Nomogram of Cervical Length at Mid-trimester in Normal Thai Pregnant Women

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Background: *As cervical length decreases in the second trimester, the risk of spontaneous preterm birth increases, especially when effacement occurs early in the second trimester, and it is often detected on ultrasound examination before it can be identified by physical examination. To date, only two Thai nomograms of transvaginal cervical length have been reported.*

Objective: *To establish a new Thai nomogram as a reference for evaluation of transvaginal cervical length in a tertiary Thai hospital in Bangkok (Rajavithi Hospital: RH) during gestational age (GA) 16 to 24 weeks.*

Material and Method: *This research was approved by the ethics committee of RH (No. 055/2558). A total of 286 normal Thai pregnant women who attended the antenatal clinic (ANC) at RH between May 1, 2015 and November 30, 2015 were included. All were cases of singleton gestation with no medical or obstetric complications and no fetal congenital anomalies; and all had GA confirmed by Crown Rump Length (CRL) before GA of 14 weeks. Cervical length measurement was performed by a single operator using transvaginal ultrasonography (7.5 mHz Voluson E8) during GA of 16 to 24 weeks. The subjects attended follow-up sessions in the antenatal care clinic until delivery.*

Results: *One hundred and ninety-six cervical measurements were analysed (90 patients were excluded: 7 because of preterm labor, and 83 because they were lost to follow-up). The mean maternal age was 29.49±6.5 years, and the most common pregnancy status was nullipara (48.3%). The mean CL of nulliparous, multiparous and overall women were 37.87, 39.46 and 38.70 mm respectively. The CL values were constant during the examined GA.*

Conclusion: *The mean cervical length of normal Thai pregnant women between GA of 16 to 24 weeks examined transvaginally was 38.70 mm.*

Keywords: *Cervical length (CL), Transvaginal ultrasonography*

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Preterm birth is the leading cause of neonatal death (demise in the first 28 days of life), and it is responsible for 27 percent of neonatal deaths worldwide[1]. Preterm birth is also the second most common reason for death (after pneumonia) in children younger than five years of age[2]. Cervical shortening (effacement) is one of the first steps in the parturition process, preceding labor by several weeks. As cervical length decreases in the second trimester, the risk of spontaneous preterm birth increases[3], especially when effacement occurs early in the second trimester. Because effacement begins at the internal cervical os and progresses caudally[3], it is often detected on ultrasound investigation before it can be identified by physical examination.

The causes of preterm cervical shortening are often unclear. It has been attributed to several factors, including occult uterine activity, uterine overdistention, congenital or acquired cervical insufficiency, decidual hemorrhage, infection, inflammation, and biological variations. To determine the risk of preterm delivery or outcomes of cervical incompetence, a nomogram of cervical length is essential. Ethnicity may affect the length of the cervix, and reference values for each ethnic group should therefore be relevant and reliable. Cervical lengths (CL) of less than 25 mm or 20 mm in previous preterm births and non-history preterm births respectively have been defined as short CL by the American College of Obstetricians and Gynecologists (ACOG)[4].

To the best of our knowledge, only two nomograms of transvaginal cervical length in the Thai population have been reported (in 1997[5] and 2015[6]). The present study was designed to create a new Thai

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nomogram of transvaginal cervical length in a tertiary Thai hospital in Bangkok (Rajavithi Hospital) during gestational age (GA) 16 to 24 weeks.

Material and Method

The present study was undertaken of normal Thai pregnant women who attended for antenatal care at Rajavithi Hospital, Bangkok, Thailand, between May 1st, 2015 and October 31st, 2015. The protocol of this research was reviewed and approved by the ethics committee of Rajavithi Hospital (No. 055/2558), and all participants gave written informed consent. Inclusion criteria were Thai pregnant women with singleton pregnancy without any medical or obstetrical complications or fetal congenital anomalies, whose GA was confirmed by Crown Rump Length (CRL) before GA of 14 weeks. Cervical length (CL) was measured by transvaginal sonography (TVS) during weeks 16 to 24 by the first author, and subjects who had risk factors of incompetent cervix or preterm delivery, history of LEEP[7,8], or history of preterm delivery, were excluded.

Cervical length was obtained at 16 to 24 weeks by transvaginal examination using a 7.5 mHz vaginal probe attached to a Voluson E8 ultrasound platform (GE medical, Kretztechnik GmbH, Austria). Patients lay in the lithotomy position after emptying their bladder. A clean vaginal probe covered by a condom was inserted slowly into the anterior fornix of the vagina until the cervix as well as the echogenic endocervical mucosa along the length of the cervical canal were clearly visualized in the sagittal plane, and the image was then magnified to 50 to 75%. In cases with T- or V-shaped cervix, CL was measured from the internal to external os in linear fashion (Fig. 1), while in cases with curved cervix (Fig. 2), CL could be measured in either of two ways: Distance A if the distance from the apex of the curved cervix drawn perpendicular to the straight line between the internal and external os was less than or equal to 5 mm; or Distance B the linear distance between internal os to the apex of the curved cervix plus the linear distance from the apex of the curved cervix to the external os, and this was used if it was more than 5 mm. A vaginal probe was applied with appropriate pressure on the cervix. A curved cervix is usually long, whereas a short cervix is more often straight. CL was obtained 3 times for each subject, and the shortest measurement was used for analysis. All subjects were examined by a single researcher (WS), and short CL was defined as a cervical length ≤25 mm in every case in the present study.

Sample size was calculated from mean and SD of previous Thai studies of cervical length normative data[5] using the equation $n = \frac{(Z_{\alpha/2})^2 \times (SD)^2}{d^2}$ [9] . The calculated required number in each gestational age was 16 cases using d = 12%. Twenty percent of the total subjects required were added to allow for the possibility of patients being lost to follow-up. The total number of cases needed in each GA was therefore 20 (16 plus 4).

Statistical analysis

Data were analyzed using SPSS software package version 17.0 (SPSS Inc, Chicago, USA) to calculate the mean and 5th, 10th, 90th and 95th percentile values of CL. ANOVA was used to compare CL of nulliparous and multiparous women to detect any between-group differences.

Results

Three hundred and eighty-seven pregnant women were enrolled in the study but only 286 cases

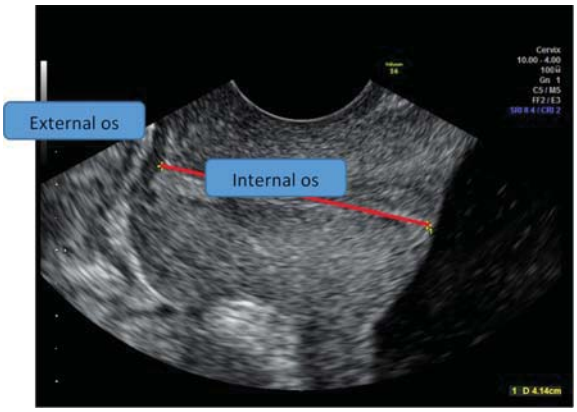

Fig. 1 Ultrasound image of transvaginal cervical length in cases of T or V-shaped cervix.

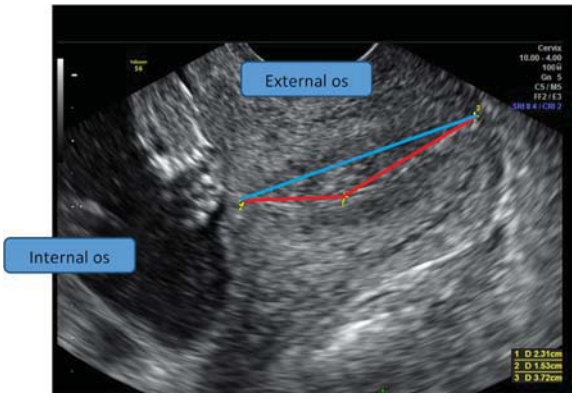

Fig. 2 Ultrasound image of transvaginal cervical length in cases of curved cervix.

(137 nulliparous and 149 multiparous women) were included for analysis. One hundred and one women were excluded (18 had abortions, 56 had not had GA confirmed before 14 weeks, 3 had previous preterm birth; furthermore there were 3 cases of multifetal pregnancies, 3 of myoma uteri, 2 of gestational diabetes mellitus (GDM), 1 of fetal cystic hygroma, and 15 cases did not come to CL TVS examination). Eighty-three patients (29.0%) were lost to follow-up after one CL TVS examination, and the delivery outcomes of these groups are therefore unknown. Delivery of the remaining 203 cases were recorded as follows: 196 term deliveries (96.5%) and 7 preterm deliveries (3.5%). Only the data of the 196 term parturients were analysed (Fig. 3). Their mean age was 29.5 (18 to 43) years and their demographic data are depicted in Table 1. No factors affecting CL were observed, as shown in Table 2.

Cervical length of examined gestational age are presented in Fig. 4. The mid-trimester cervical lengths were quite similar in every examined GA. The mean CL was remarkably constant, averaging 38.70 mm (Fig. 4).

Cervical length (CL) in each gestational age in terms of mean $\pm$ SD, minimum, maximum and percentile are shown in Table 3. The mean CLs of nulliparous women, multiparous women and the overall population were 37.87, 39.46 and 38.70 mm respectively.

Discussion

The nomograms of transvaginal CL in both previous Thai studies in 1997[5] and 2015[6] were quite consistent in every GA, and the mean CL in the early

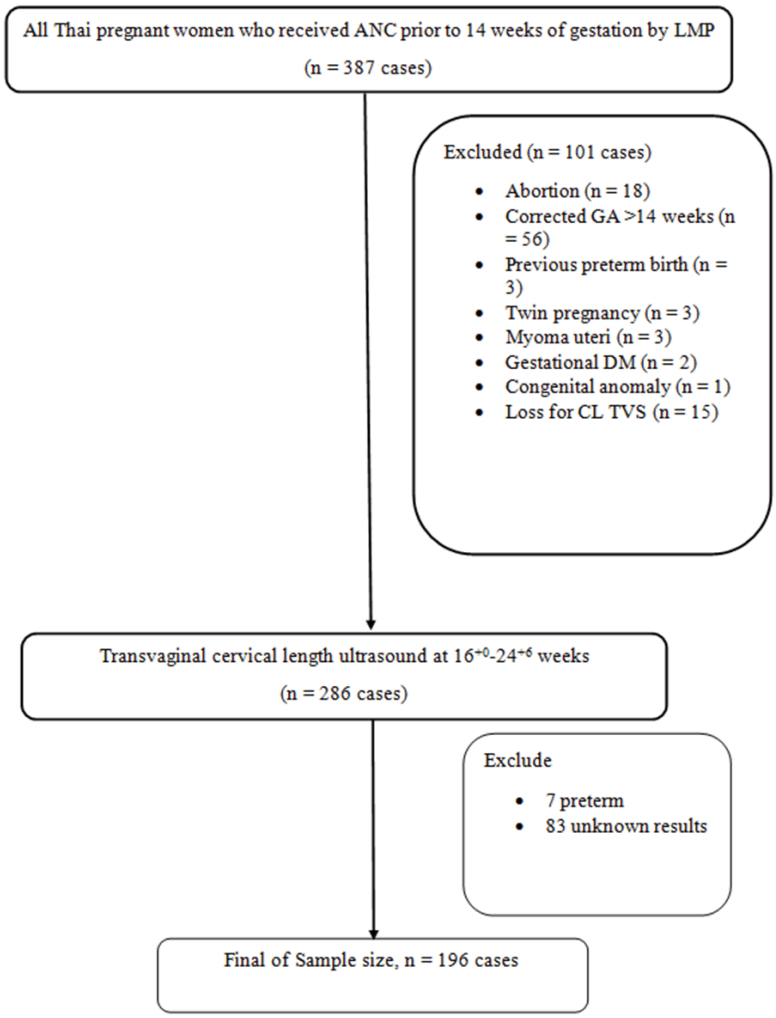

Fig. 3 Diagram of study.

Table 1. Baseline characteristics of the subjects (n = 196 cases)

Characteristics	Number	Percent
Age (years) mean ± SD (min-max)	29.5±6.5 (18 to 43)	
BMI (kg/ m^2) mean±SD (min-max)	22.7±4.3 (14.56 to 36.89)	
Gravidity		
1	71	36.2
2	77	39.3
3	33	16.8
4	15	7.7
Parity		
0	93	47.4
1	69	35.2
2	25	12.8
3	9	4.6
Abortion		
0	159	81.1
1	31	15.8
2	6	3.1
Delivery time		
Term	196	100.0
Route of delivery		
Vaginal delivery	108	55.1
Cesarean section	83	42.3
V/E and F/E	5	2.6
Birth weight (gm) *p*-value = 0.019		
BW ≥2,500	185	94.4
BW <2,500	11	5.6

V/E = vacuum extraction; F/E = forceps extraction

Table 2. Associated factors and cervical length

Factors	n	Mean	SD	95% Confidence Interval for Mean		Minimum	Maximum	*p*-value
Gravidity								0.083
1	132	38.38	6.62	37.24	39.52	22.40	61.70	
2	133	39.34	7.14	38.12	40.57	25.30	60.20	
3	65	40.93	6.95	39.21	42.66	28.30	58.90	
4	22	40.55	6.50	37.67	43.44	26.30	51.60	
Parity								0.006*
0	170	38.38	6.85	37.35	39.42	22.40	61.70	
1	121	39.62	6.95	38.37	40.87	25.30	56.60	
2	46	42.36	6.68	40.37	44.34	29.60	58.90	
3	15	38.91	5.67	35.77	42.05	26.30	45.50	
Abortion								0.986
0	290	39.36	6.77	38.57	40.15	22.40	61.70	
1	52	39.43	8.22	37.15	41.72	26.30	60.20	
2	10	39.03	5.53	35.08	42.98	32.50	49.80	

* = significant difference by ANOVA

and later reports were similar (42.4 and 41mm respectively). Surprisingly, previous studies[10-13], found that CL varied from 35.5 to 38.0 mm, which is similar to CL in the present study (39.35 mm).

Compared with previous Thai studies, CL in the present study was not very different, despite the varying GA ranges (Table 4). The mean CL in the Thai studies of 1997[5], 2015[6], 2016[14] and the present study were 42 mm, 41 mm, 35.66 mm and 38.70 mm, respectively. The mean CLs in Asian studies were 35[15] and 37[12] mm (Table 4). The mean Thai cervical length is around 38.70±6.43 mm which is similar to that of Asian and Caucasian women. The cervical length of Thai subjects in the present study did not vary significantly as gestational age increased (Table 3), and this is in keeping with the results of a previous northern Thai study[5] and with those of foreign reports[15,16].

The mean CL in nulliparous (N), multiparous (M) and the overall (O) population in the present study were significantly different (M>O>N), and this is similar to the results of a previous Thai study in Siriraj Hospital[6] and to the findings of foreign papers[10-13] (Table 4); however, there were not many significant differences between M, O, and N in an older previous Thai study in northern Thailand[5]. Different geographic factors and study periods have been posited as explanations for these variations.

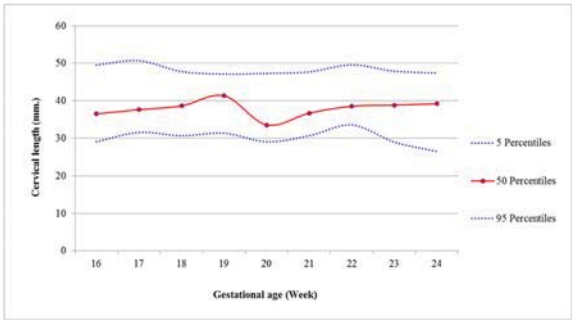

Fig. 4 Cervical length in each gestational age.

Table 3. Normative data of cervical length for each gestational age

GA	n	Mean	SD	Minimum	Maximum	Percentiles				
						5	10	50	90	95
16	20	37.52	5.90	28.80	51.60	29.00	29.40	36.45	45.65	49.55
17	21	39.76	6.21	29.60	51.10	31.50	31.70	37.60	49.10	50.70
18	23	39.00	6.31	26.30	49.80	30.60	31.50	38.60	47.20	47.80
19	21	39.66	5.45	31.20	47.70	31.30	31.40	41.30	45.60	47.10
20	21	36.26	7.14	29.00	53.80	29.00	29.40	33.50	46.30	47.30
21	22	38.26	5.59	28.00	47.80	30.60	33.10	36.65	45.80	47.70
22	23	40.88	6.44	29.60	54.90	33.50	34.00	38.50	49.40	49.60
23	23	38.59	6.80	28.70	54.10	28.90	30.00	38.80	46.90	47.90
24	22	38.11	7.64	22.40	56.50	26.40	29.00	39.15	46.70	47.40
Total	196	38.70	6.43	22.40	56.50	29.00	30.50	38.10	47.50	49.40

(n = number of examination)

Table 4. Comparison of previous transvaginal cervical length measurement and present studies

Studies	Cervical length (mean ± SD)	GA	Operator
Tongsong T 1997[5], Thailand	42.409±.00 mm	14 to 40 weeks	Multiple
Wanitpongpan P 2015[6], Thailand	41.00±11.00 mm	20 to 24 weeks	Multiple
Pattanapanyasat N 2016[14]	35.66 mm	18 to 23 weeks	Multiple
Hebbar S 2006[15], Malaysia	35.40±0.58 mm	20 to 24 weeks	Two staff
Leung TN 2005[12], Hong Kong China	37.90±6.50 mm	18 to 22 weeks	NA
Present study 2016	38.70±6.43 mm	16 to 24 weeks	Single

(NA = not available)

The oretically, significant gestational changes also occur in the cellular compartment of the cervix. Apoptosis of stromal cells was shown to be involved in cervical remodeling in a human study[17]. The number of apoptotic nuclei seen in the laboring cervix is greater than in the nonlaboring one, and it has been suggested that there is an increase in the rate of apoptosis as pregnancy progresses to term. Apoptosis is followed by infiltration of macrophages and neutrophils that add to disorganization and dispersion of the collagen and elastin fibers[17]. Ultrasound findings have shown that multiparous women have lower elasticity than nulliparous women[18], and this may be the cause of long cervical length in the former group. Having had previous abortions did not affect cervical length, and is different from the findings of the study by Health et al[7] in 1998.

The strengths of the present study were: 1) the enrolled gestational age (16 to 24 weeks) included the gestational age (16 to 24 weeks) recommended by the ACOG[4]; 2) there was an adequate calculated sample size; 3) accurate GA was confirmed by CRL before 14 weeks gestation; 4) the study used a single operator (WS); and 5) CLs were examined only once in each case.

A limitation of this study was that only 71% (203) of study cases (286) followed-up until delivery; however, in spite of the time constraints, the sample size was adequate in every GA.

Conclusion

The mean CL of nulliparous women, multiparous women and the overall population were 37.87, 39.46 and 38.70 mm respectively. The mean cervical length of Thai pregnant women whose GA was 16 to 24 weeks was 38.70 mm, and the fifth percentile of cervical length was 29.00 mm.

What is already known on this topic?

Reports of nomograms of Thai cervical length have been published in two previous studies which showed that the Thai mean cervical length was shorter than that of Caucasians. Cervical length did not alter with increasing gestational age, and parity was a factor associated with shorter cervical length (the mean cervical length of multiparous women was greater than that of their nulliparous counterparts).

What this study adds?

The present study created a new nomogram of CL during GA 16-24 weeks. The mean cervical length in this study was similar to those of previous studies, and this nomogram's findings should therefore be used as the normal mean cervical length in Thai pregnant women in GA 16 to 24 weeks.

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Potential conflicts of interest

None.

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