth; Cervicovaginitis.

Introduction

Preterm birth remains one of the primary causes of perinatal morbidity and mortality. It is now clear that intrauterine infection plays a major role in the pathogenesis of preterm birth, which itself is responsible for 70% of perinatal deaths and almost one half of long-term neurologic morbidity [1]. It was postulated that vaginal organisms found in bacterial vaginosis (BV) may first ascend into the choriodecidual space. Preterm labor and delivery are then caused by a maternal and fetal response to choriodecidual bacterial colonization. In some women, bacteria cross the intact chorioamniotic membranes into the amniotic fluid, and some of the fetuses ultimately become infected.

Cervical length is also an independent risk factor in the pathogenesis of preterm labor [2-4]. The risk of preterm delivery appears to be inversely proportional to that of cervical length, increasing significantly with shorter cervical length measurements [5]. Inflammation of the maternal-fetal interface is a common cause of cervical shortening, particularly before 31-32 weeks' gestation [6]. Such inflammation may not arise solely from either an infectious or a vascular insult but rather from both. With regard to infection, bacterial vaginosis has often been related to cervical shortening and preterm birth [7, 8].

Therefore a simple method of identifying the presence of bacterial vaginosis may be useful in screening for patients at risk for preterm labor. In a prospective study of 107 pregnant women, an increased vaginal pH significantly predicted the presence of bacterial vaginosis [9].

The purpose of this prospective study was to determine the possible association among vaginal fluid pH, cervicovaginitis and cervical length in singleton pregnancies at 16-22 weeks of gestation.

Materials and Methods

A total of 240 asymptomatic singleton pregnancies at 16-22 weeks of gestation were included to the study. The patients were divided into the following groups: group A, negative for vaginitis and cervicitis (no infection group, n = 60; 25%); group B, positive for vaginitis and cervicitis (infection group, n = 72; 30%); group C, possible or negative for vaginitis and positive for cervicitis (n = 51; 21.3%); group D, positive for vaginitis and possible or negative for cervicitis (n = 57; 23.8%). The study was conducted in accordance with the guidelines as described in the Helsinki Declaration (as revised in Tokyo 2004) on human experimentation. Informed consent was obtained from all patients.

Each patient was questioned with regard to last normal menstruation. Gestational age according to last menstruation was compared with gestational age as determined by using ultrasonography (US). Where sonar was performed in the first trimester of pregnancy, we determined the gestational age according to the last menstrual period, with a discrepancy of one week. For the second trimester, the limit was two weeks, and for the third trimester, the limit was three weeks.

Vaginal infection was diagnosed as follows: After the insertion of a vaginal speculum, the vaginal pH was determined by using pH-Universal indicator sticks (E. Merck, Darmstadt, Germany; pH range, 1-14). Vaginal secretion was obtained from

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Table 1. — *Demographic characteristics of the patients (n = 240).*

Variable	Average	Minimum	Maximum
Age (years)	27.4 ± 4.6	18	39
Gestational age (weeks)	20.3 ± 1.4	18	22
Vaginal pH	4.9 ± 0.8	3	8
Parity	0.6 ± 0.6	0	2
Gravida	1.9 ± 0.9	1	5
Cervical length (mm)	35.8 ± 6.0	23	72

Table 2. — *Wet mount vaginal smear and whiff test results (n = 240).*

Variable	Percentage
Döderlein's bacilli	38.3
Clue cells	37.5
Positive whiff test result	12.9
More leukocytes than epithelial cells	18.8
Trichomonas vaginalis	17.9
Vaginal infection*	51.3

*Infection was diagnosed if at least one of the following criteria was present: Trichomonas vaginalis, positive whiff test result, clue cells.

Table 3. — *Diagnosis of cervicitis in the study group (n = 240).*

Variable	Percentage
Discharge	34.1
Red cervix	38.7
Ulceration	39.5
Cervical infection*	53.8

*Infection was diagnosed if 2 or 3 of the stipulated variables were present.

the lateral vaginal walls by using the blunt end of a wooden spatula and applied to two locations on a glass slide. The whiff test was executed by adding a drop of 10% potassium hydroxide solution to one of these locations. The test result was positive if an unpleasant fishy odor resulted. A drop of 0.9% sodium chloride solution was then added to the second location, and coverslips were placed over both. Each location was then microscopically examined at × 100 and × 400 magnification by using a phase contrast light microscope for the presence of clue cells, Döderlein's bacilli, *Trichomonas vaginalis,* and white blood cells on the sodium chloride solution side and for the mycelia of *Candida albicans* on the potassium hydroxide side. Vaginitis, for the purpose of this study, was diagnosed if at least one of the following was present: (1) *T vaginalis,* (2) positive whiff test result, and (3) clue cells. Cervicitis was diagnosed if at least two or three of the following was present at the inspection of the cervix: (1) red cervix, (2) discharge, (3) ulceration.

Each patient was then subjected to transabdominal US to measure the crown-rump length or biparietal diameter, femur length, and trunk circumference. Thereafter, a vaginal ultrasonographic investigation was performed with a 140° vaginal probe covered by a sterile condom. The internal cervical os was viewed on a sagittal plane, and the probe was then manipulated until the entire cervical canal could be visualized. Markers were placed at the furthest points between the internal os and the external os to measure cervical length in millimeters. Ultrasonic assessment was performed by one of the investigators.

Patients were followed to delivery and hospital records were reviewed to extract obstetric information. Preterm delivery was defined as delivery at or prior to 36 weeks of gestation. Abnormal pH was defined as a pH of > 5.0. Patients with cervicovaginitis (n = 72) were compared with those without any trace of infection (n = 60).

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL). Values are given as mean ± standard deviation. We compared variables between groups using the Student's unpaired *t*-test. To test for an association in the case of categoric data, we used the χ^2 test. Correlations between variables were calculated with Pearson's correlation coefficient; $p < 0.05$ was considered statistically significant.

Results

The mean gestational age was 20.3 ± 1.4 years. We found a significant association among cervicovaginitis, cervical length and vaginal pH. There was a significant correlation between elevated vaginal pH (> 5.0) and shortened cervical length (r = -0.59, $p < 0.001$). Vaginal fluid pH > 5.0 was associated with increased risk of preterm delivery (OR 4.3, 95% CI 2.0, 9.3; $p = 0.001$) as well as delivering an infant of less than 2,500 g (OR 4.0, 95% CI 1.4, 11.0; $p = 0.009$). The results are summarized in Tables 1-4 and Figures 1-3.

Table 4. — *Comparison between group A (no infection) and group B (infection).*

Variable	Group A (n = 60)	Group B (n = 72)	*p*
Age (years)*	26.7 ± 4.7	27.2 ± 4.5	0.55
Gestational age (weeks)*	20.6 ± 1.4	20.3 ± 1.2	> 0.05
Gravida*	1.8 ± 0.9	1.9 ± 0.9	0.58
Parite*	0.5 ± 80.61	0.65 ± 0.67	0.54
Trichomonas vaginalis**	–	26 (36.1)	
Clue cells**	–	56 (77)	
Positive whiff test result**	–	21 (29.2)	
Döderlein's bacilli**	37 (61.7)	13 (18.1)	
More leukocytes than epithelial cells**	–	26 (36.1)	
Cervical length (mm)*	39.4 ± 7.2	32.4 ± 4.5	< 0.001
Vaginal pH*	4.2 ± 0.58	5.6 ± 0.86	< 0.001
Gestational age at birth (weeks)*	38 ± 0.9	36.9 ± 1.4	< 0.001
Birth weight (g)*	3336 ± 320	3053 ± 404	< 0.001
Preterm birth (weeks)**	1 (1.7)	18 (25)	< 0.001

Values in parantheses are percentages, *Values are mean ± SD, ** Values are the number of patients.

Table 5. — *Comparison between the groups of vaginal pH ≤ 5 (n =172) and pH > 5 (n = 68).*

Variable	pH ≤ 5 (n = 172)	pH > 5 (n = 68)	*p*
Age (years)*	27.3 ± 4.8	27.6 ± 4.05	0.64
Gestational age (weeks)*	20.4 ± 1.3	20.2 ± 1.2	0.21
Clue cells**	52 (30.2)	38 (55.9)	< 0.001
Positive whiff test result**	12 (7)	18 (27.9)	< 0.001
Cervicitis**	68 (39.5)	61 (89.7)	< 0.001
Vaginitis**	70 (40.7)	53 (77.9)	< 0.001
Cervicovaginitis**	24 (14)	48 (70.6)	< 0.001
Cervical length (mm)*	37.8 ± 5.7	30.9 ± 3.2	< 0.001
Gestational age at birth (weeks)*	37.8 ± 1.2	36.6 ± 1.2	< 0.001
Birth weight (g)*	3272 ± 356	3005 ± 398	< 0.001
Preterm birth (weeks)**	14 (8.1)	19 (27.9)	< 0.001
Birth weight < 2500 g**	7 (4.1)	10 (14.7)	0.006

Values in parantheses are percentages, *Values are mean ± SD, ** Values are the number of patients.

Fig. 1

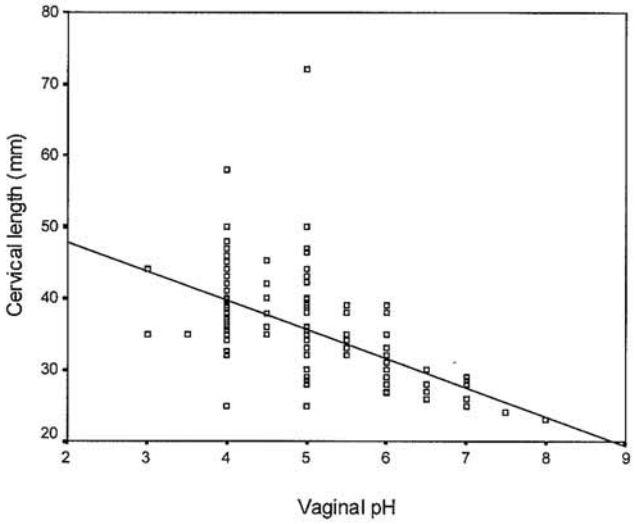

Fig. 2

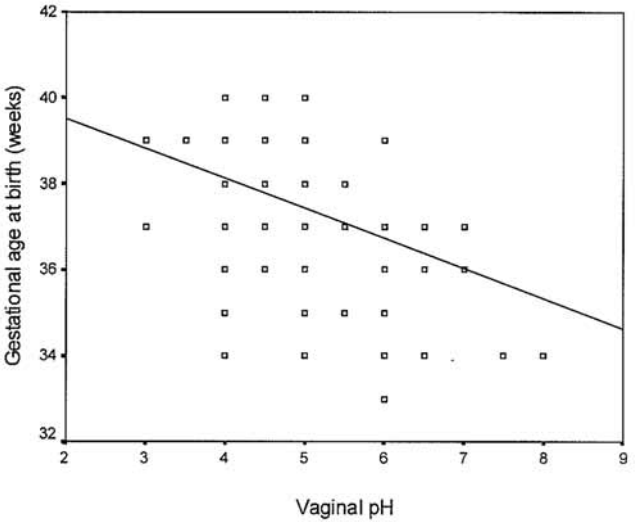

Fig. 3

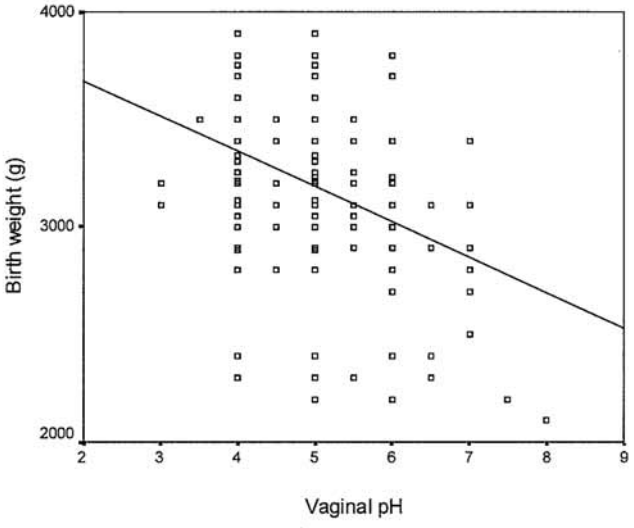

Figure 1. — Linear regression analysis of vaginal pH and cervical length (mm) in singleton pregnancies at 16-22 weeks of gestation with a correlation coefficient of r = -0.65; $p < 0.001$.

Figure 2. — Linear regression analysis of vaginal pH and gestational age at birth (weeks) in singleton pregnancies at 16-22 weeks of gestation with a correlation coefficient of r = -0.45; $p < 0.001$.

Figure 3. — Linear regression analysis of vaginal pH and birth weight (g) in singleton pregnancies at 16-22 weeks of gestation with a correlation coefficient of r = -0.37; $p < 0.001$.

Discussion

The cause of preterm birth is multifactorial. Pathophysiologic changes preceding clinical indicators of preterm labor include the presence of inflammatory cytokines in amniotic fluid during the second trimester, fetal fibronectin expression in cervicovaginal mucus, shortening of the cervix on US examination, and an increase in maternal salivary estriol. It is important to note that the clinical presentation is strongly influenced by the dominant factor in the pathogenesis. For example, a short cervix is a particularly important risk factor in patients who deliver their neonates before 26 weeks' gestation [10].

A recent meta-analysis performed by Leitich *et al*. [11] confirmed that BV was associated significantly with adverse pregnancy outcome and that the risk of preterm delivery at < 37 weeks of gestation, as calculated in the main analysis, was > 2-fold in women with BV.

An elevated vaginal pH level is a well-known characteristic of bacterial vaginosis. In their study, Hauth *et al*. [12] concluded that women with an early pregnancy vaginal pH, those whose pH was 5.0 or greater had a significantly increased incidence of subsequent preterm birth at < 37, < 35, or < 32 weeks' gestation. Women whose vaginal pH was 5.0 or less also had significantly fewer subsequent spontaneous preterm births and fewer newborn infants weighing less than 2,500 g or less than 1,500 g.

Our study contributes to this finding because we found a significant correlation between an elevated vaginal pH (> 5.0) and a shortened cervical length (r = -0.59, $p < 0.001$). Vaginal fluid pH > 5.0 was associated with increased risk of preterm delivery (OR 4.3, 95% CI 2.0, 9.3; p = 0.001) as well as delivering an infant of less than 2,500 g (OR 4.0, 95% CI 1.4, 11.0; $p = 0.009$). Therefore it seems as if an elevated vaginal pH could be used as a tool in screening for patients at risk for preterm labor.

In conclusion, an elevated vaginal fluid pH in women at 16-22 weeks of gestation seems to be associated with a decreased cervical length and increased risk of preterm delivery. In cases in which US examination is not available, however, an elevated vaginal pH may be a simple and useful predictor.

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