The Prevalence and Pregnancy Outcomes of Short Cervix in Low Risk Singleton Pregnancy from Universal Cervical Length Screening

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Abstract

Objective: To study the prevalence of short cervix in low risk singleton pregnancy.

Methods: A retrospective descriptive study was conducted in 1099 low risk singleton pregnant women who came for antenatal care at 16-24 weeks of gestation during February 2016 to January 2017 by reviewing medical records. Pregnant women who had previous history of cervical incompetence, spontaneous preterm labor, preterm premature rupture of membranes (PPROM), Loop electrosurgical excision procedure (LEEP), conization and severe congenital anomaly or chromosomal abnormality were excluded. Transvaginal ultrasound for cervical length (CL) measurement referred to Society for Maternal-Fetal Medicine (SMFM) was performed. The short cervix was defined as CL less than or equal to 25 mm.

Results: The mean gestational age for CL measurement was 19.68±1.62 weeks of gestation and mean CL was 37.37±6.66 mm. The prevalence for short cervix ≤25, ≤20 and ≤15 mm was 1.73, 0.27 and 0.18 %, respectively. All pregnancy that had short cervix received micronized progesterone or 17-hydroxyprogesterone caproate (17OHP-C). Arabin pessary was used in six pregnancies and no case for cervical cerclage. Most of pregnancy delivered ≥37 weeks of gestation whereas preterm delivery was 6.46% (55/852) and late preterm was occurrences 4.23% (36/852). The major cause of preterm delivery was spontaneous preterm labor 47.27% (26/852) and preterm premature rupture of membrane 30.91% (17/852).

Conclusion: The prevalence of short cervix in low risk singleton pregnancy was 1.73%.

Keywords: cervical length, short cervix, preterm, singleton pregnancy

ความชุกและผลลัพธ์การตั้งครรภ์ของภาวะปากมดลูกสั้นในสตรีตั้งครรภ์เดี่ยวความเสี่ยงต่ำจากการตรวจวัดความยาวปากมดลูกแบบคัดกรองทุกราย

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาความชุกและผลลัพธ์การตั้งครรภ์ของภาวะปากมดลูกสั้นในสตรีตั้งครรภ์เดี่ยวความเสี่ยงต่ำ

วิธีดำเนินการวิจัย: ทำการศึกษาย้อนหลัง (retrospective descriptive) ในสตรีตั้งครรภ์เดี่ยวความเสี่ยงต่ำ 1,099 ราย ที่มาฝากครรภ์ระหว่างอายุครรภ์ 16-24 สัปดาห์ โดยการทบทวนเวชระเบียน ระหว่าง กุมภาพันธ์ 2559 ถึง มกราคม 2560 ได้ทำการคัดออกหากสตรีตั้งครรภ์มีประวัติของ cervical incompetence มีประวัติการคลอดหรือน้ำเดินก่อนกำหนดในครรภ์ก่อน มีประวัติผ่าตัดปากมดลูกโดย Loop electrosurgical excision (LEEP) หรือ Conization รวมถึงทารกในครรภ์มีความผิดปกติหรือมีโครโมโซมผิดปกติที่รุนแรงในครรภ์ปัจจุบัน ทำการวัดความยาวปากมดลูกโดยการอัลตราซาวด์ทางช่องคลอด ขั้นตอนการวัดอ้างอิงจาก Society for Maternal-Fetal Medicine (SMFM) สตรีตั้งครรภ์มีความยาวปากมดลูกสั้นเมื่อวัดได้น้อยกว่าหรือเท่ากับ 25 มิลลิเมตร

ผลการวิจัย: อายุครรภ์เฉลี่ยในการวัดความยาวปากมดลูกคือ19.68±1.62 สัปดาห์ ความยาวปากมดลูกเฉลี่ยเท่ากับ 37.37±6.66 มม. พบความชุกของภาวะปากมดลูกสั้น ≤25, ≤20 และ ≤15 มม. ร้อยละ 1.73, 0.27 และ 0.18 ตามลำดับ สตรีตั้งครรภ์เดี่ยวที่มีความยาวปากมดลูกสั้นทุกรายจะได้รับยา micronized progesterone หรือ 17-hydroxyprogesterone caproate (17OHP-C) และมีการใช้ห่วงรัดปากมดลูก (Arabin pessary) ในสตรีตั้งครรภ์ 6 ราย สตรีตั้งครรภ์ส่วนใหญ่ร้อยละ 93.54 (797/852) คลอดทารกครบกำหนด ≥37 สัปดาห์ คลอดก่อนกำหนดร้อยละ 6.46 (55/852) ซึ่งส่วนใหญ่จะเป็น late preterm 34-$36^{6/7}$ สัปดาห์ร้อยละ 4.23 (36/852) สาเหตุของการคลอดก่อนกำหนดได้แก่ spontaneous preterm labor ร้อยละ 47.27 (26/852) และน้ำเดินก่อนกำหนดร้อยละ 30.91 (17/852)

สรุป: ความชุกของปากมดลูกสั้นในสตรีตั้งครรภ์เดี่ยวความเสี่ยงต่ำเท่ากับร้อยละ 1.73

คำสำคัญ: ความยาวปากมดลูก, ปากมดลูกสั้น, การคลอดก่อนกำหนด, สตรีตั้งครรภ์เดี่ยว

Introduction

Preterm birth is a global problem; the incidence is 10.6% of all live births in 2014[1]. In past 5 years, our institute had preterm birth rate are 12.9, 12.14, 10.79, 10.63 and 9.09% respectively. The most common cause of preterm birth are spontaneous preterm labor and PPROM[2]. Premature birth is the most common cause of neonatal death and disability due to prematurity especially respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), retinopathy, pulmonary hypertension, etc[2]. The reported medical fee for prematurity treatment in Thailand 2008 is 1,992,025,000 baths per year [3], which is high cost.

For this reason, many institutions have worked for preterm prediction and prevention by screening risk factor such as previous spontaneous preterm delivery, cervical surgery, asymptomatic bacteriuria and bacterial vaginosis, etc[4]. At present, the previous spontaneous preterm delivery, PPROM and short cervical length (CL) are strong risk factors for preterm labor and delivery in the next pregnancy[5-6]. Therefore, there is recommendation for cervical measurement in pregnancy who ever had spontaneous preterm labor and delivery[7-8] but the universal CL screening is not routinely recommended. However, the benefits of universal CL screening are still mentioned in some studies [9].

There are several effective treatment options if short CL has been identified, such as progesterone, cervical cerclage and cervical pessary. Progesterone (17 hydroxyprogesterone caproate (17OHP-C)/ micronized progesterone) plays an important role on preventing preterm birth in singleton pregnancy with a history of previous preterm birth or short CL. Aside from progesterone, cervical cerclage is also useful for previous preterm birth with short CL[7]. For cervical pessary, its role is still controversy for the prevention of preterm birth[10-11]. The Society for Maternal Fetal Medicine did not recommend it in routine practice and currently cervical pessary is used mainly in clinical trial or research protocol[12].

Our institute has confronted uneventful events of preterm births. For that reason, the preterm screening and prevention programs have been implemented since February 2016. CL measurement and ultrasound screening have been launched for all singleton pregnant women at their gestational ages of 16-24 weeks. Actually, CL measurement should be done only in high risk singleton pregnancy who had previous preterm birth. However, universal cervical length screening may provide benefit because low risk cases with short cervix can be detected. These pregnant women should be also treated because of preterm births have an effect on family and annual government statement of expenditure. Therefore, the objective of this study focused on the prevalence of short cervix in low risk singleton pregnancy. Outcomes of these women were also determined.

Materials and Methods

A retrospective descriptive study was conducted by reviewing medical records of pregnant women who came for antenatal care during February 2016 to January 2017 at Department of Obstetrics and Gynecology, Faculty of Medicine, Navamindradhiraj University. The study was approved by Vajira Institutional Review Board (Registered Number 099/60). Eligibility criteria were singleton pregnancy; gestational age is between 16-24 weeks of gestation. Exclusion criteria were history previous cervical incompetence, spontaneous preterm labor, PPROM, Loop electrosurgical excision procedure (LEEP), conization and severe congenital anomaly or chromosomal abnormality. The gestational age was calculated from last menstrual period (LMP) and confirmed by ultrasound for all pregnancy.

Transvaginal ultrasound for CL measurement was performed by well-trained physicians and confirmed by maternal fetal medicine (MFM) staff inter/intra observer variability in all case with short cervix which is less than or equal to 25 mm. All physicians were trained by MFM staff and step for measurement was referenced from Society for Maternal-Fetal Medicine (SMFM)[8]. Pregnant women who had short cervix were treated with 200 mg vaginal micronized progesterone suppositories daily

until $36^{6/7}$ weeks or 250 mg 17OHP-C intramuscularly weekly until 36 weeks. Additional treatments such as cervical pessary or cervical cerclage may be considered.

Lemeshow formula was used to calculate sample size. The prevalence from a previous study of Temming et al. was 2%[13]. The sample size was calculated using 5% level of statistical significance and 1 % for acceptable error. This resulted in total of 753 subjects needed. Data collection included maternal demographic, antenatal characteristics and delivery outcomes. BMI was calculated from self-reported pre-pregnancy weight (kg) divided by square of height (m^2). Neonatal low birth weight is less than 2500 grams and birth asphyxia was defined as 5-minute Apgar score less than 7[14].

Statistical analysis was performed using SPSS software package version 22.0 (SPSS Inc., Chicago IL, USA). The prevalence was presented with 95% CI. Quantitative data were presented using mean ± SD or median and Quartile range where appropriated. Qualitative data were presented frequency distribution and percentage.

Results

Total 1,099 pregnant women who met the criteria were enrolled. Maternal demographic and antenatal characteristics are presented in Table 1. The mean maternal age was 27.71±6.63 years old. Most of them graduated under Bachelor degree and was employee. There was similar percentage in parity; nulliparous and multiparous were 48.23 and 51.77, respectively. Pregnancy women generally had normal weight before pregnant; overweight and obesity were rather high (38.03%). The mean gestational age for cervical length measurement was 19.68±1.62 weeks of gestation.

Table 1:

Maternal antenatal characteristics (n=1099)

Characteristic	Over all (n = 1,099)
Age (year)	27.71 ± 6.63
Education	
Primary school	256 (23.29)
Secondary school	601 (54.69)
Bachelor degree or above	242 (22.02)
Occupation	
Employee	699 (63.60)
Civil servant	65 (5.92)
Housewife	174 (15.83)
Other	161 (14.65)
Parity	
Nulliparous	530 (48.23)
Multiparous	569 (51.77)
BMI (kg/m2)	22.49 ± 4.48
Underweight (<18.5)	187 (17.02)
Normal weight (18.5-24.9)	494 (44.95)
Overweight (25.0-29.9)	176 (16.01)
Obesity (≥ 30)	242 (22.02)
GA for CL measurement (week)	19.68 ± 1.62

Data are presented as number (%) or mean±standard deviation

Abbreviation: BMI = body mass index; GA = gestational age; CL = cervical length; n = number; SD = standard deviation

For delivery outcomes; Most of pregnancy delivered ≥37 weeks of gestation (93.54%) whereas preterm delivery was 6.46% and mostly was late preterm delivery (4.23%) as showed in table 2. The majority of preterm causes were spontaneous preterm labor (47.27%) and premature ruptured of membrane (30.91%). Cesarean section delivery was 41.55%; focusing on the indications for cesarean section was previous cesarean section 36.16% and the second was cephalopelvic disproportion (34.18%). There was low neonatal birth weight 7.98% and birth asphyxia (Apgar score <7) at 5 and 10 minutes of age were 1.06% and 0.7% respectively.

Table 2:

Delivery outcomes (n = 852)

Outcome	Over all (n = 852)
GA at delivery (weeks)	38.52 ± 1.77
≤ 28	6 (0.70)
28+1-34	13 (1.53)
34+1-36+6	36 (4.23)
≥ 37	797 (93.54)
Route of delivery	
Normal vaginal delivery	484 (56.81)
Cesarean section	354 (41.55)
Other	14 (1.64)
Indication for CS (n = 354)	
Previous CS	128 (36.16)
CPD	121 (34.18)
Non reassuring FHR	42 (11.86)
Other	63 (17.80)
Preterm cause (n = 55)	
Spontaneous preterm labor	26 (47.27)
PPROM	17 (30.91)
Indicated preterm	12 (21.82)
Neonatal birth weight (g)	3079 ± 489.29
< 2500	68 (7.98)
≥ 2500 g	784 (92.02)
Apgar score at 1 minute	
Apgar score <7	33 (3.87)
Apgar score ≥7	819 (96.13)
Apgar score at 5 minutes	
Apgar score <7	9 (1.06)
Apgar score ≥7	843 (98.94)
Apgar score at 10 minutes	
Apgar score <7	6 (0.70)
Apgar score ≥7	846 (99.30)

Data are presented as number (%) or mean±standard deviation

Abbreviation: GA = gestational age; CS = cesarean section; CPD = cephalopelvic disproportion; FHR = fetal heart rate; PPROM = preterm premature rupture of membrane; n = number; SD = standard deviation

Table 3 demonstrated that mean CL from transvaginal ultrasound measurement was 37.37±6.66 mm (95%CI 36.98-37.76). The short CL less than or equal to 25 mm was found 19 cases (1.73%; 95% CI 1.044-2.687). There were three cases (0.27%; 95%CI 0.056-0.796) had cervical length ≤ 20 mm whereas two cases (0.18%; 95% CI 0.022-0.656) had cervical length ≤15 mm that was defined as very short cervix.

All nineteen pregnant women who had short CL received progesterone (micronized progesterone for 12 cases and 17OHP-C for 7 cases). Progesterone drug form consideration was depended on medical welfare and pregnant women requirement. There were six pregnant women who received cervical pessary. Their CL were 8.3, 16.7, 20.5, 22.4, 24.2 and 24.6 mm. Cervical pessary was inserted in women who had CL 8.3 and 16.7 mm at 20 and 24 weeks of gestation, respectively. Both gave birth at respective 24 and 26 weeks due to PPROM. Others four cases delivered at term (after 37 weeks of gestation). There were 5 cases who received only progesterone and had preterm delivery. One case with CL 21.8 mm had indicated preterm delivery at 30-weeks due to placenta previa with active bleeding. Another case with CL 20.8 mm was stillbirth at $23^{2/7}$ weeks because of PPROM. Three cases with CL 23.7 mm, 20.7 mm and 20.8 mm delivered at $35^{6/7}$, $33^{4/7}$ and $36^{3/7}$ weeks, respectively. Others eight cases, including one case with very short CL of 14. 2 mm, delivered at term.

There was no significant difference in parity between short and normal CL. However; our study found that most pregnant women who had short cervix were nulliparity. Pregnancy with short CL had tendency for preterm delivery more than normal CL and the causes of preterm delivery were spontaneous preterm labor and PPROM. There was also more neonatal low birth weight and birth asphyxia at 5 and 10 minutes in pregnancy with short CL (table 4). The cause of this finding was likely due to more rate of extremely (< 28 weeks) and early (< 34 weeks) preterm delivery among this group.

Discussion

The prevalence of short cervical length ≤ 25 mm and ≤ 20 mm in low risk singleton pregnancy were 1.73 and 0.27%, respectively, which is rather low in our institute. Previous studies found prevalence of short cervical length ≤ 25 mm were 0.9, 0.89 and 0.45%[15-17]. Whereas, Moeun S reported short cervical length less than or equal 20 mm was 0.47%[16]. This may be due to ethnic difference and even though Asian populations are also different. However, prevalence of short cervix in low risk singleton pregnancy (no previous preterm delivery and cervical surgery such as LEEP, conization) is low.

Table 3:

Prevalence of short cervix (n = 1099)

Cervical length	All participants (n = 1099)	
	n (%)	95% CI
CL (mean±SD)	37.37 ± 6.66	(36.98 - 37.76)
CL ≤ 25 mm.	19 (1.73)	(1.044 - 2.687)
CL ≤ 20 mm.	3 (0.27)	(0.056 - 0.796)
CL ≤ 15 mm.	2 (0.18)	(0.022 - 0.656)

Data are presented as number (%), mean±standard deviation and 95%CI
Abbreviation: CL = cervical length; CI = confidence interval

Table 4:

Pregnancy characteristic and delivery outcomes between short CL and normal CL

Characteristic and delivery outcomes	Short CL (n=19) n (%)	Normal CL (n=833) n (%)	p-value*
Parity			
P0	12 (3.0)	310 (97.0)	0.029
≥P1	7 (1.5)	523 (98.5)	
GA at delivery (week)			
≤28	3 (50.0)	3 (50.0)	<0.001
28+1-34	2 (15.4)	11 (84.6)	
34+1-36+6	2 (5.6)	34 (94.4)	
≥37	12 (1.5)	785 (98.5)	
Cause of preterm			
Spontaneous preterm labor	4 (15.4)	22 (84.6)	<0.001
PPROM	2 (11.8)	15 (88.2)	
Indicated preterm	1 (8.3)	11 (91.7)	
Neonatal birth weight (g)			
< 2500	6 (8.8)	62 (91.2)	0.002
≥2500	13 (1.7)	771 (98.5)	
Apgar score at 1 minute			
< 7	5 (15.2)	28 (84.8)	0.001
≥7	14 (1.7)	805 (98.3)	
Apgar score at 5 minutes			
< 7	3 (33.3)	6 (66.7)	0.001
≥7	16 (1.9)	827 (98.1)	
Apgar score at 10 minutes			
< 7	3 (50.0)	3 (50.0)	<0.001
≥7	16 (1.9)	830 (98.1)	

Data are presented as number (%)

* Fisher's exact test

Abbreviation: CL = cervical length; G = gravida; P = parity; GA = gestational age; PPROM = preterm premature rupture of membrane

The average gestational age for CL length measurement is 19.68 ± 1.62 weeks while doing fetal anomaly scan which is appropriate gestational age and convenient for pregnant women. In our study found that all pregnancy who had short cervix is primigravida and preterm prevention was considered. Therefore, universal cervical length screening may be useful in these pregnancies. According to low prevalence of short cervix in low risk singleton pregnancy and universal cervical length screening increases workload and cost for ultrasound examination, therefore the value of universal length screening is still controversial.

This is retrospective study and there are many physicians performed CL measurement. However, all physicians were trained by MFM staff and in the case of short cervix which is less than or equal to 25 mm was repeated and confirmed by MFM staff at the same day. Then, this pregnancy was received micronized progesterone or 17OHP-C after giving information about risk of preterm birth, progesterone effectiveness for preterm prevention and route of drug administration. Pregnant women preferred in difference form of progesterone due to route of drug administration, convenience, satisfaction and including medical welfare even though the American College of Obstetricians and Gynecologists (ACOG) recommended vaginal progesterone in singleton pregnancy with no prior spontaneous preterm birth and SMFM still confirmed 17OHP-C 250 mg intramuscularly weekly for singleton previous preterm delivery[18-19]. There were six cases for cervical pessary whereas no cervical cerclage because of most of our short cervix were primigravida or multigravida without previous preterm delivery.

For delivery outcome, preterm delivery in our study is only 6.46%. This is not representing the entire population because of we included only low risk singleton pregnancy who come to visit antenatal care unit between 16-24 weeks of gestation. In addition, we have no delivery information for 247 cases which delivery at others hospital. Four in six cases of cervical pessary delivered at term which corresponding with previous study; using cervical pessary in short cervix without prior preterm delivery had lower rate of spontaneous preterm delivery less than 34 weeks of gestation[20]. Although two cases delivered extremely preterm but pregnancy could be prolonged for 2-4 weeks. In our study, there are some pregnancies that had short cervix lost follow up or non-compliance that affected to preterm delivery. Moreover, we lacked of cervical surveillance for CL measurement every 1-2 week in short cervix cases. We supposed that if CL is shortened during follow up, additional treatments should be provided. In case very short cervix (CL ≤ 15 mm), cervical cerclage may be another option even if primigravida or multigravida without previous preterm delivery. The mostly cause of preterm delivery was preterm labor and PPROM which is similar other studies[2]. As we know, pregnancy that had previous preterm delivery and short cervix is high risk for recurrence preterm[5-6]. However, short cervix in primigravida or nulliparous is also significant for preterm labor and delivery. In other words; these pregnancies are liable to have cervical incompetence. For this reason, prophylaxis preterm labor should be considered in all pregnancies that had short cervix. The cesarean section rate is 41.55% that is higher than WHO recommendation due to previous cesarean section was indicated. Neonatal low birth weight and birth asphyxia were mainly associated with preterm birth. Short and long term neonatal outcomes were not collected which is limitation due to retrospective study.

There are nineteen cases of short cervix so we could not identify the risk factors for short cervix. Micronized progesterone had higher price in our institute and was not covered by some medical welfare. Thus, vaginal progesterone could not be used in all pregnancies. Because of the prevalence of short cervix in low risk singleton pregnancy is rather low. The cost and benefit for universal cervical length screening in low risk pregnancy should be the further study. Moreover, the risk factor for short cervix was also interested.

Conclusion

The prevalence of short cervix in low risk singleton pregnancy is low. The benefit and cost should be explored in individual institute. However, preterm prevention should be considered when short cervix was detected.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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