International Journal of Gynecology and Obstetrics xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo

CLINICAL ARTICLE

# Vaginal fluid pH and buffer capacity for predicting false preterm labor in Japanese women

Taketoshi Noguchi, Toshiyuki Sado, Katsuhiko Naruse, Hiroshi Kobayashi *

*Department of Obstetrics and Gynecology, Nara Medical University, Nara, Japan*

ARTICLE INFO

*Article history:*
Received 5 August 2015
Received in revised form 16 November 2015
Accepted 22 February 2016

*Keywords:*
Buffering capacity
Prediction
Preterm delivery
Preterm labor
Threatened preterm labor
Vaginal pH

ABSTRACT

*Objective:* To determine the relationship between preterm labor and delivery, and the pH and buffer capacity of vaginal secretions. *Methods:* Between January 1, 2009 and March 31, 2012, two cohorts of patients at 22–36 weeks of pregnancy were enrolled in a prospective cohort study at Nara Medical University Hospital, Japan. Patients experiencing preterm contractions and a control group of patients experiencing normal pregnancies were included. The pH and buffer capacity of vaginal secretions were measured and compared. *Results:* Of the 237 patients enrolled, 48 (20.3%) were experiencing symptoms of preterm labor and 189 (79.7%) were included in the control group. The pH was higher ($P < 0.001$) and the buffer capacity was lower ($P = 0.0135$) in the vaginal secretions of the patients experiencing preterm contractions compared with the control group. There was no difference in the pH and buffer capacity of the vaginal secretions of symptomatic patients who would experience preterm delivery and those who would not. Receiver operating characteristic curve analyses demonstrated that vaginal-secretion pH and buffer capacity could differentiate between patients experiencing preterm contractions and those not, but could not differentiate between patients who would experience preterm delivery and those who would not. *Conclusion:* Vaginal-secretion pH and buffer capacity could be useful in diagnosing preterm labor; further studies are needed to determine potential practical diagnostic criteria.


## 1. Introduction

The most common obstetric complication experienced during pregnancy is preterm delivery; it is currently the leading cause of perinatal morbidity and mortality worldwide [1]. It is difficult to discriminate between patients who will actually experience preterm delivery and those who experience preterm uterine contractions but do not undergo delivery until at least full term, with more than half of patients thought to be at risk of preterm delivery ultimately experiencing a full-term delivery [2]. The multifactorial etiology of preterm labor [2,3] explains this difficulty in identifying specific biomarkers for preterm delivery.

Recent attempts to accurately predict preterm delivery have included the use of ultrasonographic measurements of the cervix [4,5] and measuring (cervico)vaginal fluid properties [6], including fetal fibronectin (fFN) [7] and phosphorylated insulin-like growth factor-binding protein 1 [8]. Analytical tests using fFN have demonstrated some accuracy in predicting spontaneous preterm delivery among patients experiencing symptoms of preterm labor [9–13] and a quantitative phosphorylated insulin-like growth factor-binding protein 1 test has demonstrated accuracy in predicting preterm delivery among patients experiencing preterm labor [14] and in patients during the first trimester of pregnancy [15]. Additionally, considerable interest has been shown in developing safe, effective, simple, and inexpensive biomarker assays for predicting preterm delivery [16,17].

The novel idea explored in the present study originated from the concept that saliva provides protection against dental erosion and caries [18]. The healthy oral microbiota performs a protective role against pathogenic bacteria. Significant correlations have been demonstrated between an increased risk of dental caries and both saliva *Streptococcus mutans* counts and buffer capacity [19]. In comparison with healthy controls, patients with dental erosion have demonstrated larger decreases in pH following citric acid rinses or drinking orange juice, with the pH of patients' saliva remaining decreased for a longer period of time [20]. Low saliva buffer capacity has been found to be a risk factor for the development of dental caries [18,20]. It was hypothesized that, similarly, reductions in vaginal buffer capacity could result in a decrease in vaginal pH, and that this could, in turn, influence the likelihood of preterm labor and delivery.

Consequently, the aim of the present study was to evaluate the pH and buffer capacity of vaginal secretions of patients who were pregnant to identify any associations between these values and preterm labor. To the best of our knowledge, no previous studies have investigated the association between preterm labor and the buffer capacity of vaginal secretions.

* Corresponding author at: Department of Obstetrics and Gynecology, Nara Medical University, 840 Shijo-cho, Kashihara, 634-8522, Japan. Tel.: +81 744 29 8877; fax: +81 744 23 6557.
*E-mail address:* hirokoba@naramed-u.ac.jp (H. Kobayashi).

http://dx.doi.org/10.1016/j.ijgo.2015.11.018
0020-7292/

**Table 1**
Patient characteristics among all study participants (cohorts 1 and 2).[a]

| Variable | Control patients (n = 189) | Patients exhibiting symptoms of preterm labor (n = 48) | Patients who delivered at term after demonstrating symptoms of preterm labor (n = 30) | Patients who delivered preterm after demonstrating symptoms of preterm labor (n = 18) | *P* value |
|---|---|---|---|---|---|
| No. of vaginal mucus samples | 501 | 118 | 75 | 43 | |
| Parity | | | | | 0.112 |
| 0 | 97 | 19 | 13 | 6 | |
| 1 | 65 | 18 | 9 | 9 | |
| 2 | 27 | 11 | 8 | 3 | |
| Age, y | 29.5 ± 5.54 (16–43) | 30.8 ± 4.41 (22–39) | 31.2 ± 4.60 (22–39) | 30.1 ± 3.99 (23–37) | 0.255 |
| Neonate weight at delivery, g | 3018.5 ± 372.2 | 2770.8 ± 572.4 | 2942.0 ± 441.2 | 2485.6 ± 647.5 | 0.007[b] |
| Duration of pregnancy at recruitment, wk | 27.2 ± 3.94 | 31.2 ± 2.87 | 31.4 ± 3.18 | 30.9 ± 2.25 | <0.001[c] |
| Duration of pregnancy at delivery, wk | 38.8 ± 1.2 | 36.8 ± 1.86 | 37.7 ± 0.90 | 35.2 ± 2.00 | <0.001[d] |
| Vaginal secretion pH | 4.05 ± 0.34 | 4.38 ± 0.54 | 4.35 ± 0.536 | 4.44 ± 0.52 | <0.001[e] |

[a] Values are given as number, number (percentage), mean ± SD (range), or mean ± SD, unless indicated otherwise.
[b] Significant differences were observed between the control group and patients exhibiting symptoms of preterm labor ($P = 0.007$), between the control group and patients who delivered preterm after demonstrating symptoms of preterm labor ($P = 0.004$), and between patients who delivered at term after demonstrating symptoms of preterm labor and patients who delivered preterm after demonstrating symptoms of preterm labor ($P = 0.016$).
[c] Significant differences were observed between the control group and patients exhibiting symptoms of preterm labor ($P < 0.001$), between the control group and patients who delivered at term after demonstrating symptoms of preterm labor ($P < 0.001$), and between the control group and patients who delivered preterm after demonstrating symptoms of preterm labor ($P < 0.001$).
[d] Significant differences were observed between the control group and patients exhibiting symptoms of preterm labor ($P < 0.001$), between the control group and patients who delivered at term after demonstrating symptoms of preterm labor ($P < 0.001$), between the control group and patients who delivered preterm after demonstrating symptoms of preterm labor ($P < 0.001$), and between patients who delivered at term after demonstrating symptoms of preterm labor and patients who delivered preterm after demonstrating symptoms of preterm labor ($P < 0.001$).
[e] Significant differences were observed between the control group and patients exhibiting symptoms of preterm labor ($P < 0.001$), between the control group and patients who delivered at term after demonstrating symptoms of preterm labor ($P < 0.001$), and between the control group and patients who delivered preterm after demonstrating symptoms of preterm labor ($P < 0.001$).

## 2. Materials and methods

The present study included data from two prospective cohorts enrolled at Nara Medical University Hospital, Japan, between January 1, 2009 and March 31, 2012. The first cohort study (cohort 1) examined the pH of patients vaginal secretions only and enrolled patients attending the study hospital owing to symptoms of preterm labor and a control group between January 1, 2009 and December 31, 2009. Following this, the second prospective cohort (cohort 2) examined the pH and buffer capacity of vaginal secretions, enrolling further patients experiencing preterm labor and a control group between January 1, 2010 and March 31, 2012. Both cohorts were enrolled according to the same criteria; the preterm-labor groups comprised patients at 22–36 weeks of pregnancy attending the study hospital owing to increasingly symptomatic uterine contractions at shorter than 10-min intervals, who had cervical dilation up to 3 cm or had premature effacement of the cervix. The control groups enrolled patients at 22–36 weeks of pregnancy who were experiencing no pregnancy complications, had no systemic diseases, and where not regularly taking any medications. Patients were recruited to the control groups when attending routine prenatal checkups. The exclusion criteria for all potential study participants included preterm rupture of membranes, cervical dilatation greater than 3 cm, multiple pregnancies, non-reassuring fetal testing, chronic hypertension, pre-eclampsia, pre-existing diabetes, gestational diabetes mellitus, lupus erythematosus, abruptio placenta, intrauterine growth restriction, fetal anomalies, placenta previa, clinical signs of

**Table 2**
Patient characteristics among study participants in cohort 2.[a]

| Variable | Control patients (n = 96) | Patients exhibiting symptoms of preterm labor (n = 27) | Patients who delivered at term after demonstrating symptoms of preterm labor (n = 16) | Patients who delivered preterm after demonstrating symptoms of preterm labor (n = 11) | *P* value |
|---|---|---|---|---|---|
| No. of vaginal mucus samples | 179 | 59 | 34 | 25 | |
| Parity | | | | | 0.118 |
| 0 | 48 | 8 | 6 | 2 | |
| 1 | 33 | 12 | 5 | 7 | |
| 2 | 15 | 7 | 5 | 2 | |
| Age, y | 30.2 ± 5.19 (18–40) | 30.9 ± 4.32 (22–39) | 31.1 ± 4.68 (22–39) | 30.5 ± 3.70 (23–35) | 0.550 |
| Neonate weight at delivery, g | 2955.9 ± 358.3 | 2638.9 ± 565.0 | 2809.5 ± 415.8 | 2390.7 ± 654.3 | 0.011[b] |
| Duration of pregnancy at recruitment, wk | 28.1 ± 3.84 | 31.0 ± 3.00 | 31.4 ± 3.30 | 30.5 ± 2.39 | <0.001[c] |
| Duration of pregnancy at delivery, wk | 38.7 ± 1.30 | 36.7 ± 2.08 | 37.8 ± 0.95 | 35.2 ± 2.29 | <0.001[d] |
| Buffer capacity | 0.743 ± 0.372 | 0.668 ± 0.457 | 0.747 ± 0.639 | 0.671 ± 0.301 | 0.014[e] |

[a] Values are given as number, number (percentage), mean ± SD (range), or mean ± SD, unless indicated otherwise.
[b] Significant differences were observed between the control group and patients exhibiting symptoms of preterm labor ($P = 0.016$), and between the control group and patients who delivered preterm after demonstrating symptoms of preterm labor ($P = 0.023$).
[c] Significant differences were observed between the control group and patients exhibiting symptoms of preterm labor ($P < 0.001$), and between the control group and patients who delivered at term after demonstrating symptoms of preterm labor ($P = 0.0015$).
[d] Significant differences were observed between the control group and patients exhibiting symptoms of preterm labor ($P < 0.001$), between the control group and patients who delivered at term after demonstrating symptoms of preterm labor ($P < 0.001$), between the control group and patients who delivered preterm after demonstrating symptoms of preterm labor ($P < 0.001$), and between patients who delivered at term after demonstrating symptoms of preterm labor and patients who delivered preterm after demonstrating symptoms of preterm labor ($P = 0.0048$).
[e] Significant differences were observed between the control group and patients exhibiting symptoms of preterm labor ($P = 0.0135$), and between the control group and patients who delivered preterm after demonstrating symptoms of preterm labor ($P = 0.0465$).

Please cite this article as: Noguchi T, et al, Vaginal fluid pH and buffer capacity for predicting false preterm labor in Japanese women, Int J Gynecol Obstet (2016), http://dx.doi.org/10.1016/j.ijgo.2015.11.018