The efficacy of the measurement of cervical length at 18-22 weeks of gestation for the prediction of preterm delivery in low risk asymptomatic pregnancies

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Abstract

Objective: The aim of this study was to determine the relationship between cervical length and gestational weeks and to evaluate the efficacy of the measurement of the cervical length in predicting preterm delivery.

Methods: In this prospective study, we performed cervical length measurement by vaginal ultrasonography at 18 and 22 weeks of gestation in 337 women with asymptomatic singleton pregnancies. The distribution of cervical length was established according to gestational weeks. We then assessed the relation between the length of the cervix and the risk of preterm delivery. Delivery occurring at less than 37th week was referred as preterm delivery.

Results: Preterm delivery (before 37 weeks) occurred in 25 pregnancies (7.4%). The mean cervical length in the preterm group was 33.2±5.7 mm while it was 37.8±4.8 mm in the term group, and the difference was statistically significant (p<0.001). It was found that cervical length did not change significantly between 18th and 22nd weeks of gestation in cases resulted with term delivery, and the 5th, 50th and 95th percentile values of cervical length were 30, 38 and 46 mm respectively. The area under the receiver-operating characteristics curve (ROC) was 0.74 (95% CI: 0.62-0.85) for the prediction of preterm delivery (p<0.001). The values of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and OR for the prediction of preterm delivery at 18-22 gestational weeks cervical length ≤30 mm were (5th percentile) 36.6%, 92.6%, 28.1%, 94.8 and 7.1 (95% CI: 2.8-17.8), respectively.

Conclusion: Cervical length measurement is considered to be a useful method for preterm delivery prediction in asymptomatic patients.

Key words: Cervical length, preterm delivery, cut off.

Düşük riskli asemptomatik gebeliklerde 18-22. gebelik haftaları arasında servikal uzunluk ölçümünün preterm doğum öngörüsündeki değeri

Amaç: Çalışmamızda, servikal uzunluğun gebelik haftası ile olan ilişkisini ve preterm doğumu öngörmedeki değerini belirlemeyi amaçladık.

Yöntem: Bu prospektif çalışmada; 18-22. gebelik haftaları arasında, 337 asemptomatik tekil gebeliğin transvajinal ultrasonografi ile servikal uzunluk ölçümü yapıldı. Servikal uzunluğun gebelik haftasına göre dağılımı çıkarıldı. Servikal uzunluk ile preterm doğum arasındaki ilişki değerlendirildi. Preterm doğum sınırı olarak 37 hafta alındı.

Bulgular: Yirmi beş gebelik preterm doğumla (<37 hafta) sonuçlandı (%7.4). Preterm doğum yapan gebelerde ortalama servikal uzunluk 33.2±5.7 mm, term doğum yapanlarda da 37.8±4.8 mm bulundu ve aradaki fark istatistiksel olararak anlamlıydı (p<0.001). Term doğum ile sonuçlanan olgularda 18-22 gebelik haftaları arasında servikal uzunluğun değişmediği saptandı ve servikal uzunluğun 5, 50 ve 95. persentil değerleri sırasıyla 30, 38 ve 46 mm bulundu. 18-22 gebelik haftaları arasında servikal uzunluğun, preterm doğumu öngörmedeki değerini araştırdığımızda; ROC (alıcı çalışma karakteristiği) eğrisi altındaki alan 0.74 (%95 CI: 0.62-0.85; p<0.001) ve ≤30 mm (5. persentil) servikal uzunluk için %36.6 duyarlılık ve %92.6 özgüllük, %28.1 pozitif prediktif değer (PPD), %94.8 negatif prediktif değer (NPD) ve göreceli olasılık oranı (OR) 7.1 (%95 CI: 2.8-17.8) tespit edildi.

Sonuç: Asemptomatik gebelerde preterm doğumu öngörmede servikal uzunluk ölçümünün faydalı olacağı düşünülmektedir.

Anahtar sözcükler: Servikal uzunluk, preterm doğum, eşik değer.

deomed.

Introduction

Preterm delivery (PTD) is defined as the delivery occurred before 37th week of gestation. Although its prevalence varies according to societies, it is between 5 and 13%. Preterm delivery is the most significant reason of perinatal mortality and morbidity today. It would be an appropriate approach to determine risk factors for decreasing preterm delivery rates, and to predict the preterm delivery diagnosis.[1-3] It has been reported that risk scoring systems, digital examination of cervix, analysis of cervix by ultrasonography and various biochemical reagents can be used to predict preterm delivery beforehand.

Evaluation of cervical length (CL) can be done transabdominally, transperineally and transvaginally. However, the most preferred and suggested method is to measure cervical length by ultrasonography. Cervical length is 25-70 mm, and width of endocervical canal is 2-4 mm during pregnancy.[2] The period between 18th and 24th week of gestation is recommended for the measurement of cervical length. Many studies reported that the shortest cervical length measured between these weeks is associated with PTD. It is difficult to distinguish cervix and sub-segment before 14-16t weeks of gestation, and measurement of cervical length should be done after this period since it causes faulty measurement. Also, it has been reported that there was no significant difference between cervical lengths measured before 14th week of gestation, and significant cervical changes occurred after this period in pregnant women who had preterm and term delivery.[4,5] On the other hand, Greco et al. reported in their study that cervical length could be measured between 11 and 14 weeks of gestation, and short cervix was associated with early PTD.[6]

In our study, we aimed to determine the relationship between cervical length and gestational week and to predict preterm delivery in this way by measuring cervical length via transvaginal ultrasonography between 18 and 22 weeks of gestation.

Method

In this study, we aimed to investigate the relationship between gestational week & PTD with cervical length measured in asymptomatic pregnant women who admitted to our clinic between 01.08.2009 and 01.02.2011 and were at low risk in terms of preterm delivery. Study protocol was established for this research and required approval was obtained from Ethics Committee of Clinical Researches. All patients were informed and their written consents were received.

Our study group was consisting 337 women with singleton pregnancy at 18-22 weeks of gestation. Gestational week was based on last menstrual period (LMP), or for those who did not know their LMP, crown-rump length at first trimester or biparietal diameter at second trimester. Women with preterm delivery history, previous cervical failure, undergone cervical circlage, or pregnant women with preterm contractions, those with placenta praevia, or structural or karyotype anomalies at fetus, having preeclampsia or eclampsia, those below 18 years old, and those with systemic disease, uterine mullerian anomaly or uterus myomas were all excluded from the study. Preterm delivery limit was considered as 37 weeks.

Ultrasonographic measurements were done by a single specialist with transvaginal approach (7 MHz) by Toshiba Xario ultrasound device. Also, by transabdominal approach, biometric evaluations of fetus together with detailed fetal structures were analyzed. The probe was proceeded within vagina by transvaginal ultrasonography, and sagittal image of cervix was obtained by taking care not to pressure on cervix. Cervical measurements were done at a view as covering 3/4 of the screen and where internal os, external os, cervical canal and endocervical mucosa can be viewed at the same time. When the length between internal os and external os cannot be measured on a straight line due to the curved cervix, measurements taken as linear sections were summed up and cervical length was calculated. Measurements were performed three times on each pregnant woman and the shortest one with the best image quality was recorded.

Statistical methods

Patient data was analyzed by SPSS 20 package program (SPSS Inc., Chicago, IL, USA). Descriptive analyses (mean, standard deviation, standard error and percentile distribution) were done. Parameters were tested by Kolmogorov-Smirnov test to check whether they were within normal range. Statistical analyses were carried out by using *independent samples* T test to compare parameters within normal range, and Mann-Whitney U test to compare parameters not within nor-

mal ranges. One-way Anova test was used to compare cervical lengths according to gestational weeks. Homogeneity of variants was evaluated by Levene test. Also, the impact of cervical length measurements for predicting preterm delivery was evaluated by ROC curve analysis. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and relative odds ratio (OR) of threshold values were calculated. P<0.05 was considered statistically significant.

Results

Our study included 337 pregnant women complying with research criteria. Totally 312 pregnancies resulted at or above 37 weeks, and 25 pregnancies resulted below 37 weeks. Preterm delivery rate was found to be 7.4%. Also, ten of preterm deliveries were at or below 34 weeks. Early preterm delivery rate was found to be 3%. There was no difference between pregnancies resulting in term delivery and pregnancies resulting in preterm delivery in terms of maternal age, gravid, parity, abortus and gestational week in which evaluation was performed. While mean cervix length was 37.8±4.8 mm of term delivery group, it was 33.2±5.7 mm in preterm delivery group (p<0.001). Other definitive characteristics of the groups are given in **Table 1.**

In cases resulted in term delivery, mean cervix lengths for each week between 18 and 22 weeks of gestation were 37.9±4.9, 37.8±5.2, 38±5.1, 37.4±4, 37.6±4.4 and 37.8±4.8 mm, respectively; and it was found that CL measurements did not change significantly according to gestational weeks (p=0.98). **Table 2** shows CL distributions according to gestational weeks. Also, percentile distribution of CL between 18 and 22 weeks of gestation is shown at **Table 3.** Cervical length was found to be 30 mm, 38 mm and 46 mm for 5th percentile, 50th percentile and 95th percentile, respectively. In terms of the relationship between cervical length and parity, mean CL was 36.5±4.2 mm in nullipara pregnancies, 37.5±4.3 mm in primipara pregnancies, and 39.2±5.8 mm in multipara pregnancies; and it was found that there was a significant difference among them.

Considering the significance of cervical length between 18 and 22 weeks of gestation for predicting PTD, the field below ROC curve was found to be 0.74 (95% CI: 0.62-0.85, p<0.001). So, measuring cervical length between 18th and 22nd weeks of gestation was

Table 1. Definitive characteristics of term and preterm delivery cases.

|	Term delivery cases (n=312)	Preterm delivery (n=25)	p
Maternal age	30.7±6	29.3±5.9	0.27
Gestational week	19.6±1.4	19.4±1.4	0.1
Gravida	2.5±1.5	2.0±1.1	0.067
Parity	1.1±1.5	0.8±0.9	0.141
Abortus	0.3±0.5	0.2±0.5	0.257
Cervical length (mm)	37.8±4.8	33.2±5.7	0.000
Delivery week	38.9±1.1	34±2.3	0.000
Newborn weight (g)	3319.0±465.9	2468.8±688.4	0.000

Table 2. Cervical length (mm) measurements in term delivery cases according to gestational week at 95% CI.

Gestational week	Case Number	Mean	Shortest	Longest
18	97	37.9±4.9	25	52
19	77	37.8±5.2	26	57
20	52	38±5.1	26	56
21	39	37.4±4.0	29	46
22	47	37.6±4.4	28	51
Total	312	37.8±4.8	25	57

Table 3. Percentile distribution of cervical length between 18th and 22nd weeks of gestation.

Percentile	3rd	5th	10th	25th	50th	75th	95th
Cervical length (mm)	29	30	32	35	38	40	46

found to be a useful scanning method for predicting PTD. The sensitivity was 32% and the specificity was 96.2% for ≤29 mm CL (3rd percentile); the sensitivity
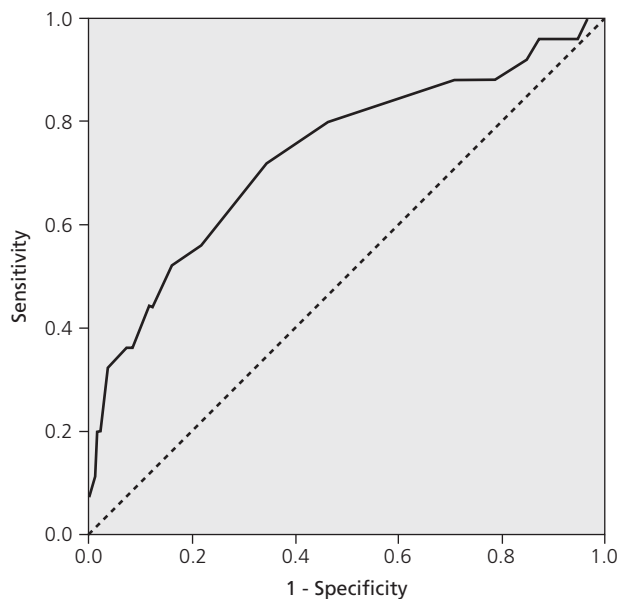
Fig. 1. The ROC curve of the prediction of cervical length for preterm delivery.

was 36.6% and the specificity was 92.6% for ≤30 mm CL (5th percentile); and the sensitivity was 44% and the specificity was 88.1% for ≤32 mm CL (10th percentile). Predictivity of ROC curve and CL to predict PTD has been given in **Fig. 1** and **Table 4.**

Discussion

Preterm delivery is the most significant reason for neonatal mortality and morbidity. Predicting and preventing preterm delivery and its complications are one of the most critical missions of obstetrics. Today, many studies have reported that evaluating cervix by transvaginal ultrasonography may be helpful for predicting PTD.

PTD was found in 7.4% of pregnancies in our study, and mean CL was found to be 37.8±4.8 mm in pregnancies resulted in term delivery and it was 33.2±5.7 mm in pregnancies resulted in preterm delivery. In cases resulted in term delivery, mean CL between 18 and 22 weeks of gestation was found to be 37.9±4.9, 37.8±5.2, 38±5.1, 37.4±4, 37.6±4.4 and 37.8±4.8 mm, respectively, and it was found that cervical length did not change significantly according to gestational weeks. Also, percentile distribution of cervical length between 18th and 22nd weeks of gestation was found to be 30 mm at 5th percentile, 38 mm at 50th percentile and 46 mm at 95th percentile. Gramellini et al. reported in their study where they measured CL by TV USG on 321 pregnants (185 nullipara and 136 multipara cases) that cervical length decreased by gestational week (r2=085, p<0.01).[7] Qu et al. conducted a study on 5277 pregnants and reported that mean CL significantly decreased with gestational week and it was 38.8±4.0 mm between 22 and 24 weeks of gestation, and 34.6±4.8 mm between 28 and 32 weeks of gestation.[8] Also Liabsuetrakul et al. reported that CL was decreased with gestational week between 24 and 34 weeks of gestation.[9] In our study,

Table 4. The impact of cervical length measured between 18th and 22nd weeks of gestation for predicting preterm delivery.

Threshold cervical length (mm)	Sensitivity	Specificity	PPV	NPV	OR (95% CI)
≤29 (3rd percentile)	32	96.2	40	94.6	11.8 (4.3-32.6)
≤30 (5th percentile)	36	92.6	28.1	94.8	7.1 (2.8-17.8)
≤32 (10th percentile)	44	88.1	22.9	95.2	5.8 (2.5-13.8)

NPV: negative predictive value, **OR:** odds ratio, **PPV:** positive predictive value.

CL did not change significantly with gestational week and we consider the reason that gestational week range is very narrow compared to other studies.

In terms of the relationship between cervical length and parity, mean CL was found to be 36.5±4.2 mm in nullipara pregnancies, 37.5±4.3 mm in primipara pregnancies and 39.2±5.8 mm in multipara pregnancies (p<0.05). While Gramellini et al.[7] reported that there was no relationship between CL and parity, Liabsuetrakul et al.[9] reported that CL was significantly longer in multipara cases. Iams et al. found that mean CL at 24th week of gestation was 34.0±7.8 mm nullipara cases, 36.1±8.4 mm in multipara cases while mean CL at 28th week of gestation was 32.6±8.1 mm in nullipara cases and 34.5±8.7 mm in multipara cases. They reported that this difference was statistically significant; however, it did not have any clinical significance.[10]

Considering the significance of cervical length between 18 and 22 weeks of gestation for predicting PTD, field under ROC curve was found to be 0.74 (95% CI: 0.62-0.85, p<0.001). The sensitivity was 32% and the specificity was 96.2% for ≤29 mm CL (3rd percentile); the sensitivity was 36.6% and the specificity was 92.6% for ≤30 mm CL (5th percentile); and the sensitivity was 44% and the specificity was 88.1% for ≤32 mm CL (10th percentile). Çelik et al. researched the relationship between CL and PTD on 58,807 singleton pregnancies at 20+0-24+6 weeks of gestation, and found the field under ROC curve for predicting delivery as 0.90, 0.82, 0.78 and 0.62, respectively before 28th week, at 28-30, 31-33, and 34-36 weeks of

gestation. They showed that CL measurement is a useful scanning method for predicting especially early PTD cases. They also reported that 5% false-positivity value of CL had 66% sensitivity for predicting delivery before 28th week of gestation, 40.1% sensitivity for predicting delivery at 28-30 weeks of gestation, 32.6% sensitivity for predicting delivery at 31-33 weeks of gestation, and 12.7% sensitivity for predicting delivery at 34-36 weeks of gestation.[3]

Iams et al. found threshold values by CL measurements at 24th and 28th weeks in 2915 singleton pregnants with low risk. When threshold value was accepted as 30 mm at 24th week of gestation, sensitivity was 54%, specificity was 76.3%, PPV was 9.3% and NPV was 97.4% for predicting deliveries before 35th gestational week, and when threshold value was accepted as 30 mm at 28th week of gestation, sensitivity was 69.9%, specificity was 68.5%, PPV was 7% and NPV was 98.5%.[10] Barber et al. performed a study where they measured CL on 2351 pregnant women between 18 and 22 weeks of gestation, and similar to our study, they reported that threshold CL had low sensitivity and high specificity for predicting preterm delivery (<37 weeks). They reported sensitivity as 26% and specificity as 98% for 3rd percentile, sensitivity as 34% and specificity as 97% for 5th percentile, and sensitivity as 39% and specificity as 92% for 10th percentile (**Table 5**). They also reported that CL measurement would be helpful for PTD risk in asymptomatic pregnants during routine fetal examination between 18th and 22nd weeks of gestation.[11]

Table 5. Comparison of studies researching the impact of transvaginal CL in asymptomatic pregnancies with low risk for predicting preterm delivery.

Studies	Case number	USG (GW)	Result (GW)	Threshold value (mm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Current study	337	18-22	<37	≤30	36	92.6	28.1	94.8
Tongsong et al.[12]	730	28-30	<37	<35	65.9	62.4	19.4	92.8
Iams et al.[10]	2915	24	<35	≤30	54	76.3	9.3	97.4
		24	<35	≤25	37.3	92.2	17.8	97
	2531	28	<35	≤30	69.9	68.5	7	98.5
		28	<35	≤25	49.4	86.8	11.3	98
Fukami et al.[13]	3030	16-19	22-31	≤30	50	98.5	8.3	99.9
			32-36	≤30	18.2	98.9	33.3	97.6
Pires et al.[14]	338	21-24	<37	<20	18	98.1	40	94.8
			<35	<20	27.3	97.9	30	97.6
Barber et al.[10]	2351	18-22	<37	<30	39	92	31	94
Qu et al.[8]	5277	22-24	<37	<30	3	99	19	96

GW: gestational week, NPV: negative predictive value, PPV: positive predictive value, USG: ultrasonography.

In the study performed by Qu et al., it was shown that CL threshold value below 30 mm had 3% sensitivity and 99% specificity for predicting PTD between 22nd and 24th weeks of gestation. Also, it was found that OR was 5.2 if CL was lower than 30 mm for PTD, 11.1 mm if CL was lower than 25 mm, and 13.8 mm if CL was lower than 15 mm.[8] In Turkey, Özdemir et al. conducted a study on 79 singleton pregnant women between 20 and 24 weeks of gestation, and when 27 mm was threshold value, they found sensitivity as 77.8%, specificity as 100%, PPV as 100%, NPV as 97% and OR as 33.5 for PTD prediction.[15] The sensitivity and specificity values of the study seem quite high, which may be caused by insufficient number of cases. Hibbard et al. measured cervical lengths of 760 pregnant women between 16 and 22 weeks of gestation and found CL as 30 mm at 10th percentile, 27 mm at 5th percentile, and 22 mm at 2.5 percentile. They reported relative risks of cervical length for deliveries before 37th week of gestation as 3.8 for 10th percentile, 5.4 for 5th percentile, and 6.3 for 2.5 percentile.[16] Barber et al. presented ORs of 3rd, 5th and 10th percentile values of cervical length for PTD as 25.47 (95% CI: 15.5-41.73); 16.98 (95% CI: 11.51-25.05) and 7.55 (95% CI: 5.44-10.5), respectively. In our study, OR values were found to be lower for PTD, as 11.8 (95% CI: 4.3-32.6) for 3rd percentile, 7.1 (95% CI: 2.8-17.8) for 5th percentile, and 5.8 (95% CI: 2.5-13.8) for 10th percentile.[11]

Conclusion

Consequently, transvaginal cervical length measurement is a useful method for PTD scanning in asymptomatic pregnancies with low risk. It has been reported that cervical length has a high specificity for predicting preterm delivery and the value of ≤30 mm can be used as threshold.

Conflicts of Interest: No conflicts declared.

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