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Original Research

Anterior Uterocervical Angle and Prediction of Preterm Labor in Cases with an Inconclusive Cervical Length: A Prospective Cohort Pilot Study

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Abstract

Background: Cervical length measurement is still the most widely used method to predict preterm labor. Recent studies have reported that in addition to cervical length, uterocervical angle (UCA) may also be useful in predicting preterm labor. The main purpose of this study was to evaluate the use of the anterior UCA to predict preterm labor in symptomatic pregnant women with a cervical length of 20 to 30 mm. **Methods**: In this prospective cohort study, 48 patients with a cervical length of 20 to 30 mm who applied to the emergency department with any preterm labor symptoms, between September 2019 and February 2020, were included as the study group. Cervical length and anterior UCA were measured at the first admission. Of these 48 patients, 12 patients who gave birth before 37 weeks were called the 'preterm labor group', and 36 patients who gave birth at 37 weeks or later were named the 'preterm threatened but delivered at term' group. The control group consisted of 46 healthy pregnant women who were matched with the study group in terms of age, body mass index (BMI), and the gestational week at which anterior UCA was measured. The three groups were compared in terms of anterior UCA values. **Results**: The cervical lengths of the 'preterm labor' and 'preterm threatened but delivery at term' groups were similar and shorter than the control group (25.4 mm, 25.1 mm, and 35 mm, respectively, $p < 0.001$). Anterior UCA value in the 'preterm labor' group (116.1) was found to be significantly higher than both 'preterm threatened but delivered at the term' group (100.2) and the control group (98.6) ($p = 0.001$). Receiver operating curve (ROC) analysis was performed to determine a threshold value of anterior UCA that could predict preterm labor in symptomatic pregnant women with a cervical length of 20 to 30 mm. Area under curve (AUC) analysis of anterior UCA for estimation of preterm labor was 0.647 ($p = 0.014$, 95% confidence interval (CI) = 0.52–0.77). According to this analysis, the threshold value of anterior UCA was determined as 95.3, with 72% sensitivity, and 63% specificity. **Conclusion**: The anterior UCA can be used to better predict preterm labor in symptomatic pregnant women with a cervical length of 20 to 30 mm without cervical effacement and dilation.

Keywords: cervical length; preterm birth; preterm labor; uterocervical angle

1. Introduction

Preterm labor is defined as the presence of uterine contractions of sufficient strength and frequency for the progressive dilation and effacement of the cervix between the 20th and 37th weeks of pregnancy, while deliveries occurring before 37 weeks of gestation are called preterm birth [1]. Preterm birth, which is the biggest contributor to neonatal morbidity and mortality, is reported to be responsible for 70% of neonatal deaths [2]. In most cases, less than 10% of pregnant women diagnosed with preterm labor give birth within the following 7 days, so it is still a challenge for obstetricians to distinguish which unexpected preterm labor will lead to preterm delivery [3].

Considering the neonatal problems and health expenditures brought by preterm births, many inflammatory markers, proteins, or hormones have been investigated in the prediction of preterm birth, but they are not cost-effective enough for daily routine use [4]. When the studies carried out to date are evaluated, it is seen that the most reliable method for estimating the risk of preterm birth is still the measurement of cervical length by transvaginal ultrasonography [5]. It has been stated that fetal fibronectin, which is the most studied biomarker in the prediction of preterm delivery, is not more effective than cervical length alone, and more randomized controlled studies are needed to recommend its use in combination with cervical length in routine [4–6].

According to meta-analyses, pregnant women with a cervix length less than 20 mm measured by transvaginal sonography are at high risk for the possibility of giving birth before 34 weeks, and a measurement over 30 mm has been reported as low risk [7]. There is uncertainty in terms of the

risk of preterm delivery in pregnant women with a cervical length of 20 to 30 mm, and repeated cervical length measurements are required in these cases. A reduction of more than 10% in the cervical length of these pregnant women within three weeks has been associated with an increased risk of preterm birth [8].

Another tool investigated in terms of preterm birth prediction is the anterior uterocervical angle (UCA) measurement. It has been shown by many studies that the risk of preterm birth increases in patients with an anterior UCA of 105 and above, measured by transvaginal ultrasonography in the second trimester [9–12]. In another study, it was determined that the combined use of maternal history, cervical length, and anterior UCA could predict approximately 40% of preterm births [10]. In a study by Lynch *et al*. [11], a final UCA of 105 degrees and above measured before 25 weeks of gestation in asymptomatic women with a cervical length less than 2.5 cm was associated with an increased risk of preterm birth before 34 weeks of gestation.

In this study, we aimed to determine the use of anterior UCA measurement in predicting preterm labor in symptomatic pregnant women with a cervical length of 20 to 30 mm but without cervical effacement and dilatation.

2. Materials and Methods

This prospective cohort study was conducted with 94 pregnant women who applied to the Umraniye Training and Research Hospital, Department of Obstetrics and Gynecology, between September 2019 and February 2020, and had their pregnancy follow-up and delivery in our hospital. The study group consisted of 48 pregnant women who applied to the obstetrics and gynecology emergency outpatient clinic with preterm labor symptoms before 37 weeks of gestation, with a cervical length between 20 to 30 mm, but without cervical dilatation or effacement. The control group consisted of 46 healthy pregnant women who applied to the antenatal outpatient clinic for routine pregnancy follow-up. The control group was formed by matching with the study group in terms of age and body mass index (BMI) and gestational week at which anterior UCA was measured.

Afterward, the study group was divided into two groups according to their weeks of delivery. 12 pregnant women who gave birth before 37 weeks of gestation were defined as the ‘preterm labor group’ and 36 pregnant women who gave birth at or after 37 weeks were defined as the ‘preterm threatened but delivered at term group’. As the primary outcome, the preterm labor group, preterm threatened but delivered at term group, and control group were compared in terms of anterior UCA.

Inclusion criteria of the study group:

• Those between the ages of 18–41 years, with a singleton pregnancy between 24 and 36 weeks of gestation;

• Those who do not have cervical effacement or dilation and whose cervical length measured by transvaginal ultrasonography is between 20 to 30 mm;

• Those with painful uterine contractions lasting 30 seconds, which can be demonstrated by cardiotocography 4 times in 20 minutes or 6 times in 60 minutes;

• Those who did not receive any progesterone treatment due to cervical shortness or those who did not use any tocolytic treatment for contractions.

Exclusion criteria of the study group:

• Those who have been diagnosed with cervical insufficiency or have a history of preterm labor or cervical operation (loop electrosurgical excision procedure or conization) or congenital uterine anomaly;

• Those with multiple pregnancies or conditions complicating pregnancy such as intrauterine growth retardation, polyhydramnios, oligohydramnios, premature rupture of membranes, placental abruption, placenta previa, hypertensive disorders, diabetes mellitus, gestational diabetes, known fetal anomaly or any other maternal systemic or autoimmune diseases.

In the pregnancy follow-up protocol of our clinic, routine cervical length or anterior uterine-cervical angle measurement is not performed in healthy pregnancies if there is no history of preterm labor or risk factor for preterm birth. The control group consisted of pregnant women who did not have a history of preterm labor and did not have preterm labor symptoms. The pregnant women included in the control group were selected from the healthy singleton pregnant women who came to the routine follow-ups. After routine examination and fetal biometric measurements, pregnant women who met the inclusion criteria were given detailed information about the study protocol. Cervical lengths and anterior UCA were measured after obtaining written consent from the pregnant women who voluntarily agreed to participate in this study.

Inclusion criteria of the control group:

• Those with a single pregnancy between the ages of 18–41 years who had their pregnancy follow-up and delivery in our clinic;

• Those who did not show any sign of preterm labor during the pregnancy and gave birth at term;

• Those who do not have any pregestational or gestational disease.

Exclusion criteria of the control group:

• Those with multiple pregnancies or conditions complicating pregnancy such as intrauterine growth retardation, polyhydramnios, oligohydramnios, premature rupture of membranes, placental abruption, placenta previa, hypertensive disorders, diabetes mellitus, gestational diabetes, known fetal anomaly or any other maternal systemic or autoimmune diseases.

After the participants were informed about the study and their consent was obtained, cervical length and anterior UCA measurements were made. Sonographic evaluation of all participants was performed by a single experienced perinatologist with the transvaginal probe of the Hitachi Pro sound F37 trademark ultrasound device (Guangzhou Rongtao Medical Technology Co., Ltd., Guangzhou, Guang-

dong, China). The cervical length measurement of the participants was done in accordance with the recommendations of American College of Obstetricians and Gynecologists (ACOG) [13]. For the anterior UCA measurement, in the same sagittal section, the first line of the angle was drawn along the endocervical canal between the internal os and the external os, the second line was drawn along the anterior uterine lower segment, and the angle between these two lines was measured.

Statistical Analysis

Power analysis of the study was performed using the G*Power (v3.1.9.2, Heinrich-Heine-Universitat, Dusseldorf, Germany) program to determine sample sizes [14]. The power of the study is expressed as 1-β (β = Type II error probability) and has 80% power. Assuming that the effect size (d = 0.598) will be observed according to the effect size coefficients determined by Cohen [15], it was determined that the required number of patients should be 92 (46 for the study group, and 46 for the control group). Although we calculated the minimum number of participants by power analysis at the beginning of the study, we included 50 participants in each group, considering that there might be dropouts. After the dropouts, there were 48 participants in the study group, and 46 participants in the control group, with a final design study of 94 participants.

Statistical analysis was performed with Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM Corp., Chicago, IL, USA). The normal distribution of the variables was evaluated using the Kolmogorov-Smirnoff test. The homogeneity of variances between groups was evaluated with Levene's test. Comparisons between groups in terms of demographic features and sonographic measurements were evaluated by One-Way ANOVA and Chi-square test. The post-Hoc test was used to determine the difference obtained in the comparison of more than two groups. The *p*-value was interpreted by making Bonferroni and Tamhane's T2 corrections. Statistical significance was accepted at $p < 0.05$ for all values. The significance of UCA between the three groups was tested with the Kruskal-Wallis test, and the Mann-Whitney U test was used to determine the difference obtained in the comparison of more than two groups. Receiver operating curve (ROC) was used to determine the effectiveness of anterior UCA in predicting preterm labor and to determine the significant threshold value.

3. Results

There was no significant difference between the three groups in terms of maternal age, BMI, smoking, and obstetric history ($p > 0.05$, for each). The average gestational week at which anterior UCA was measured was 29.1 in the 'preterm labor group', while the 'preterm threatened but delivered at term group' was 31.5 and 31.4 in the control group ($p = 0.039$). As expected, the gestational age and birth weight of the 'preterm labor group' were significantly lower than the other two groups ($p < 0.001$, $p < 0.001$, respectively) (Table 1).

The mean cervical lengths of the 'preterm labor' and 'the preterm threatened but delivered at term' groups were similar and significantly shorter than the control group (25.4 mm, 25.1 mm, and 35.1 mm, respectively, $p < 0.001$). The anterior UCA value in the 'preterm labor group' (116.1) was found to be significantly higher than both 'preterm threatened but delivered at term' (100.2) and the control groups (98.6) ($p = 0.001$) (Table 2).

ROC analysis was performed to determine a threshold value of anterior UCA that could predict preterm labor in symptomatic pregnant women with a cervical length of 20 to 30 mm. Area under curve (AUC) analysis of anterior UCA for estimation of preterm labor was 0.647 ($p = 0.014$, 95% confidence interval (CI) = 0.52–0.77). According to this analysis, the threshold value of anterior UCA was determined as 95.3 with 72% sensitivity and 63% specificity (Fig. 1).

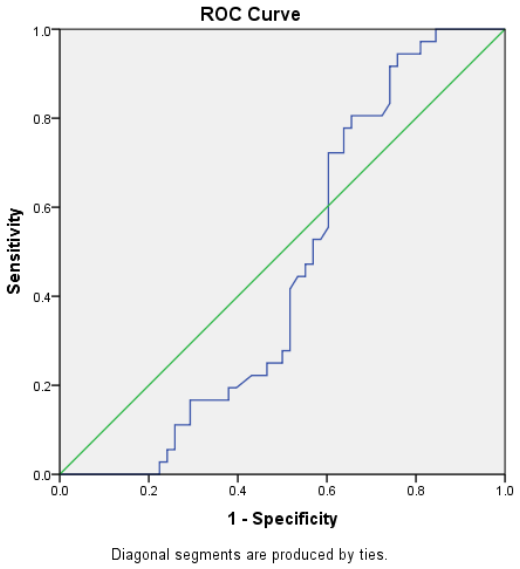

Fig. 1. ROC analysis of anterior UCA to predict preterm delivery in symptomatic pregnant women with a cervical length of 20 to 30 mm. ROC, receiver operating curve; UCA, uterocervical angle.

Of the 12 pregnant women in the 'preterm labor group', 4 (33.3%) were delivered vaginally, and 8 (66.7%) were delivered by cesarean section. Of the 36 pregnant women in the 'preterm threatened but delivered at term group', 24 (66.7%) were delivered vaginally, and 12 (33.3%) were delivered by cesarean section. Of the 46 pregnant women in the control group, 25 (54.3%) were delivered vaginally, and 21 (45.7%) were delivered by cesarean section.

Table 1. Demographic characteristics of the three groups.

	Preterm labor group (n = 12)	Preterm threatened but delivered at term group (n = 36)	Control group (n = 46)	Total (n = 94)	*p*-value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
	n (%)	n (%)	n (%)	n (%)	
Age (years)	27 ± 6.9	27 ± 5.3	28.7 ± 4.8	27.8 ± 5.3	0.290*
BMI (kg/m^2)	27.4 ± 5	27.9 ± 5.4	28 ± 3.4	27.9 ± 4.4	0.889*
Smoking	1 (0.8)	4 (1)	4 (0.8)	9 (0.9)	0.760**
Gravida	2.8 ± 2	2.1 ± 1.2	2.3 ± 1.4	2.3 ± 1.4	0.427*
Number of previous curettages	4 (33)	10 (27)	8 (17)	22 (23)	0.544**
Number of previous cesarean sections	4 (25)	8 (22)	17 (36)	29 (30)	0.351**
Gestational age at which anterior UCA measured (week)	29.1 ± 4.7^{ab}	31.5 ± 3.5	31.4 ± 1.2	31.1 ± 2.9	**0.039***
Gestational age at birth (week)	32.5 ± 2.8^{ab}	37.8 ± 1.6	37.8 ± 2.1	37.1 ± 2.7	**<0.001***
Birth weight (kg)	2170 ± 648^{ab}	3172 ± 387	3075 ± 438	2997 ± 549	**<0.001***

* One-Way ANOVA; ** Chi-square test; BMI, body mass index; UCA, uterocervical angle; SD, standard deviation.

Groups were compared by One-Way ANOVA, followed by post-Hoc analyses for two group pairwise comparisons with the Bonferroni correction for multiple testing. Bold, statistically significant.

[a] Represents a comparison between the 'preterm labor group' and the 'preterm threatened but delivered at term group', $p < 0.05$.

[b] Represents a comparison between the 'preterm labor group' and the control group, $p < 0.05$.

Table 2. Comparison of ultrasonographic measurements of the three groups.

	Preterm labor group (n = 12)	Preterm threatened but delivered at term group (n = 36)	Control group (n = 46)	Total (n = 94)	*p*-value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Anterior uterocervical angle	116.1 ± 12.2^{ab}	100.2 ± 8.1	98.6 ± 24.2	101.5 ± 18.9	**0.001**
Cervical length (mm)	25.4 ± 2.1^{b}	25.1 ± 2.5^{c}	35.1 ± 7.2	30 ± 7.3	**<0.001**

Groups were compared by One-Way ANOVA and Kruskal-Wallis, followed by post-Hoc analyses and the Mann-Whitney U test for two group pairwise comparisons with the Bonferroni correction for multiple testing. Bold, statistically significant.

[a] Represents a comparison between the 'preterm labor group' and 'preterm threatened but delivered at term group', $p < 0.05$.

[b] Represents a comparison between the 'preterm labor group' and the control group, $p < 0.05$.

[c] Represents a comparison between the 'preterm threatened but delivered at term group' and the control group, $p < 0.05$.

4. Discussion

In this study, we determined that anterior UCA was significantly higher in the preterm labor group in symptomatic pregnant women with a cervical length of 20 to 30 mm compared to both 'preterm threatened but delivered at term group' and the control group.

Cervical length and fetal fibronectin measurements are still the most frequently used and reliable tools in the evaluation of preterm birth diagnosis [16]. The sensitivity of fetal fibronectin is low, special laboratory tests are required for its quantitative measurement, and it may not be possible to reach these resources in every clinic [17]. Cervical length measurement, on the other hand, is a non-invasive, inexpensive, reliable, and reproducible method and is still the most widely used tool for preterm birth prediction [1]. It was observed that when the cervical length cut-off value is taken as 20 mm, it can predict the probability of giving birth within 7 days with 75% probability and 79% sensitivity [18]. The main challenge is the uncertainty about the pregnant group with a cervical length of 20 to 30 mm, which requires repeated cervical length measurements in follow-up. In repeated cervical length measurements, a shortening of more than 10% of the cervical length at 3-week intervals was found to be associated with an increased risk of preterm birth [8]. However, the fact that 3 weeks is a long time, and repetitive transvaginal measurements increase the burden on both patients and the health system has led to the need to question the use of other methods in predicting preterm birth.

In addition to shortened cervical length, changes in the uterine cervical angle have also been associated with preterm delivery. A wide UCA is thought to be associated with a more direct, linear outlet of uterine contents to

the cervix. However, the narrower UCA resulting in a less direct force on the internal cervical os is more protective against cervical effacement and dilatation [19,20].

According to a study, UCA measurement was found to be more reliable than cervical length measurement in terms of intra and interobserver differences [21]. Although we only included singleton pregnancies in this study, it has been proven that UCA is as effective in twin pregnancies as in singleton pregnancies in the prediction of preterm birth [12]. It has been shown that UCA can be measured via transabdominal ultrasound after micturition, just as in cervical length measurement, in patients who are not willing to undergo transvaginal examination [22].

In a study conducted on 972 women, it was shown that measuring the cervical length of 25 mm or less was successful in predicting preterm labor with a sensitivity of 63% and a false-negative rate of 97%. In the same study, anterior UCA of 105 degrees and above was found to be associated with preterm birth, and it was shown that a value of 105 degrees and above could predict preterm birth with a sensitivity of 81% and a false-negative rate of 99% [9].

In a different study published in 2020, cervical length and UCA were evaluated in terms of prediction of preterm birth in pregnant women who were in the risk group for preterm birth. A UCA of 105 degrees and above predicted preterm delivery, with a sensitivity of 86.1% and a specificity of 60.4%, while a cervical length of 25 mm or less predicted preterm delivery with a sensitivity of 27.8% and a specificity of 85.8%. The authors emphasize that a UCA greater than 105 degrees provides a high diagnostic performance in predicting preterm birth in high-risk patients compared to cervical length measurement [23].

Singh *et al*. [24] evaluated UCA measured by transvaginal sonography at 16 to 24 weeks of gestation in terms of the prediction of spontaneous preterm birth. Spontaneous preterm labor risk was found to be higher in pregnant women whose UCA was measured above 95 degrees (86.7% sensitivity, 93.0% specificity, 83.0% positive predictive value, 94.6% negative predictive value, $p < 0.001$). The UCA $\geq$105 degrees and 95 to 105 degrees were found to be significantly associated with spontaneous preterm births at $<$34 weeks and 34 to 37 weeks, respectively [24].

Another study, published in 2021, evaluated the diagnostic performance of UCA alone and UCA together with cervical length in predicting preterm labor in pregnant women with the threat of preterm labor. While the sensitivity and specificity of the UCA of 110.9 degrees and above in predicting preterm birth were 65.1% and 43.6%, the sensitivity and specificity of UCA of 110.9 degrees and above together with a cervical length shorter than 34 mm were 48.8% and 68.4%. The authors stated that UCA measurement can be used together with cervical length to increase diagnostic performance in predicting preterm birth [25].

The main problem of the studies in the literature about UCA measurement is the heterogeneity of the patient groups and the cut-off values of UCA [26]. Similar to the studies mentioned above, we also showed that wide anterior UCA is associated with preterm birth in this study. We found that a 95.3 degree anterior UCA can predict preterm labor with 72% sensitivity and 63% specificity in symptomatic pregnant women with a cervical length of 20 to 30 mm.

To the best of our knowledge, this is the first study in the literature examining the use of anterior UCA in the prediction of preterm labor in symptomatic patients with a cervix of 20 to 30 mm. The low number of participants was the limitation of this study since we included a very specific patient group to avoid heterogeneity in the study.

5. Conclusion

In conclusion, we think that anterior UCA can be combined with cervical length to better assess the risk of preterm delivery. It should be noted that the patient population of our study is too small to draw a firm conclusion and the results need to be confirmed by studies with larger patient groups.

Availability of Data and Materials

Data supporting the findings of this study are available in the OSF data repository (https://www.covgen.org/osf-home) with DOI identifier 10.17605/OSF.IO/VS4ZY.

Author Contributions

İE and RNB designed the research study. İE and EAD were responsible for the examination of the patients participating in the study and data collection. İK and MD were responsible for data interpretation and statistical analysis. İK was responsible for the writing and MD was responsible for the language editing of the manuscript. EAD was responsible for the creation of tables and figures. RNB was responsible for the supervision and the final version of the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The Local Ethics Committee of Umraniye Training and Research Hospital, Istanbul, Turkey has approved this study (Ethics Committee Approval No: B.10.1.TKH.4.34.H.G.P.0.01/187). The study protocol was maintained in accordance with the Declaration of Helsinki, and informed consent was obtained from all the participants.

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Conflict of Interest

The authors declare no conflict of interest.

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