



PREDICTION OF SPONTANEOUS PRETERM BIRTH USING ANTERIOR CERVICAL ANGLE-A PROSPECTIVE STUDY

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ABSTRACT

Background: Identifying women 'at risk' for preterm labour remains a major challenge as the current screening modalities have a prediction rate of only 55 – 69 %. Novel screening tool is the transvaginal measurement of Anterior cervical angle(ACA).

Methods: This is a prospective cohort study carried out on 674 pregnant women with singleton pregnancies between 18 to 23 weeks of gestation at Amrita Institute of Medical Sciences, Kochi from June 2017 till May 2019. Transvaginal sonography was done to measure the cervical length(CL) and ACA.

Results: out of 674 pregnancies 96 had spontaneous preterm labour, accounting to 14 % incidence. A wide ACA 108.8 at 18 – 23 weeks of pregnancy, predicted increased risk of spontaneous preterm delivery with a sensitivity of 78 %, specificity of 77.7 %, p value of < 0.001. Cervical length of 2.9 cms performed better than Anterior cervical angle in the present study. ACA failed to predict the risk of spontaneous preterm labour in Multiparous women.

Conclusion: Based on our results and analysis, a wider Anterior cervical angle (108.8) has significant association with increased risk of preterm labour. Among Cervical length & ACA, CL of 2.9 cms showed superior results as a predictor of spontaneous preterm labour in the present study. There is a need for revision of the cut off for cervical length as 2.5 cms (10th percentile) did not show a better prediction than 2.9 cms in our study population. However, larger multicentre studies are needed to prove it.

KEYWORDS : Preterm labour, Anterior cervical angle (ACA), Cervical length (CL), transvaginal ultrasonography, NICU admissions, Multiparous

INTRODUCTION:

Preterm birth at < 37 weeks of pregnancy accounts for 75 % of neonatal deaths and 50 % long term morbidity world wide. ^[1] Incidence of preterm birth in India is as high as 12.9 % in 2010 and tops the list among all countries. ^[2] As per WHO estimates in November 2016, out of 27 million babies born each year, 3.3 million babies are born premature. ^[3] Spontaneous preterm labour (sPTL) accounts for 40 - 50 % of these cases. Hence prediction of spontaneous preterm labour must be carried out prudently in all pregnant women.

Identifying the women at risk for preterm labour is a major challenge. Until now, a previous history of spontaneous preterm birth (SPTB) and a short cervix (CL < 25mm on Transvaginal Ultrasonography (TVU)) were the best screening tools to identify these at-risk women. These can identify only 55 % to 69 % of spontaneous preterm labour. ^[4] Hence development of new predictive strategies for spontaneous preterm births (SPTB) is necessary. As pregnancy advances, the force of the pregnant uterus is shifted to the cervix causing the cervical angle to be either closed (acute inclination) or open (obtuse inclination). These Pelvic angles can be visualized and measured during TVU examination performed in second trimester of pregnancy and are being quoted as a novel marker in predicting preterm delivery.

Our objective is to evaluate whether this Anterior cervical angle can predict risk of SPTL in singletons pregnancies and to evaluate the performance of cervical length in comparison with Anterior cervical angle in prediction of spontaneous preterm labour.

METHODS:

Selection Process & Study Design:

After getting approval from Institutional Ethics committee, this prospective cohort study was carried out on 674 pregnant women with singleton pregnancies, attending the Department of Obstetrics & Gynaecology as a part of Antenatal visit between 18 to 23 weeks of gestation at Amrita Institute of Medical Sciences, Kochi from June 2017 till September 2019. Women who did not consent for Transvaginal ultrasonography, multifetal pregnancy, polyhydramnios, fetus with growth abnormalities / congenital anomalies, medically or surgically indicated preterm births and women with cervical cerclage were excluded from the study.

sensitivity of Anterior cervical angle in predicting spontaneous preterm birth < 37 weeks is found to be 80 %. With 20 % allowable error and 95 % confidence interval, the minimum sample size comes to 20. We have included 96 cases. This gives the estimate with 99 % confidence and only 10 % allowable error.

Technical information:

Transvaginal Ultrasonography of cervix - Informed consent was obtained from all participants. After emptying bladder, a 4 - 8 MHz transvaginal transducer was placed in the anterior vaginal fornix and a sagittal section of the cervix is obtained following the Perinatal Quality Foundation guidelines 2015 with a field of view of cervix occupying 75 % of the image. Anterior and posterior cervical width and echogenicity was similar for both portions. External os is identified as a small triangular area at the inferior portion of cervical canal. Cervical canal is visualized as a linear echogenicity between the interface of anterior & posterior walls of cervix. Cervical length is measured with a straight line caliper drawn from the internal to the external os (Line 1). Another straight line from the internal os to the inner wall of anterior myometrium of lower uterine segment is drawn (Line 2). Angle between the two lines is taken as Anterior cervical angle. Offline measurement of ACA was done on stored images. [FIGURE1]

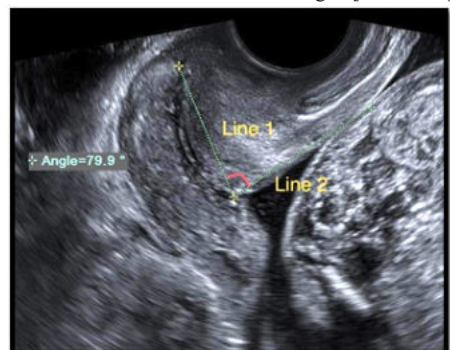


Figure1: Measurement Of Anterior Cervical Angle And Cervical Length In Transvaginal Sonography

Pregnancies were followed up till delivery. Maternal demographic

Based on previously published article by Dziadosz et al (2016) ^[5], the

data, scan findings (ACA & CL), gestational age at birth & mode of delivery, birthweight, sex of the infant and adverse perinatal outcomes in terms of NICU admissions, duration of NICU stay, short term neonatal complications were obtained from the hospital's electronic medical records, Labour registers as well as through telephonic conversation and entered in Microsoft Excel.

Statistics:

Data collected from 674 samples were analysed statistically using IBM SPSS Statistics version 20.0 software. All the measurable variables were presented as Mean ± Standard Deviation (SD) and all the categorical variables were presented as in percentage. Univariate analysis of categorical variables were analysed by Chi square test and continuous variables by Student's t test.

Receiver Operating characteristic curve was used to find the optimal cut off of ACA and CX length for predicting spontaneous preterm birth. Statistical significance of the correlation between Anterior cervical angle and cervical length in Term & Preterm births was studied by computing Correlation co-efficient. Multivariate logistic regression was applied to find the significant independent risk factors for Preterm delivery. p value < 0.05 was considered as statistically significant.

RESULTS:

During the study period, 1000 screening transvaginal sonographies were performed between 18-23 weeks of gestation. Of these, 176 cases were delivered preterm due to medical/obstetric indications and 150 cases did not have perinatal follow-up. Hence, 326 cases were excluded from the study. On analysis of the remaining 674 cases, 96 cases (14%) had spontaneous preterm delivery (< 37 weeks of gestation) and 578 cases had a term delivery (>= 37 weeks).

Influence of Demographic details on Outcome:

A significant difference in the socioeconomic status, parity index between both groups were noticed with higher incidence of preterm labour in low socioeconomic group, nulliparous women, diabetes complicating pregnancy & in multiparous women with prior preterm labour.

Anterior Cervical Angle & Preterm Labour:

The Mean Anterior cervical angle in those women who delivered preterm was found to be 117.7 and in those women who delivered term was 95.2. This difference is statistically significant with p value of < 0.001.

Receiver Operating Characteristic Curves (ROC) were generated to evaluate the validity parameters of ACA. When women who delivered preterm (< 37 weeks) were compared to term (> 37 weeks), the area under the curves was 0.835 (p < 0.001; 95 % confidence interval(CI) 0.792 – 0.877). A point was chosen on the ROC curve corresponding with ACA of 108.8, for optimal sensitivity (78.1%), Specificity of 77.1 %; Positive predictive value [PPV] 36.8 %, Negative predictive value [NPV] 95.5%]. [TABLE 1].

Table 1: ROC & Validity Parameters For ANTERIOR CERVICAL ANGLE (ACA) & CERVIX LENGTH (CL)

Parameter	Area under curve	Value	Sensitivity	Specificity	Positive Predictive value	Negative predictive value	p value
ACA (°)	0.835	108.85	78.1%	77.7 %	36.8 %	95.5 %	< 0.001
CL (mm)	0.996	29	94.8%	97%	84.3%	99.1%	0.017

In this study population, 204 women had ACA > 108.8, of which 75 women (36.8%) had a preterm delivery, while of 470 women with ACA < 108.8, only 21 (4.4 %) delivered preterm. (p value < 0.001) [FIGURE 2].

There was a significant negative correlation of Anterior cervical angle and gestational age at delivery in women who delivered preterm. No correlation between ACA & gestational age at delivery was noted in term group. No statistically significant correlation exists between ACA and Birth weight at delivery in either of the groups. [TABLE 3]

Table 2: Anterior Cervical Angle Of 108.8 And Correlation With Gestational Age At Delivery & Birth Weight.

Group	Variable	ACA	
		r - value	p - value
Preterm	Gestational age at delivery	-0.235	0.021

	Birth weight	-0.060	0.564
Term	Gestational age at delivery	-0.010	0.809
	Birth weight	-0.058	0.162

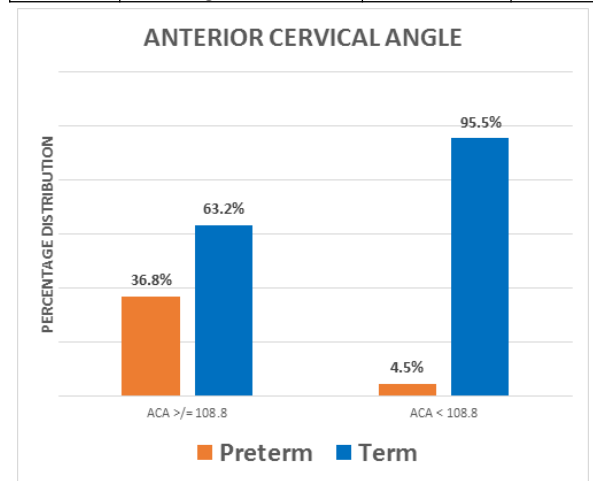


Figure 2: Distribution Of Cases With Anterior Cervical Angle Of 108.8 In The Present Study

Cervical length & Preterm Labour:

The mean cervical length in women who delivered preterm was found to be 2.4 cms & those who delivered at term was 3.4 cms. The difference is statistically significant. (p value < 0.001).

Receiver Operating Characteristic Curve (ROC) was generated to evaluate the validity parameters for Cervical length in our study population. When women who delivered preterm were compared to term, the area under the curves was 0.996 (p value: 0.017; 95 % CI, 0.993 - 0.999) for a cut off of 2.9 cms with the sensitivity of 94.8%, specificity of 97 %; Positive predictive value [PPV] 84.3 %, Negative predictive value [NPV] 99.1%]. [TABLE 1]

In this study population, 91 women had CL 2.9 cms, of which 74 women (81%) had preterm delivery, while of 583 women with CL > 2.9 cms, only 22 (3.8 %) delivered preterm. (p value: 0.017).

Multivariate analysis of risk factors for preterm labour:

A multivariate analysis of the risk factors was performed by Logistic regression revealed that ACA and CL are the only two independent risk factors with statistical significance for occurrence of Spontaneous preterm labour nullifying the effect of confounding factors like Parity, socioeconomic status & diabetes complicating pregnancy. Patients with ACA 108.8 had 11.29 times higher risk of preterm labor than ACA < 108.8 and CL 2.9 cms shows 543.35 times high risk of preterm labour than CL > 2.9 cms. [TABLE 3]

Table 3: multivariate Analysis Of Risk Factors In Our Study Population

Variables	Odds Ratio	95% Confidence interval	p value
ACA 108.8	11.93	4.036 - 35.285	< 0.001
CL 2.9 cms	543.35	166.012 - 1778.416	< 0.001
Parity – Nullipara	1.36	0.453 - 4.111	0.581
Socioeconomic status – Low	2.53	0.668 - 9.575	0.972
Diabetes in pregnancy	1.08	0.161 - 7.310	0.934

Multivariate analysis of the confounding risk factors in multiparous women revealed that history of prior preterm labour & CL were the only two independent risk factors with statistical significance for occurrence of spontaneous preterm labour. ACA 108.8 was not statistically significant (p value: 0.381) in the multiparous group.

Perinatal outcomes:

Mean gestational age at delivery in preterm group was 35 weeks, as compared to 38 weeks 6 days, in women who delivered Term. This was statistically significant (p value < 0.001). Out of the 96 preterm deliveries, the majority of 66 cases (68.8 %) delivered between 35 - 36 weeks of gestation. The lower and upper limit of gestational age at delivery in the preterm group was 24 weeks and 36 weeks 6 days respectively.

There was a slightly higher rate of Caesarean to vaginal deliveries in Preterm (14.6 %) & Term (13.8%) groups, however the difference was statistically insignificant. There was a statistically significant difference in the mean birth weight in preterm and term groups (2.43 kg and 3.02 kg). Out of 96 babies born preterm, 58 babies (60%) had low birth weight of < 2.5 Kg. Sex ratio of Female to male babies remained statistically insignificant in both preterm and term groups.

DISCUSSION:

In our study, after excluding confounding factors like maternal age, BMI and Gestational age at scan, an incidence of 14 % of preterm labour was noted. However, the difference in parity, socioeconomic factors, prior preterm labour, diabetes complicating pregnancy remained statistically significant. But, multivariate analysis showed that only significant confounding factor among these risk factors is the prior history of preterm labour in multiparous women.

Similar association between history of Prior preterm labour and preterm delivery in current pregnancy was noted in study by Sur et al with a statistically significance (p value < 0.001, OR 3.15, 95 % confidence interval 1.957-0.0693) and Dziadosz et al (2016)^[5] with a statistical significance of p value 0.005.

ACA & relationship with preterm delivery:

ROC curve was made to ascertain the cut off of ACA and was chosen to be 108.8 for a AUC: 0.835, p value < 0.001, 95 % confidence interval of 0.792 – 0.877, sensitivity of 78 %, specificity of 77.7%, positive predictive value of 36.8% and negative predictive value of 95.5 %.

The cut off of ACA taken by Sur et al (2017), was obtained by calculating Mean anterior cervical angle as 127.66 for Preterm delivery < 37 weeks with p value 0.004, 95 % CI 4.6329-194.2615, sensitivity of 80 %, specificity of 88.23 %.^[6] The cut off of ACA taken by Dziadosz et al (2016), was obtained by making an ROC. The cut off of anterior cervical angle was taken as 95 for preterm delivery < 37 weeks with p value < 0.001, sensitivity of 80 %, specificity of 53 %, positive predictive value 14 %, negative predictive value 95%.^[5] The cut off of ACA taken by Farras Llobet et al (2017), was obtained by calculating Mean anterior cervical angle as 105.16 for Preterm delivery < 37 weeks with p value 0.015, 95 %.^[7] On analysing the validity parameters of previous studies, there is significant differences at the gestational age at scan in second trimester ranging from 14 weeks till 25 weeks. This could possibly be the factor responsible for differences in Cut off ACA in all studies.

Sur et al (2017) found significant differences in Mean ACA between preterm (< 37 weeks) & term groups in first trimester (114.2 Vs 93) and in second trimester (127.6 Vs 103.6).^[5] Similar results were reported by Farras Llobet et al (2017) suggesting the angle during second trimester was wider in women who delivered preterm (< 34 weeks) as compared to those who delivered term (105.1 Vs 94.53).^[6] Sepulveda et al had also confirmed that pregnant women with wide ACA are prone to deliver preterm (< 34 weeks) compared to term (106.1 Vs 99.5).^[8] In our study, this relationship of wider ACA in second trimester was confirmed as women who delivered preterm (< 37 weeks) had an ACA 117.7 Vs 95.2 in the term group.

ACA & cervical length:

Sepulveda et al studied that ACA was independent of CL measurements and could be used as a combined screening test when including Maternal age, H/o Prior preterm labour, CL expressed in MoM (Multiple of Median) & ACA expressed as z score), with detection rate of 37.6 % with fixed false positivity of 10 %.^[9] Similar results of independency of ACA & CL was found in our study. However, the predictive model for combined testing of ACA and CL did not reveal a significant difference when measured separately.

Our study showed that measurement of cervical length of 2.9 cms was superior for predicting the occurrence of spontaneous preterm labour (< 37 weeks) as compared to Anterior cervical angle in our study population. Similar comparison was performed by Dziadosz et al (2016) and stated that ACA of > 95 performed well compared to CL 2.5 cms as a screening tool, in regards to higher sensitivity & negative predictive value. They concluded that combination of ACA and CL measurements may be the best predictor of preterm labour in their population.^[5] [TABLE 4]

Strengths:

Study was performed in a large cohort of singleton pregnancies with a

Preterm labour, which is a well-defined outcome. It was a prospective study done with real-time Transvaginal sonography with no selection bias unlike other studies which did measurements of previously stored images after knowing the outcome. Multivariate analysis of confounding risk factors like Prior Preterm birth, Parity, Socio-economic status, Diabetes in pregnancy was studied.

Limitation:

We evaluated ACA at 1 point during the pregnancy between 18 – 23 weeks. It is unknown whether serial evaluation of ACA would correlate more strongly with the risk of preterm delivery.

CONCLUSION:

The aim of the present study was an attempt made to study the Anterior cervical angle measured at 18 – 23 weeks by transvaginal sonography for predicting spontaneous preterm labour (< 37 weeks) in singleton pregnancies. Based on our results and analysis, a wider Anterior cervical angle (108.8) has significant association with increased risk of preterm labour. Among Cervical length & ACA, CL of 2.9 cms showed superior results as a predictor of spontaneous preterm labour in the present study. There is a need for revision of the cut off for cervical length as 2.5 cms (10th percentile) did not show a better prediction than 2.9 cms in our study population. However, larger multicentre studies are needed to prove it.

SUMMARY:

Wider Anterior cervical angle (108.8) has significant association with increased risk of preterm labour. Among Cervical length & ACA, CL of 2.9 cms showed superior results as a predictor of spontaneous preterm labour in the present study. There is a need for revision of the cut off for cervical length as 2.5 cms (10th percentile) did not show a better prediction than 2.9 cms in our study population. However, larger multicentre studies are needed to prove it.

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