

Prediction of Spontaneous Preterm Delivery at Siriraj Hospital, Thailand

Prapat Wanitpongpan, M.D., Buraya Phattanajindakun, M.D., Kusol Russameecharoen, M.D., Monsak Chuchotirot, M.D.

Department of Obstetrics & Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

Objective: To assess the significance of various parameters that attribute to preterm delivery before 35 weeks in Thai women with normal singleton pregnancies.

Methods: A cohort analytical study enrolling 1,027 Thai pregnant women was carried out. Those who had risk factors of preterm labour, indicated preterm birth or the cases with fetal anomalies were not included. Nineteen parameters including cervical length at mid-trimester were assessed. The cutoff value for short cervix in this study was defined at less than 30 mm. Univariate and logistic regression analysis were used to determine the significance of each parameter.

Results: From the 19 parameters, logistic regression analysis demonstrated that short cervix is the only parameter that is associated with preterm delivery before 35 weeks ($p=0.019$) (OR = 3.77; 1.24-11.49). There is a trend towards significance for history of preterm birth ($p=0.089$). Amniocentesis or Cesarean delivery of the mothers had no effect on the incidence of preterm labour in the current pregnancy ($p=0.73$ and 0.53 respectively).

Conclusion: For Thai women with normal singleton pregnancies, those who have cervical length measured at mid-trimester less than 30 mm have 3.8 times higher risk of preterm delivery than those who have normal cervical length. Short cervix and history of previous preterm birth should be used as important predictors of preterm labour.

Keywords: Preterm delivery, short cervix, Thai pregnant women

Siriraj Med J 2015;67:155-159

E-journal: <http://www.sirirajmedj.com>

INTRODUCTION

Preterm delivery (PTD) is one of the most challenging problems in modern maternity care. Although there has been advancement in newborn care and progressive increment of survival rate of prematurely born babies, early PTD is still the leading cause of infant death and short term morbidities and long term physical and mental disabilities in those who survived.

Various efforts to reduce this condition seem to be unsatisfactory and the incidence has been stable for decades or even increasing.¹⁻² Early detection of women at risk of PTD and providing effective managements e.g. progesterone supplement or cervical cerclage are the current appropriate interventions to reduce PTD. There are solid evidences about some parameters e.g. history of previous preterm births, short cervical length and smoking that are significantly associated with PTD.³⁻⁹ Since some biological parameters have some ethnic variation, we decided to conduct a study to assess the reliability of many clinical parameters as a predictor of PTD among Thai pregnant women who had no known risks for PTD.

Correspondence to: Prapat Wanitpongpan

E-mail: prapatw@hotmail.com

Received 16 January 2015

Revised 7 April 2015

Accepted 8 April 2015

MATERIALS AND METHODS

This was a cohort analytical study conducted in the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital between 2008 and 2010. Thai singleton pregnant women were eligible if both the mothers and the babies were healthy. The cases with known risk factors for PTL e.g. twins pregnancies, uterine fibroids, history of cervical surgery and prematurely delivered from obstetric indications were excluded from the study. The study was approved by the institutional ethical committee and all the participants gave their informed consent before the beginning of the study. The participants' antenatal books and the 19 parameters were reviewed. Gestational age was determined by correct menstrual history and/or ultrasound examination before 20 weeks of gestation. At mid-trimester, an ultrasound examination was performed to rule out fetal anomalies and transvaginal ultrasound examination was performed to measure the cervical length using 7.5 MHz vaginal probe attached to Voluzon E8 ultrasound platform (GE Medical, Kretztechnik GmbH, Austria). The cervical length was measured by the recommended method reported earlier.¹⁰ Value less than 5th percentile was taken as a critical value of short cervix. After delivery the investigators reviewed delivery documents and all the outcome data were recorded. Mean and standard deviation of demographic data of participants were calculated. We performed univariate analysis using either Chi-square test or Fisher' Exact test to examine the individual parameters contributing significantly to PTD before 35 weeks. Then logistic regression analysis was used to determine the association between each parameter and PTD. Statistical significance was set at p-value <0.05. The statistical software package SPSS version 18.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS

During the study period, 1,027 pregnant women were enrolled but only 947 cases were analyzed. Maternal data and pregnancy outcomes have been presented in Table 1. Those who delivered

TABLE 1. Characteristics of 947 participants.

Characteristics	Mean \pm SD	Range
Age (yrs)	27.8 \pm 7.2	15-45
Pre pregnancy weight (kg)	50.7 \pm 10.8	43-82
Height (cm)	155.2 \pm 16.5	146-172
Parity	0.56 \pm 0.7	0-4
Gestational age at birth (wks)	38.4 \pm 1.7	26-42
Newborn birth weight (g)	3,073.7 \pm 468.4	810-4,860

after 37 weeks (n=832) were separately analyzed for mean cervical length. Deliveries before 37 weeks occurred in 71 (7.5%) cases and 38 (4.0%) cases delivered before 35 weeks. Mean (and 95% confidential interval) of cervical length of nulliparous, multiparous women and overall population were 40 (29.4-49.2) mm, 42.1 (31.9-54) mm and 41 (30.6-52) mm respectively. Short cervix, defined as less than 5th percentile of normal value, in overall population was 30.6 mm. The most common parameter presented in the group that delivered after 35 weeks was hard working (n=181). The most common parameter presented in the group that delivered before 35 weeks was age >35 years (n=8).

The results of univariate analysis of 19 parameters have been demonstrated in Table 2. In the PTD group, the prevalence of women who were older than 35 years, smoking during pregnancy, history of previous preterm births, the use of abusive substances, short cervical length, small for gestational age fetuses and maternal anemia were higher. The results of logistic regression analysis have been presented in Table 3 which demonstrated that short cervix was a single parameter that was significantly associated with PTD before 35 weeks (p=0.019) (OR = 3.77; 1.24-11.49). There was a trend towards significance for history of preterm births (p=0.89).

DISCUSSION

In this study the incidence of preterm delivery before 37 wks and 35 wks were 7.5% and 4.0% respectively which was lower than 13.6% of a previous global report.¹ This could be the result

TABLE 2. Studied parameters.

Factors	Delivery >35 wks	PTL<35 wks	p value
SGA	5 (0.6%)	1 (3.4%)	0.035
Smoking	6 (0.7%)	2 (5.3%)	0.038
CL <30 mm	36 (4.2%)	4 (12.9%)	0.045
Age >35 years	101 (11.1%)	8 (21.1%)	0.069
History of PTL	30 (3.3%)	3 (7.9%)	0.142
Drug abuse	4 (0.4%)	1 (2.6%)	0.186
Anemia	36 (3.9%)	3 (7.9%)	0.203
Alcohol drinking	5 (0.6%)	1 (2.6%)	0.218
Poor weight gain	23 (3.0%)	2 (6.9%)	0.492
BMI <19 kg/m ²	175 (19.2%)	5 (13.5%)	0.522
Cesarean delivery of the mother	19 (3.1%)	1 (4.3%)	0.531
Hard working	181 (19.9%)	6 (15.8%)	0.679
Low income (<5,000 Baht/month)	52 (5.7%)	1 (2.6%)	0.718
Amniocentesis	58 (6.4%)	3 (7.9%)	0.731
Anxiety	90 (9.9%)	3 (7.9%)	0.839
Graduate less than primary school	156 (17.2%)	6 (15.8%)	1.0
Threaten abortion	40 (4.4%)	1 (2.6%)	1.0
Genito-urinary tract infection	27 (2.9%)	1 (2.6%)	1.0
Age <17 years	17 (1.9%)	0 (0%)	NA

SGA= small for gestational age; estimated fetal weight was less than 10 percentile of each gestational age, smoking = regular smoking more than 10 cigarettes/day through the pregnancy, drug abuse = regular use of abusive substances through the pregnancy, anemia = maternal hematocrit <30%, alcohol drinking = regular alcohol drinking through the pregnancy, poor weight gain = maternal weight gain <0.5 kg/week in 2nd half of pregnancy, hard working = a work that required a standing >6 hours/day or lifting heavy objects that weighed more than 30 kg/day, anxiety = feeling stressful with somatic symptoms e.g. headache or insomnia or loss of appetite

TABLE 3. Logistic regression analysis.

	Adjusted OR	95% CI of adjusted OR	p value
CL<30 mm	3.77	1.24-11.49	0.019
Hx of PTL	3.02	0.85-10.8	0.089
Age >35 yr	1.83	0.72-4.67	0.20
Anemia	2.0	0.45-8.95	0.363

from the exclusion of the cases with known risk factors for PTD and the cases with indicated PTD. Because late PTD has almost the same morbidity/mortality rate as term delivery, we focused on earlier PTD i.e. before 35 wks. We also analyzed the association between PTD at very early gestational age and the parameters, but the number of the cases was too small to show any significant association. The results of our study confirmed the findings of other studies reporting that short cervix is the strongest predictor of PTD.^{4-6,8,11-13} We

chose 30 mm as a cutoff for short cervix for Thai pregnant women, because our study found that the cervix of Thai pregnant women is a little longer than those of the western population.¹⁴ The studies of CL in Asian population also showed the same trends.¹⁵⁻¹⁷ We believed that using CL<30 mm as a predictor allow more time to manage the cases properly than using 25 mm or 15 mm as a cutoff value. Whether the universal screening of cervical length at mid-trimester should be encouraged to become a daily practice in Thailand, is still a question. We have proposed 30 mm as a new cutoff value for those who are ready to make a move. The history of previous preterm birth has been advocated to be one of the strongest predictors of PTD.^{3-5,18} Our study showed only a trend towards significant association. This could be the result of small number of cases (n=3) in the PTD group that had a history of previous preterm births. Although

there was no significant association in this study, we encourage the obstetricians to use the history of previous preterm births as a predictor of PTD, because of the previous strong evidences. As the precise mechanisms of PTD have remained inconclusive, many previous studies have pointed out that inflammation plays a major role in the onset of preterm labour.¹⁹⁻²⁰ Amniocentesis has become more common procedure in recent obstetric care due to more cases of advanced maternal age. This invasive procedure could, more or less, trigger a set of maternal inflammatory responses via either introduction of microorganisms into the amniotic cavity or tissues injury after the procedure and might lead to preterm labour. Allergic reaction has been found to be another possible mechanism of preterm labour.²¹⁻²³ There are bunches of evidence which demonstrate the association between Cesarean delivery and allergic diseases in the offspring.²⁴⁻²⁶ A recent meta-analysis showed a 20% increase in the subsequent risk of asthma in children who had been delivered by Cesarean section.²⁷ The evidence suggests that being delivered by Cesarean section alters the intestinal microorganisms ecosystem that modulates the development of the immune system in later life. The subsequent maladaptive immune response to the stimuli might lead to the imbalanced development of T-helper type 1 and 2 cells and production of cytokines and inflammatory mediators that might be related to the onset of preterm labour when that person gets pregnant. Our study did not show a significant correlation between PTD before 35 weeks and history of amniocentesis or Cesarean delivery of the mothers ($p=0.73$ and 0.53 respectively). However, the larger studies could yield different results. The strength of our study was the study in a selected population that could provide the data for custom-made practice. The limitation of our study was the small number of cases in some parameters that could not show any significance. The other limitation was the limited accuracy of measurement of some subjective parameters e.g. hard working, anxiety and drug abuse. Further larger studies on some parameters that showed a trend towards significance might bring some knowledge for better understanding about preterm labour and delivery.

CONCLUSION

For Thai women with normal singleton pregnancies, those who have cervical length less than 30 mm have 3.8 times higher risk of preterm delivery than those who have normal cervical length. Short cervix should be used as an important predictor of preterm labour. Although the history of previous preterm birth and preterm delivery did not have a significant association, it should be used as one of the predictors of preterm labour.

ACKNOWLEDGMENTS

The author would like to thank Dr.Chulaluck Komoltree and Dr.Pattarawalai Talungchit for help in statistical analysis.

REFERENCES

1. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet*. 2012 Jun 9;379(9832): 2162-72.
2. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008 Jan 5; 371(9606):75-84.
3. Spong CY. Prediction and prevention of recurrent spontaneous preterm birth. *Obstet Gynecol*. 2007 Aug;110(2 Pt 1): 405-15.
4. Kagan KO, To M, Tsoi E, Nicolaides KH. Preterm birth: the value of sonographic measurement of cervical length. *BJOG*. 2006 Dec;113 Suppl 3:52-6.
5. ACOG Practice Bulletin. Assessment of risk factors for preterm birth. Clinical management guidelines for obstetrician-gynecologists. Number 31, October 2001. (Replaces Technical Bulletin number 206, June 1995; Committee Opinion number 172, May 1996; Committee Opinion number 187, September 1997; Committee Opinion number 198, February 1998; and Committee Opinion number 251, January 2001). *Obstet Gynecol*. 2001 Oct;98(4):709-16.
6. Grimes-Dennis J, Berghella V. Cervical length and prediction of preterm delivery. *Curr Opin Obstet Gynecol*. 2007 Apr;19(2):191-5.
7. To MS, Skentou CA, Royston P, Yu CK, Nicolaides KH. Prediction of patient-specific risk of early preterm delivery using maternal history and sonographic measurement of cervical length: a population-based prospective study. *Ultrasound Obstet Gynecol*. 2006 Apr;27(4):362-7.

8. Romero R. Prevention of spontaneous preterm birth: the role of sonographic cervical length in identifying patients who may benefit from progesterone treatment. *Ultrasound Obstet Gynecol.* 2007 Oct;30(5):675-86.
9. Goldenberg RL, Iams JD, Mercer BM, Meis P, Moawad A, Das A, et al. What we have learned about the predictors of preterm birth. *Semin Perinatol.* 2003 Jun;27(3):185-93.
10. Meijer-Hoogeveen M, Stoutenbeek P, Visser GH. Methods of sonographic cervical length measurement in pregnancy: a review of the literature. *J Matern Fetal Neonatal Med.* 2006 Dec;19(12):755-62.
11. Heath VC, Southall TR, Souka AP, Novakov A, Nicolaides KH. Cervical length at 23 weeks of gestation: relation to demographic characteristics and previous obstetric history. *Ultrasound Obstet Gynecol.* 1998 Nov;12(5):304-11.
12. Williams M, Iams JD. Cervical length measurement and cervical cerclage to prevent preterm birth. *Clin Obstet Gynecol.* 2004 Dec;47(4):775-83; discussion 881-2.
13. Colombo DF, Iams JD. Cervical length and preterm labor. *Clin Obstet Gynecol.* 2000 Dec;43(4):735-45.
14. Wanitpongpan P, Sutthritongsa P, S. R. Cervical length at mid-trimester in Thai women with normal singleton pregnancies. *Siriraj Med J.* 2015;67(1):33-6.
15. Leung TN, Pang MW, Leung TY, Poon CF, Wong SM, Lau TK. Cervical length at 18-22 weeks of gestation for prediction of spontaneous preterm delivery in Hong Kong Chinese women. *Ultrasound Obstet Gynecol.* 2005 Dec;26(7):713-7.
16. Hebbar S, Samjhana K. Role of mid-trimester transvaginal cervical ultrasound in prediction of preterm delivery. *Med J Malaysia.* 2006 Aug;61(3):307-11.
17. Mukherji J, Anant M, Ghosh S, Bhattacharyya SK, Hazra A, Kamilya GS. Normative data of cervical length in singleton pregnancy in women attending a tertiary care hospital in eastern India. *Indian J Med Res.* 2011 May;133:492-6.
18. Goldenberg RL, Iams JD, Mercer BM, Meis PJ, Moawad AH, Copper RL, et al. The preterm prediction study: the value of new vs standard risk factors in predicting early and all spontaneous preterm births. *NICHD MFMU Network. Am J Public Health.* 1998 Feb;88(2):233-8.
19. Romero R, Espinoza J, Kusanovic JP, Gotsch F, Hassan S, Erez O, et al. The preterm parturition syndrome. *BJOG.* 2006 Dec;113 Suppl 3:17-42.
20. Wei SQ, Fraser W, Luo ZC. Inflammatory cytokines and spontaneous preterm birth in asymptomatic women: a systematic review. *Obstet Gynecol.* 2010 Aug;116(2 Pt 1):393-401.
21. Romero R, Kusanovic JP, Munoz H, Gomez R, Lamont RF, Yeo L. Allergy-induced preterm labor after the ingestion of shellfish. *J Matern Fetal Neonatal Med.* 2010 Apr;23(4):351-9.
22. Romero R, Kusanovic JP, Gomez R, Lamont R, Bytautiene E, Garfield RE, et al. The clinical significance of eosinophils in the amniotic fluid in preterm labor. *J Matern Fetal Neonatal Med.* 2010 Apr;23(4):320-9.
23. Bytautiene E, Romero R, Vedernikov YP, El-Zeky F, Saade GR, Garfield RE. Induction of premature labor and delivery by allergic reaction and prevention by histamine H1 receptor antagonist. *Am J Obstet Gynecol.* 2004 Oct;191(4):1356-61.
24. Neu J, Rushing J. Cesarean versus vaginal delivery: long-term infant outcomes and the hygiene hypothesis. *Clin Perinatol.* 2011 Jun;38(2):321-31.
25. Romero R, Korzeniewski SJ. Are infants born by elective cesarean delivery without labor at risk for developing immune disorders later in life? *Am J Obstet Gynecol.* 2013 Apr;208(4):243-6.
26. Cho CE, Norman M. Cesarean section and development of the immune system in the offspring. *Am J Obstet Gynecol.* 2013 Apr;208(4):249-54.
27. Thavagnanam S, Fleming J, Bromley A, Shields MD, Cardwell CR. A meta-analysis of the association between Caesarean section and childhood asthma. *Clin Exp Allergy.* 2008 Apr;38(4):629-33.