Normal Reference of Cervical Blood Perfusion in Pregnancy

Thitinant Samutchaikij MD*,
Somsri Pitukkijronnakorn MD*, Panyu Panburana MD*

** Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

Objective: *To develop normal reference of cervical blood perfusion in pregnancy by using 3D power Doppler-derived FMBV at 16 to 24 weeks gestation.*

Material and Method: *The present prospective cohort study recruited the normal singleton pregnant women at 16 to 24 weeks gestation who had antenatal care and midtrimester ultrasound screening at Ramathibodi Hospital between June and September 2012. Transvaginal ultrasound (TVU) measurements of cervical length (CL), cervical volume (CV), vascularization index (VI), flow index (FI), and vascularization flow index (VFI) were performed. The pregnant women with multifetuses, severe fetal anomalies, unknown delivery status, abortion, stillbirth, and preterm birth were excluded from the present study.*

Results: The authors recruited 168 cases but 25 cases were excluded. Only 143 cases were included into the study. The mean of gestational age at ultrasound examination and delivery was 21 and 39 weeks respectively. There were no perinatal morbidity and mortality in the present study. The average values of cervical profiles of CL, CV, VI, FI, and VFI were 4.2 cm, 31.6 cm3, 6.4, 38.9, and 2.6 respectively.

Conclusion: The normal reference of cervical blood perfusion in Thai pregnant women was established. The VI, FI, and VFI of the normal term singleton pregnancy at 16 to 24 weeks gestation were 6.4, 38.9, and 2.6 respectively.

Keywords: Cervical length (CL), Cervical volume (CV), Cervical blood perfusion, Fractional moving blood volume (FMBV), Power Doppler-flow indices, 3D transvaginal ultrasound, VOCAL, Preterm birth (PTB)

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Current development of the three-dimensional (3D) ultrasound technique makes it become commercially available in the routine ultrasound scanning. The 3D power Doppler ultrasonography (PDU) is also appropriate method to assess the organ blood supply better than the conventional two-dimensional (2D) power Doppler ultrasound.

Cervical modifications leading to labor include increased softness and blood supply. Changes in tissue blood perfusion reflected as blood cell movements can be reliably assessed with estimation of the fractional moving blood volume (FMBV)[1]. There is evidence that angiogenic factors may play a role in cervical ripening and the birth process, and therefore it would be valuable to know how cervical blood circulation changes during pregnancy[2].

Cervical length (CL) measured by transvaginal ultrasound (TVU) is the only screening test that identifies early opening of the internal cervical os[3,4]. TVU CL has not been shown to associate with complications, even in women with preterm prelabor rupture of membranes, as it is not associated with increase in infection or higher inoculation of bacteria. It has been shown as less than 2% experience pain or severe discomfort[4,5].

Preterm birth (PTB) is the main cause of perinatal mortality about 75%, and its incidence increased to 12.8% in the USA in 2006. Some of the reasons may include the increase incidence of multiple gestations, assisted reproductive technology, better dating and recording of gestational age, more fetal monitoring as well as the iatrogenic deliveries[4]. According to the Ramathibodi Hospital's birth statistics, the incidence of PTB has been increasing up to 12%, similar to the PTB rate in Thailand and around the world.

As FMBV is a reliable estimation of tissue blood perfusion, it can be implemented as a complementary procedure in cervical assessment for identification of high-risk women for PTB[1].

The aim of the present study was to develop normal reference of cervical blood perfusion in pregnancy by using 3D power Doppler-derived FMBV from 16 to 24 weeks' gestation.

Correspondence to:
Pitukkijronnakorn S, Department of Obstetrics & Gynaecology, Faculty of Medicine, Ramathibodi Hospital, 270 Rama 4 Road, Phayathai, Ratchathewi, Bangkok 10400, Thailand.
Phone: 0-2201-1412, Fax: 0-2201-1416
E-mail: somsri2005p@yahoo.com

Material and Method

The present prospective cohort study recruited the normal singleton pregnant women of 16 to 24 weeks gestation who attended antenatal care and midtrimester ultrasound screening at Ramathibodi Hospital between June and September 2012. The Ethical Clearance Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University had approved the present study.

The parameters used in the present study were as follow: Cervical profiles were the totality of related characteristics of the cervix: functional cervical length, cervical volume, and cervical blood perfusion. Cervical blood perfusion was the reflection of blood cell movement through the cervix: vascularization index (VI), flow index (FI) and vascularization flow index (VFI). FMBV was based on mathematical algorithm that analyzes the power Doppler signals obtained from a region of interest (ROI) and compensated for the effect of depth, tissue interfaces, and blood characteristics. FMBV was a reliable estimation of tissue blood perfusion[1]. Functional CL was the length of the cervix from the internal to external os along the endocervical canal. It was used for calculation and prediction of preterm birth. Cervical volume (CV) was the volume of the cervix as measured by 3D ultrasound. VI was the ratio of color-coded voxels to all voxels within the volume and expressed as percentage, reflecting the number of vessels within the volume of interest[2]. FI was the mean power Doppler signal intensity from all color-coded voxels, reflecting the intensity of flow at the time of the 3D sweep[2]. VFI was the simple mathematical relationship derived from multiplying VI by FI and dividing the result by 100, reflecting both flow and vascularization[2].

All patients were examined by only one experienced operator, using a Voluson 730 Expert ultrasound system (General Electric® Healthcare) with a 7.5-MHz intracavitary probe containing both 2D and 3D modes. After a routine ultrasound screening, the patient was asked to empty her bladder and obtained TVU measurements of CL, CV and cervical power Doppler flow indices (VI, FI, and VFI). CL was measured by using 2D-ultrasound, and then changed to 3D without removing the probe. All procedures were carried out according to the manufacturer's directions.

Recommendations for the technical performance of TVU CL[4] and technique of transvaginal 3D power Doppler ultrasound[2] were followed as the guidelines. The technical performance was shown as in Fig. 1 and 2.

The authors recruited 168 cases in the present study. The pregnant women with multifetuses, severe fetal anomalies, unknown delivery status, abortion, stillbirth, and preterm birth were excluded from the present study. One hundred forty three cases of term birth were included in the study.

Statistical analyses were performed by using STATA® version 11.2. Quantitative variables were described by the following centralization and dispersion indices: mean, median, standard deviation, and variation range. For comparison of CL, CV, and power Doppler flow indices in relation to the nullipara and para cervix, we used the Student's t-test. Pearson's correlation was used to identify the relationship of CL (standard test to predict PTB) with CV and power Doppler flow indices. A p-value <0.05 was considered statistically significant.

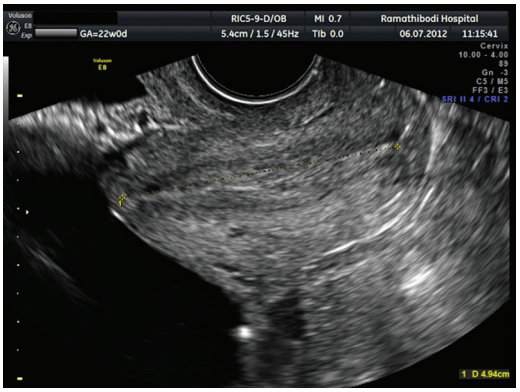

Fig. 1 The functional cervical length.

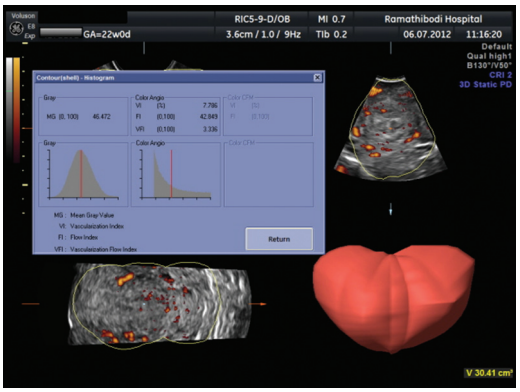

Fig. 2 The cervical volume and power Doppler flow indicies.

Results

The authors recruited 168 cases in the study, but 25 cases were excluded. Only 143 cases were included to the study. The mean of maternal age was 28.3 years old. The mean of gestational age at ultrasound examination and delivery were 21 and 38.8 weeks respectively. There were primigravida 48.4%, multigravida 40.7%, previous preterm birth 1.3%, and previous abortion 25.8% (Table 1).

Regarding the neonatal outcomes, the mean fetal weight was about 2,991.4 gm. The mean Apgar score at 1 and 5 minutes were 8.5 and 9.7 respectively (Table 1).

The term birth group, the normal ranges at 16-24 weeks gestation of cervical profiles of CL, CV, VI, FI, and VFI were 4.2 cm, 31.6 cm^3, 6.4, 38.9, and 2.6 respectively. The cervical profile at each gestational age group had no difference (Table 2).

Table 1. Baseline characteristic in population study

Maternal & neonatal outcomes	Total (n = 143) mean (SD)
Maternal age (years)	28.3 (5.3)
Gestation age (weeks)	21.0 (1.6)
Delivery (weeks)	38.8 (1.6)
Estimated fetal weight (EFW) (g)	2,991.4 (497.1)
Apgar score at 1 min	8.5 (1.3)
Apgar score at 5 min	9.7 (1.0)

The para cervix tended to have the cervical profiles higher than nullipara cervix, but there were no statistically significant difference (Table 3).

There was the correlation between CL and CV (r = 0.409, *p*-value <0.001). For the power Doppler flow indices (VI, FI, and VFI), there were inverted correlation with CL. The coefficient between CL and VI was 0.161 (*p*-value = 0.039). The coefficient between CL and FI was 0.125 (*p*-value = 0.112). The coefficient between CL and VFI was 0.153 (*p*-value = 0.05). There was statistically significant difference, except FI.

Discussion

Cervical blood perfusion had been assessed previously in pregnant and non-pregnant women using 3D-PDU indices (vascularization (VI), flow (FI), and vascularization flow (VFI) indices). Changes in tissue blood perfusion reflected as blood cell movements can be reliably assessed with estimation of FMBV. Cervical FMBV can be evaluated at the same time and in the same anatomical plane as CL estimation[1]. This was the first study of the cervical profiles in Thailand.

In the term birth group, the normal ranges at 16-24 weeks' gestation of cervical profiles of CL, CV, VI, FI, and VFI were 4.2 cm, 31.6 cm^3, 6.4, 38.9, and 2.6 respectively. Therefore, the normal reference of cervical blood perfusion in singleton term pregnancy was established in the present study. The authors found

Table 2. The normal range of cervical profiles in term birth groups

Cervical profiles, mean (95% CI)	GA 16^{+1}-20 weeks n = 34	GA 20^{+1}-22 weeks n = 75	GA 22^{+1}-24 weeks n = 34	Total n = 143
Functional cervical length (CL) (cm)	4.2 (4.0, 4.4)	4.2 (4.1, 4.3)	4.2 (3.9, 4.4)	4.2 (4.1, 4.3)
Cervical volume (CV) (cm^3)	32.0 (29.1, 34.9)	31.8 (29.7, 33.9)	30.6 (27.3, 33.9)	31.6 (30.1, 33.0)
Vascularization index (VI)	6.8 (5.2, 8.3)	6.1 (5.3, 6.9)	6.5 (5.1, 8.0)	6.4 (5.7, 7.0)
Flow index (FI)	39.3 (37.7, 40.9)	38.9 (37.6, 40.2)	38.5 (37.0, 39.9)	38.9 (38.1, 39.7)
Vascularization flow index (VFI)	2.8 (2.0, 3.5)	2.5 (2.1, 2.9)	2.6 (1.9, 3.3)	2.6 (2.3, 2.9)

GA = gestational age

Table 3. Comparison of cervical profiles between nulliparae and parae cervix in term birth group

Cervical profiles, mean (SD)	Nulliparae (n = 84)	Parae (n = 59)	*p*-value
Functional cervical length (CL) (cm)	4.16 (0.60)	4.25 (0.60)	0.379
Cervical volume (CV) (cm^3)	29.98 (9.03)	33.79 (8.60)	0.070
Vascularization index (VI)	5.88 (3.78)	7.04 (4.12)	0.084
Flow index (FI)	38.10 (5.00)	40.03 (4.93)	0.066
Vascularization flow index (VFI)	2.34 (1.73)	2.92 (1.89)	0.060

no significant difference from 16 to 24 weeks gestation in term of the cervical profile. One of the reason the examination was performed only in a short period of gestational age (16-24 weeks). As from the previous study, there was no statistical significance[2]. This did not exclude the possibility that there might be vascular changes too small to be detectable with the rather crude Doppler ultrasound technique.

PTB is the major cause of perinatal morbidity and mortality. TVU CL is the only screening test to identify the early opening process of the cervical os[4]. The mean gestational age of cervical shortening occurs between 18 and 22 weeks gestation. However, the most of recommendation for screening CL is between 16 and 24 weeks gestation. In the present study, the PTB rate was 9.49%. It was lower than worldwide incidence of PTB, which is approximately 12%[4]. One of the reasons was the loss follow-up in the present study.

As the CL is the gold standard for prediction of PTB[4,5], we expected to use the other cervical profiles to predict PTB as well. FMBV is a reliable estimation of tissue blood perfusion. It can be implemented as a complementary procedure in cervical assessment for identification of women at high risk for PTB[1].

The advantage of the present study is that all patients underwent ultrasound screening, volume acquisitions, and calculations by the single operator. This could eliminate the interpersonal validity in the study because the ultrasound is depended on operator's skill and technique. The authors followed the recommendations for the technical performance of TVU CL[4] and the technique of transvaginal 3D power Doppler ultrasound[2] as directed by the guidelines.

The limitation of the present study was the methodological difficulty, especially when drawing the contours of the cervix to get the cervical volume and vascularity by 3D ultrasound. The delineation between the cervix and the lower uterine segment is also particularly difficult, especially early in pregnancy and at mid-gestation when the lower uterine segment is thick and the cervix often curved[2].

When the cervical length is less than 10 mm, it is difficult to define where the superior and inferior cervical boundaries are. As the cervix is almost a continuation with the uterine wall. Another potential factor affecting FMBV estimation is the dynamic changes of the cervix observed during uterine contractions. These changes can alter the size and position of the cervix and thus FMBV estimation[1].

However, after getting familiar with the 3D power Doppler-derived ultrasound of the cervical profiles examination, it became easy to perform the cervical profiles assessment.

In conclusion, the normal reference of cervical blood perfusion in Thai pregnant women was established. The VI, FI, and VFI of the normal term singleton pregnancy at 16 to 24 weeks' gestation were 6.4, 38.9, and 2.6 respectively.

What is already known on this topic?

PTB is the main cause of perinatal mortality about 75%. CL measured by TVU is the only screening test that identifies early opening of the internal cervical os[3,4] but it depends on operator's experience. Cervical modifications leading to labor include increased softness and blood supply. Changes in tissue blood perfusion reflect as blood cell movements can be reliably assessed with estimation of FMBV[1]. There is evidence that angiogenic factors may play a role in cervical ripening and the birth process. Therefore, it would be valuable to know how cervical blood circulation changes during pregnancy[2]. FMBV can be implemented as a complementary procedure in cervical assessment for identification of women at high risk for PTB[1].

What this study adds?

Cervical FMBV can be evaluated at the same time and in the same anatomical plane as CL estimation[1]. The present study is the first kind of study of the cervical profiles in Thailand. In addition, the normal reference of cervical blood perfusion in Thai pregnant women has been established.

Potential conflicts of interest

None.

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ค่าอ้างอิงปกติของปริมาณเลือดบริเวณปากมดลูกในสตรีตั้งครรภ์

ฐิตินันท์ สมุทรไชยกิจ, สมศรี พิทักษ์กิจรณกร, พัญญ พันธ์บูรณะ

วัตถุประสงค์: *เพื่อหาค่าอ้างอิงปกติของปริมาณเลือดบริเวณปากมดลูกในสตรีตั้งครรภ์ด้วยการตรวจคลื่นเสียงความถี่สูงสามมิติพาวเวอร์ดอปเปลอร์ ที่ช่วงอายุครรภ์ 16-24 สัปดาห์*

วัสดุและวิธีการ: *เป็นการศึกษาแบบ prospective cohort ในสตรีตั้งครรภ์เดี่ยวอายุครรภ์ 16-24 สัปดาห์ ที่มาฝากครรภ์และได้รับการตรวจคัดกรองที่ช่วงกลางของการตั้งครรภ์ด้วยคลื่นเสียงความถี่สูงที่โรงพยาบาลรามาธิบดี ระหว่างเดือนมิถุนายน ถึงเดือนกันยายน พ.ศ. 2555 และได้รับการวัดความยาวปากมดลูก (CL) ขนาดปากมดลูก ดัชนีค่าของหลอดเลือด (IV) ดัชนีการไหลของเลือด (FI) และดัชนีการไหลของหลอดเลือด (VFI) ด้วยคลื่นเสียงความถี่สูงทางช่องคลอด ส่วนสตรีตั้งครรภ์แฝด ทารกที่มีความพิการแต่กำเนิดที่รุนแรง หรือไม่ทราบข้อมูลการคลอด การแท้ง การตายคลอด และการคลอดก่อนกำหนดจะไม่รวมในการศึกษานี้*

ผลการศึกษา: *ได้คัดเลือกสตรีตั้งครรภ์ตามเกณฑ์ที่กำหนด จำนวน 168 ราย แต่ต้องคัดออก 25 ราย ดังนั้น จึงมีเพียง 143 รายที่ได้ศึกษา โดยพบค่าเฉลี่ยของอายุครรภ์ขณะตรวจคลื่นเสียงความถี่สูงและคลอดที่ 21 และ 39 สัปดาห์ ตามลำดับ ในการศึกษานี้ไม่พบภาวะทารกทุพพลภาพและตายปริกำเนิด ค่าเฉลี่ยของปากมดลูก CL, CV, VI, FI และ VFI เท่ากับ 4.2 เซนติเมตร, 31.6 ลูกบาศก์เซนติเมตร 6.4, 38.9 และ 2.6 ตามลำดับ*

สรุป: *ได้รายงานค่าอ้างอิงปกติของปริมาณเลือดปากมดลูกในสตรีตั้งครรภ์ไทย ค่า VI, FI, และ VFI ของสตรีตั้งครรภ์เดี่ยวปกติครบกำหนดที่อายุครรภ์ 16-24 สัปดาห์ คือ 6.4, 38.9 และ 2.6 ตามลำดับ*