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Assessment of utero-cervical angle as an ultrasound screening tool to predict spontaneous preterm birth in singleton pregnancy

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***Abstract*---**Introduction: Several attempts have been made from healthcare professionals around the world to determine the effective methods for early prediction and prevention of preterm birth. Aim of Work: The aim of this study was to determine the predictive value for spontaneous preterm birth by using transvaginal ultrasonography of the uterocervical angle (UCA) in pregnant women with singleton pregnancy. Subjects and methods: This study was a prospective Case-control study that was conducted at Obstetrics and Gynecology Department at Al-Zahraa University Hospital and Kafr Elshiekh General Hospital. Results:Utero Cervical angle (UCA) was significantly increased in preterm group>95 degree compared to control group (p< 0.001). Also, CL was significantly decreased in preterm group less than 27mm compared to control group .By using ROC-curve analysis, UC can predict preterm birth with accuracy (75.4%). The sensitivity, specificity, PPV and NPV was 70%, 76%, 74.47% and 71.7% respectively (p< 0.001). CL can predict preterm birth with accuracy (66%). The sensitivity, specificity, PPV and NPV was 74%, 62%, 66.07% and 70.45% respectively (p= 0.003). Conclusion: Ultrasonographic measurement of uterocervical angle performed in routine vaginal ultrasound during second trimester is a useful strategy in the prediction of preterm birth in pregnancies and better than cervical length alone. In our research, a multivariate model combining uterocervical angle (UCA) and cervical length(CL) have a

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high predictive value to estimate the risk of extreme preterm birth in pregnancies.

Keywords---Utero-cervical Angle, Ultrasound Screening Tool, Spontaneous Preterm Birth ; Singleton Pregnancy.

Introduction

Preterm birth (PTB), is any birth before the completion of the 37 weeks of gestation, is one of the leading causes of perinatal and neonatal morbidity and mortality worldwide **[1].**

Preterm birth is estimated to complicate approximately 10-12% of pregnancies **[2].**
Although the etiology is thought to be multifactorial, the events leading to preterm birth are still not completely understood. **[3].**

In singleton pregnancies, utero-cervical angle (UCA) has shown promise as an alternative ultrasonographic tool for the prediction of sPTB(spontaneous Preterm Birth) **[4].**

This measurement evaluates the angle between the cervix and the lower uterine segment. The widening of this angle represent a flattening between the uterus and the cervix and an increased risk for sPTB. Consistent with this hypothesis, there is data that a narrower angle is associated with a decreased risk for sPTB **[5].**

Method

Patients and Methods

This study was a prospective Case-control study that was conducted at Obstetrics and Gynecology Department at Al-Zahraa University Hospital And Kafr Elshiekh General Hospital. For 100 pregnant women were included who had been attended the Hospitals. Patients were subdivided into two groups; **Group I**: 50 pregnant women with history of preterm birth (preterm group). **Group II**: 50 pregnant women with no history of preterm birth (controlgroup).

Inclusion Criteria for study group: Pregnant women age between 18 to 40 years, singleton pregnancies, prior history of preterm birth, no major malformations and women who was secheduled for an ultrasound from 30wk until time of labour

Exclusion Criteria for groups: Medically indicated preterm birth, structural or chromosomal fetal anomalies, multiple pregnancies, pregnancies conceived by assisted reproductive technology, women with vaginal bleeding, fetal heart rate abnormalities, women with cervical cerclage and women in labor at admission

Methods: Patients were subjected to:

Complete history taking: Personal history including: Name, Age, marital state, address, menstrual history: including age of Menarche, menstrual disturbance, dysmenorrhea, related symptoms, parity and Present history: of chronic diseases and medication, past history of HTN, DM, obstetric history and surgical history of operation, laparoscopic interference, treatment of hirsutism by Laser.

Examination: General examination: Vital signs (Blood pressure, Temperature, Heart rate, Respiratory rate) and signs of (Pallor, Cyanosis, Jaundice, and Lymph node enlargement). Abdominal and local clinical examination: Abdominal inspection, abdominal palpation, abdominal percussion and abdominal auscultation

Investigation: Abdominal ultrasonographic examinations performed by one investigator using a 3.5- 5-MHz transabdominal probe Fetal biometry, presentation, well-being(biophysical profile) and amniotic fluid volume will assessed by transabdominal ultrasonography by measurements in centimeters of the deepest pool of AF devoid of fetal part or umbilical cord were taken at each of these quadrants

- The values summed to give the AFI.

Vaginal ultrasonographic examination: A 5-9 MHz transvaginal probe was used. After voiding, transvaginal scan was performed to measure the cervical length The UCA is the triangular segment that measured between the lower uterine segment and the cervical canal, yielding a measurable angle.

- The first ray placed from the internal os to the external os.
- The calipers placed where the anterior and posterior walls of the cervix touch the internal and external os along the endocervical canal.

when cervix curved, the first ray also drawn from the internal os to the external os as a straight line.

- A second ray drawn to delineate the lower uterine segment.
- This ray traced up the anterior uterine segment to a distance allowed by the preloaded image.
- The anterior angle in between the two rays measured with a protractor. In the presence of funneling
- the first ray placed to measure the length of remaining cervix.
- The second caliper placed from the innermost portion of measurable cervix and extend to the lower uterine segment..

The angle measured twice first at 30 wk gestation then at 32wk of gestation.
Follow-up till delivery for occurrence of preterm or term delivery

Ethical Consideration: Study protocol had been submitted for approval by Institutional Review Board, Al-Azhar University. Informed verbal consent had been obtained from each participant sharing in the study. Confidentiality and personal privacy had been respected in all levels of the study.

Statistical analysis : IBM SPSS-22 program (Inc, Chicago, IL, USA) has been used to preform statistical analysis. Data have been examined for normal distribution via the Shapiro Walk testing. Qualitative data have been presented as frequency and relative percentage. Chi square testing (x2) has been utilized to determine change among 2 or more groups of qualitative variables. Quantitative data have been presented as mean ± SD (Standard deviation). Nondependent sample t-testing has been utilized in comparing among 2 nondependent groups of normal distribution variables (parametric data) &Mann-Whitney testing. P value < 0.05 was judged significant. ROC-curve was built to permit choice of threshold values for testing findings and comparisons of various testing approaches. Areas under ROC curves and their standard errors have been calculated via the technique of Cantor, and matched via the normal distribution, with correction for association of notes resulting from the same cases. AUC of ROC shows: 0.90 – 1 = excellent, 0.80-0.90 = good, 0.70-0.80 = fair; 0.60-0.70 = poor; and 0.50-0.6 = fail. The optimal cut-off point has been recognized at point of maximum accurateness.

Results

The mother age in preterm group ranged from 26 to 38 years with mean ±SD= 32.6± 3.7 years while the in control group the mother age ranged from 26 to 38 years with mean ±SD= 32.3± 3.5 years with no statistical significant difference (p=0.557) between the two groups. Likewise, there was no statistically significant difference between the two groups regarding weight (p=0.918), height (p=0.987) and BMI (p=0.906). (Table 1)

Table (1)
Comparison between the two groups regarding demographic characteristics

		Group I (Preterm group) (n = 50)		Group II (Control group) (n = 50)		Test value	P-value
		N	%	n	%		
Age (years)	Mean± SD	32.6± 3.7		32.3± 3.5		^{Z}MWU= 0.56	0.557
	Median (IQR)	33.0 (30.0- 36.0)		33.0 (30.0- 35.0)			
	Range	26.0- 38.0		26.0- 38.0			
Weight (Kg)	Mean± SD	81.7± 10.3		81.8± 10.5		^{Z}MWU= 0.104	0.918
	Median (IQR)	80.5 (72.0- 92.0)		79.0 (72.0- 92.0)			
	Range	67.0 – 98.0		68.0 – 98.0			
Height (cm)	Mean± SD	168.7± 6.6		168.7± 5.5		T= 0.016	0.987
	Median (IQR)	168.5 (163.0- 174.0)		168.0 (165.0- 173.0)			
	Range	158.0 – 180.0		158.0 – 180.0			
BMI (Kg/m^2)	Mean± SD	28.9± 4.6		28.8± 3.8		T=0.119	0.906
	Median	28.0 (25.3- 31.3)		28.7 (26.0- 31.5)			
	Range	21.6 – 38.9		22.1 – 36.4			

p≤0.05 is considered statistically significant, p≤0.01 is considered high statistically significant,

There was no statistically significant difference between women who delivered preterm (group I) and control group regarding prior dilation and curettage (p=0.171) and prior cervical conization (p=0.617). Likewise, there was no statistically significant difference between the two groups regarding prior cervical LEEP (p=0.790) and abnormal pap smear (p=0.499). Table (2)

Table (2)
Comparison between the two groups regarding prior intervention

		Group I (Preterm group) (n = 50)		Group II (Control group) (n = 50)		Test value	P-value
		n	%	n	%		
Prior dilation and curettage	No	40	80.0%	34	68.0%	X^2= 1.871	0.171
	Yes	10	20.0%	16	32.0%		
Prior cervical conization	No	49	98.0%	47	94.0%	X^2= 1.042	0.617 FET
	Yes	1	2.0%	3	6.0%		
Prior cervical LEEP	No	42	84.0%	41	82.0%	X^2= 0.071	0.790
	Yes	8	16.0%	9	18.0%		
Abnormal pap smear	No	38	76.0%	35	70.0%	X^2= 0.457	0.499
	Yes	12	24.0%	15	30.0%		

p≤0.05 is considered statistically significant, p≤0.01 is considered high statistically significant,
-comparison between groups done by Pearson Chi-Square test and Fischer- Exact test (FET)

It was noticed that NICU admission was significantly increased in preterm group compared to control group (p<0.001). Concerning female fetus, there was no statistically significant difference between the both groups (p= 0.689). (Table 3)

Table (3)
Comparison between the two groups regarding neonatal characteristics

		Group I (Preterm group) (n = 50)		Group II (Control group) (n = 50)		Test value	P-value
		N	%	n	%		
Female Fetus	No	27	54.0%	25	50.0%	X^2= 0.160	0.689
	Yes	23	46.0%	25	50.0%		
NICU admission	No	11	22.0%	29	58.0%	X^2= 13.5	<0.001
	Yes	39	78.0%	21	42.0%		

p≤0.05 is considered statistically significant, p≤0.01 is considered high statistically significant,

-comparison between groups done by Pearson Chi-Square test
UC angle was significantly increased in preterm group compared to control group (p< 0.001). Also, CL was significantly decreased in preterm group compared to control group (p= 0.015). (Table 4)

Table (4)
Comparison between the two groups regarding UC and CL

		Group I (Preterm group) (n = 50)		Group II (Control group) (n = 50)		Test value	P-value
		N	%	n	%		
UC	Mean± SD	120.0± 27.4		93.1± 26.3		T= 5.014	<0.001
	Median (IQR)	120.5 (104.0- 140.0)		94.5 (78.0- 107.0)			
	Range	68.0 – 173.0		31.0 – 159.0			
CL	Mean± SD	27.0± 7.0		40.0± 7.1		T= 2.471	0.015
	Median (IQR)	26 (23.0- 30.0)		41.5 (36.0- 45.0)			
	Range	20.0 – 34.0		22.0 – 52.0			

p≤0.05 is considered statistically significant, p≤0.01 is considered high statistically significant,

By using ROC-curve analysis, UC can predict preterm birth with accuracy (75.4%). The sensitivity, specificity, PPV and NPV was 70%, 76%, 74.47% and 71.7% respectively (p< 0.001). (Table 5, Figure (1))

Table (5)
Validity of UCA in prediction of preterm birth

UC	
Cutoff value	≥95
AUC (95% CI)	0.754 (0.658 - 0.834)
Sensitivity	70.0%
Specificity	76.0%
PPV	74.47
NPV	71.70
Accuracy	75.4 %
P value	<0.001

PPV= Positive Predictive Value, NPV= Negative Predictive Value, AUC= Area Under Curve

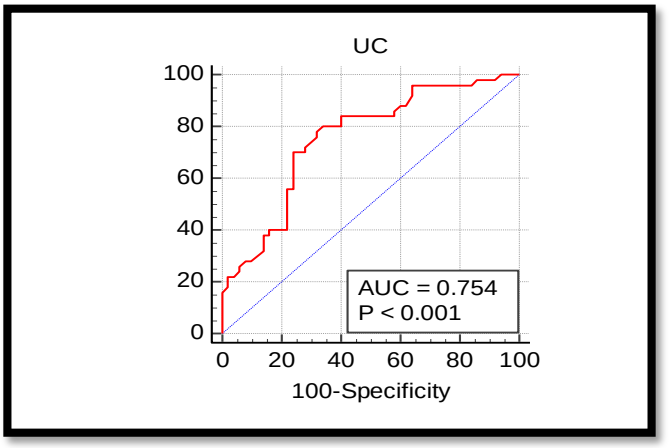

Figure (1): ROC curve of UC in prediction of preterm birth.

By using ROC-curve analysis, CL can predict preterm birth with accuracy (66%). The sensitivity, specificity, PPV and NPV was 74%, 62%, 66.07% and 70.45% respectively (p= 0.003). (Table 6, Figure (2))

Table (6)
Validity of CL in prediction of preterm birth

CL	
Cutoff value	<27
AUC (95% CI)	0.664 (0.563 - 0.756)
Sensitivity	74.0%
Specificity	62.0%
PPV	66.07
NPV	70.45
Accuracy	66.0 %
P value	0.003

PPV= Positive Predictive Value, NPV= Negative Predictive Value, AUC= Area Under Curve

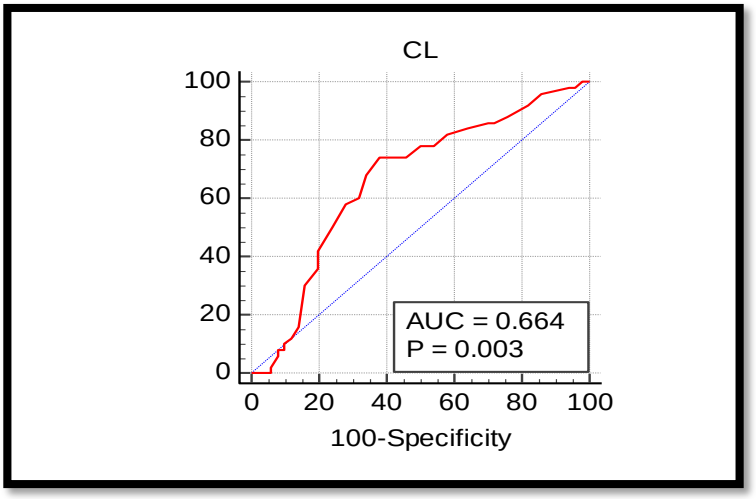

Figure (17): ROC curve of CL in prediction of preterm birth.

Discussion

Regarding the demographic characteristics among the studied groups, we revealed that the mother age in preterm group ranged from 26 to 38 years with mean ±SD= 32.6±3.7 years while in control group the mother age ranged from 26 to 38 years with mean ±SD= 32.3± 3.5 years with no statistically significant difference (p=0.557) between the two groups. Likewise, there was no statistically significant difference between the two groups regarding weight (p=0.918), height (p=0.987) and BMI (p=0.906).

In agreement with our results the study by **Farràs [6]** reported that there was no significant difference between studied groups regarding the age, and BMI (P>.05).
Regarding prior history of cervical intervention of the studied groups , we found that there was no statistically significant difference between women who delivered preterm (group I) and control group regarding prior dilation and curettage (p=0.171) and prior cervical conization (p=0.617). Likewise, there was no statistically significant difference between the two groups regarding prior cervical LEEP (p=0.790) and abnormal pap smear (p=0.499).

In agreement with our results the study by **Luechathananon (11)** reported that that there was no significant difference between studied groups regarding Prior dilatation and curettage, Prior cervical conization, Prior LEEP and Abnormal Pap (p>.05).

In contrast the study by **Dziadosz [7]** revealed that there were significant differences between studied groups regarding Prior dilatation and curettage (p=.01) while there was no significant difference between studied groups regarding, Prior cervical conization, Prior LEEP and Abnormal Pap smear (p>.05).
Regarding neonatal characteristics among the studied groups, we found that that NICU admission was significantly increased in preterm group compared to control group (p<0.001). Concerning female fetus, there was no statistically significant difference between the both groups (p= 0.689).

In agreement with our findings the study by **Farràs [6]** revealed that there was no statistically significant difference between the studied groups regarding female fetus (p= 0.346).

In agreement with our results the study by **Khamees (10)** revealed that there was high significant difference between studied groups regarding UCA (P<.001) while there was no significant difference between studied groups regarding CL (p=.062). In contrast to our findings the study by **Luechathananon [11]** reported that that there was no significant difference between studied groups regarding UCA, whereas there was significant difference regarding CL (p=.032).

While the study by **Benito (8)** revealed that there was significant difference between studied groups regarding UCA and there was no significant difference regarding CL.

Also, the studies by **Farràs [6]** and **Dziadosz [7]** revealed that there was no statistically significant difference between the studied groups UCA and CL (p>.05). As well the study by **Eser & Ozkaya (9)**revealed that there was statistically significant difference between the studied groups UCA and CL (p<.05).

By using ROC-curve analysis, UCA can predict preterm birth with accuracy (75.4%). The sensitivity, specificity, PPV and NPV was 70%, 76%, 74.47% and 71.7% respectively (p< 0.001). Also, by using ROC-curve analysis, CL can predict preterm birth with accuracy (66%). The sensitivity, specificity, PPV and NPV was 74%, 62%, 66.07% and 70.45% respectively (p= 0.003).

While the study by **Benito [8]** generated the ROC curves to assess the capacity of UCA and CL to predict sPTB before 32 and 34 weeks of pregnancy. ROC curves were used to select the optimal cutoff to predict sPTB before 28 weeks. The cutoff that demonstrated the best predictive ability was 117 degrees with sensitivity of 80% and specificity of 79.4% for sPTB before 28 weeks. On the other side, a CL of 25 mm presented a sensitivity of 25% and a specificity of 99.4%. Tables 2 and 3 show the risk of sPTB using the cutoff points selected in ROC curves for both UCA and CL measurements.

The study by **Luechathananon [11]** revealed that the use of UCA from TVS ≥110.97 degrees as a predictor for preterm birth in threatened preterm labor patients had sensitivity and specificity of 65.1% and 43.6%, respectively. The NPV of UCA >110.97 degrees were 77.3% (range 65.3%-86.7%), which implies that a UCA <110.97 degrees in pregnancies with threatened preterm labor has low likelihood of preterm birth.

Data from the **Luechathananon [11]** study found that the diagnostic performance of TVS-CL(transvaginal sonography of CL) was higher than TVS-UCA. However, the combination of both parameters could increase the accuracy of cervical condition assessment for preterm prediction. Determination of the TVS-UCA is easy to perform without additional cost from TVS-CL measurement. We propose that the high NPV of TVS-UCA with TVS-CL means it could be used in clinical practice in threatened preterm labor management to support the judgement of admission and use of tocolytic agents.

Cutoff value of uterocervical angle is 95 degree which increased in preterm group than control group.

Cutoff value of cervical length is 27mm which decreased in preterm group than control group.

Conclusion:

Ultrasonographic measurement of uterocervical angle performed in routine vaginal ultrasound during second trimester is a useful strategy in the prediction of preterm birth in pregnancies and better than cervical length alone. In our research, a multivariate model combining uterocervical angle (UCA), cervical length have a high predictive power to estimate the risk of extreme preterm birth in pregnancies.

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