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ULTRASONOGRAPHIC AND CLINICAL EVALUATION OF THE CERVIX IN PREDICTION OF PRETERM BIRTH

By

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ABSTRACT

Background: Prematurity is the leading cause of infant mortality worldwide. Correct and appropriate evaluation of cervical status has become important in predicting spontaneous onset of labor with widespread use of ultrasonography in obstetrical practice.

Objective: To evaluate the cervix clinically and ultrasonography during pregnancy as a preterm birth predictor.

Patients and methods: This was a prospective observational study included one hundred and twenty four pregnant women. The participants were divided in to two groups: Group A included 82 pregnant women had previous history of preterm birth with or without other risk factor, and Group B: included 42 pregnant women with no risk factors for preterm birth with and with prior normal labor. All cases were selected from Obstetrics and Gynecology Department, Al-Azhar University Hospital (Al-Hussein) during the period from January 2021 to July 2021.

Result: There was a significant difference between the groups in term of preterm labor history, short cervix, threatened abortion, interval ≤18 months and vaginal discharge that they were significantly more frequent in group A. The predictive role of cervical length measurement in mm was evaluated by ROC curve between 20 to 24 weeks. Cervical length ≤25mm has sensitivity 100%, specificity 64%, PPV 52.4% and the NPV 100%. The cervical length was significantly lower in group A compared to group B. There was a significant difference between preterm and term delivery of preterm labor history, and short cervix.

Conclusion: The role of ultrasound in the prediction of preterm birth, cervical length, low anterior thickness, fundal thickness and posterior thickness were found to be significant predictors of preterm delivery. Cervical length measured in transvaginal sonography has acceptable consistency for screening and early diagnosis of spontaneous preterm deliveries in low risk women.

Keywords: Prematurity, Cervical length, Preterm deliveries, Ultrasound.

INTRODUCTION

Spontaneous preterm delivery accounts for approximately 72% of preterm deliveries and several factors can increase the risk of this type of preterm delivery. Some of them are early threatened abortion in the current pregnancy, genetic factors, demographic features and behavior features *(Dalili et al., 2013)*.

Spontaneous pre-term birth is the leading cause of neonatal mortality as more than one million die because of pre-

term birth. Premature neonates who survive have significantly higher risk of developing serious complications such as cardiovascular, respiratory dysfunction, motor and intellectual deficiencies *(Muller et al., 2015)*.

Therefore, cervical length assessment has become a widely used clinical measure for identifying women at high risk for pre-term birth as the risk of spontaneous pre-term birth is greater in women with a short cervix than women with a longer cervix *(Romero et al., 2013)*.

Correct and appropriate evaluation of cervical status has become important in predicting spontaneous onset of labor with widespread use of ultrasonography in obstetrical practice, investigators have begun to study the changes of cervical morphology by sonographic scanning and they have advocated that tranvaginal ultrasonography is a reliable method to assess the cervix uteri and lower uterine segment *(Kokanali et al., 2016)*.

The aim of this study was to evaluate the cervix clinically and ultrasonography during pregnancy as a preterm birth predictor.

PATIENTS AND METHODS

The study had been conducted at Obstetrics and Gynecology Department, Al-Azhar University Hospital (Al-Hussein). This prospective observational study included one hundred and twenty four pregnant women, during the period from January 2021 to July 2021.

Inclusion criteria: Woman who fulfilled the following criteria were included in the study: Age: 16-45, gestational age from 20-36 weeks and living fetus.

Exclusion criteria: Pregnant women less than 20 weeks of gestation, primigravida, multiple gestations, uncertain gestational age, suspected fetal growth restriction and fetal macrosomia, very obese patient (BMI > 40) for prevention of sonography false results, severe medical condition leading to termination of pregnancy, accidental hemorrhage associated with moderate or severe bleeding, and polyhydramnios and oligohydramnios.

Operational design: The procedure was explanation to all women participating in the study. A written consent was taken from every patient before starting the study with counseling about risk and benefit of study.

Women were divided into 2 groups: Group A included 82 pregnant women had previous history of preterm birth with or without other risk factor including threatened abortion in the current pregnancy, inter-pregnancy interval less than eighteen months, maternal age < twenty years or > thirty five years old for the first pregnancy, maternal weight less than forty five kilograms, smoking, uterine structure abnormalities (ex. fibroid), accidental hemorrhage with mild bleeding, polyhydraminous, oligohydraminos, premature rupture of membranes, medical diseases (as anemia, diabetes and hypertension) and fetal anomalies (Sayres, 2010 and Dalili et al., 2013), and Group B included 42 pregnant women with no risk factors for preterm birth with and with prior normal labor.

All women had been subjected to:

1. **History taking including:**

A. Personal history included name, age, residency, telephone number,

education level, occupation, marital status, years of marriage, consanguinity, number of children, age of youngest child and any special habits of medical importance.

B. Menstrual history included menarche, regularity of menses, duration of menstrual bleeding, length of cycle, amount, the presence of pain and its relation to bleeding, any abnormal bleeding and types, duration of contraception methods she had used.

C. Obstetric history included gravidity, parity, time, type and site of previous delivery, number of children, detailed history of preterm births (regarding gestational age, possible cause, method of labor, management she received and any complications), abortion (regarding gestational age, possible cause, treatment received, method of termination, any complication happened in the post abortive period and time of last abortion), last menstrual period, expected day of labor and weeks of conception, history of infertility from any cause.

D. Present history included gynecological symptoms which suggested sexually transmitted diseases as vaginal discharge, pelvic discomfort, purities, dysparunia or post coital bleeding, and urinary symptoms which suggested urinary tract infection as dysuria, frequency or urgency.

E. Past history included history of medical diseases (diabetes mellitus, hypertension, heart disease, chest disease, and rheumatic disease), any previous operations and sensitivity to any drugs

F. Family history of similar condition or diabetes.

2. Examination including:

A. General examination included general condition, height, weight, gait and vital signs (blood pressure, pulse rate, respiratory rate and temperature).

B. Abdominal examination included inspection (size, shape, scars, striae gravidarum and the presence of hernia), palpation (fundal level, the rest of abdomen to detect any abnormality and for presence of contractions), and auscultation of fetal heart sounds.

C. Vaginal examination.

D. Bimanual pelvic examination of both adenexae, and uterus for detection of any abnormality of female genitalia.

3. Investigations:

a. Routine investigations included complete blood count, blood group, Rh, group, urine analysis, fasting blood sugar, and 2 hours post prandial blood sugar.

b. Ultrasounds scan to assess the gestational age and to detect any abnormality.

4. Interventions: Gestational age was determined by last menstrual period or ultrasound in the first trimester. The initial ultrasound was done at 20-24 weeks gestational age. Abdominal ultrasound was done using a 2.5 - 7.5 MHz trans-abdominal probe with the women in the recumbent position. We assessed the fetal condition, gestational age, the presence of any fetal or uterine anomalies, the placenta and the amniotic fluid.

Study protocol had been submitted for approval by the Ethical Committee of faculty of medicine Al-Azhar University, Cairo.

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) was used to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data) & Mann-Whitney test. P value < 0.05 was considered significant. Receiver operating characteristic (ROC) curve was constructed to permit selection of threshold values for test results and comparison of different testing strategies. Areas under ROC curves and their standard errors were determined using the method of Cantor, and compared using the normal distribution, with correction for correlation of observations derived from the same cases. Value of area under a ROC curve (AUC) indicates: 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 cutoff point was established at point of maximum accuracy.

RESULTS

There was a significant difference between the groups regarding maternal age, BMI, parity, gravidity and GA **(Table 1)**.

Table (1): Demographic characteristics and clinical data among the studied groups

Groups / Parameters	**Group A** (n=82)	**Group B** (n=42)	**p**
Age (years) Mean ± SD	31.56 ± 4.73	29.11 ± 4.12	**0.005**
BMI (kg/m^2) Mean ± SD	28.6 ± 2.69	26.29 ± 2.39	**<0.001**
Parity Mean ± SD	2.12 ± 1.04	1.55 ± 1.02	**0.004**
Gravidity Mean ± SD	3.61 ± 1.44	2.43 ± 1.32	**<0.001**
GA (weeks) Mean ± SD	36.25 ± 3.41	37.76 ± 1.86	**0.009**

There was a significant difference between the groups in term of preterm labor history, short cervix, threatened abortion, interval ≤18 months and vaginal discharge, that they were significantly more frequent in group A **(Table 2)**.

Table (2): History and risk factors distribution among the studied groups

Groups / Parameters	Group A (n=82)	Group B (n=42)	P
Preterm labor history	49 (59.8%)	0	**<0.001**
Short cervix	35 (42.7%)	7 (16.7%)	**0.004**
Threatened abortion	19 (23.2%)	2 (4.8%)	**0.010**
Interval ≤ 18 months	27 (32.9%)	5 (11.9%)	**0.011**
Vaginal discharge	64 (78%)	15 (35.7%)	**<0.001**
DM	14 (17.1%)	6 (14.3%)	0.689
HTN	7 (8.5%)	3 (7.1%)	0.816
Smoking	8 (9.8%)	3 (7.1%)	0.628

The cervical length was significantly lower in group A compared to group B **(Table 3)**.

Table (3): US findings of the two studied groups

Groups / US findings	Group A (n=82)	Group B (n=42)	P
Cervical length (mm) Mean ± SD	23.96 ± 4.66	28.35 ± 2.29	**.000**

There was a significant difference between preterm and term delivery in term of preterm labor history, and short cervix **(Table 4)**.

Table (4): History and risk factors distribution between preterm and term delivery among group A

Delivery / Parameters	Preterm (n=23)	Term (n=59)	P
Preterm labor history	19 (82.6%)	30 (50.8%)	**0.008**
Short cervix	18 (78.3%)	17 (28.8%)	**<0.001**
Interval ≤ 18 months	11 (47.8%)	16 (27.1%)	0.073
DM	6 (26.1%)	8 (13.6%)	0.176
HTN	4 (17.4%)	3 (5.1%)	0.073
Smoking	4 (17.4%)	4 (6.8%)	0.146

That cervical length was significantly lower in preterm group compared to term group **(Table 5)**.

Table (5): US findings between preterm and term delivery among group A

Delivery / Parameters		Preterm (n=23)	Term (n=59)	P
Cervical length (mm) Mean ± SD		22.18 ± 2.68	27.75 ± 2.82	**<0.001**
Position	**H**	18 (78.3%)	41 (69.5%)	0.427
	V	5 (21.7%)	18 (30.5%)	
Funneling		2 (8.7%)	2 (3.4%)	0.316

The predictive role of cervical length measurement in mm was evaluated by ROC curve between 20 to 24 weeks cervical length ≤ 25mm has sensitivity 100%, specificity 64%, PPV 52.4% and the NPV 100% **(Figure 1)**.

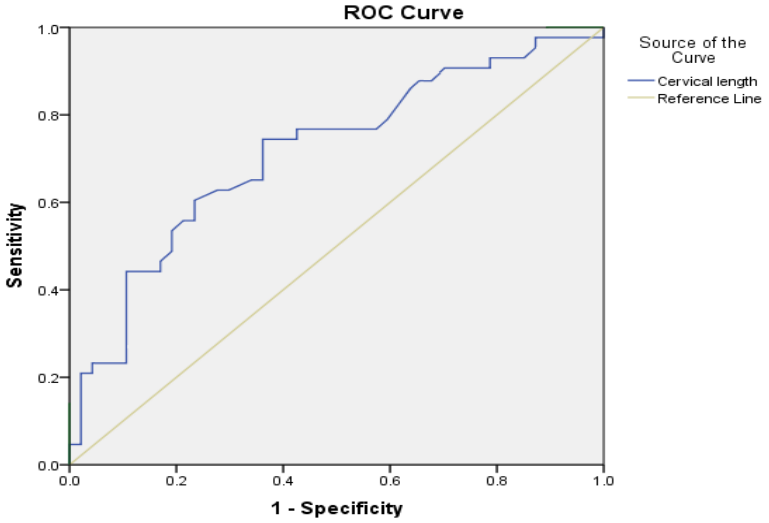

Figure (1): ROC curve for cervical length as a predictor for preterm birth

The cervical length was found to be significant predictor of preterm delivery **(Table 6)**.

Table (6): Multivariate logistic regression analysis to determine the possible predictors of preterm delivery

Analysis / Parameters	OR	S.E.	Sig.	95 % Confidence Interval for OR	
				Lower Bound	Upper Bound
Age	.242	.215	.663	.160	.550
BMI	.148	.156	.095	.116	.541
Parity	1.537	.382	.103	.737	2.338
Gravidity	.163	.107	.176	.075	.378
Cervical length	1.231	.046	**.001***	.280	1.838
H position	3.725	.055	.091	.117	8.321

DISCUSSION

Analysis of our findings, revealed that Mean ± SD of group A was 31.56 ± 4.73, and in group B was 29.11 ± 4.12 years, Mean ± SD of BMI was 28.6 ± 2.69, and in group B was 26.29 ± 2.39, and there is a significant difference between the groups regarding maternal age, BMI, parity, gravidity and GA.

In agreement with our findings, the study of *Mabrouk et al. (2020)* reported that age in group A (had previous preterm labor), and in group B (low risk pregnant women) showed that group A significantly had higher gravidity, parity and abortion.

In a study done by *Dalili et al. (2013)* reported that mean age of participants was 26.16±4.07 years with the range of 15-45 years. Mean age of subjects with term labor and that of those with spontaneous

preterm labor showed no significant difference.

Most of the risk factors for PTB are modifiable; More than 75% of PTB deaths can be prevented without intensive care. Over the past decade, seven countries have halved their deaths due to PTB by ensuring that the frontline workers are skilled in the care of premature babies and improving supplies of life-saving commodities and equipment. Despite the advances in prenatal medicine and preterm preventive measures, other countries showed an increment in PTB incidence with related morbidity and mortality *(Sherf et al., 2017)*.

In the current study, we found that there was a significant difference between the groups in term of preterm labor history, short cervix, threatened abortion, interval ≤18 months and vaginal discharge, that they were significantly more frequent in group A. *Mabrouk et al. (2020)* reported that women with previous preterm labor are significantly had more frequent vaginal discharge and previous abortion.

The same result was noted by *Ancel et al. (2010)*. They found that previous induced abortions were significantly associated with preterm birth and the risk of preterm birth increased with the number of abortions.

A history of PTB or second-trimester miscarriage is one of the strongest predictors of PTB *(Laughon et al., 2014)*. Previous studies of *Parry et al. (2012)* and *Melamed et al. (2014)* assessed the value of a short CL in combination with an obstetrical history of sPTB, *Durnwald et al. (2010)* found similar rates of CL < 25 mm at 22–25 weeks' gestation in women with a history of one previous sPTB (18–37 weeks of gestation) and in those with two or more sPTBs. Due to the limited sample size, it could not be determined whether an increasing number of prior sPTBs significantly modified the value of a short cervix in predicting a future sPTB prior to 32 or 35 weeks of gestation.

Numerous studies have clearly demonstrated that the relationship between a sonographic short cervix and spontaneous preterm birth is most sensitive when combining cervical length and obstetric history in high-risk populations with previous preterm birth *(Gudicha et al., 2021)*. A cut-off value of cervical length of 25 mm has been used by clinicians and researchers to screen for women at the highest risk of spontaneous preterm birth *(Conde-Agudelo et al., 2013)*. This group of women has been targeted with interventions to reduce the risk of spontaneous preterm birth including vaginal progesterone, cerclage and cervical pessary. In addition, current practice guidelines recommend initiation of therapy in high-risk patients with a cervical length of < 25 mm in the mid-trimester *(Lim et al., 2011)*.

In the present study, we found that cervical length was significantly lower in group A compared to group B.

McFarlin et al. (2015) found that cervical length was significantly shorter at 22–26 weeks in the spontaneous preterm birth women than in the women delivering at full term .In a study by *Ghose et al. (2014)* the mean cervical length was 33.16 mm. Almost 80% of women who had cervical length.

On the other hand, we found that in women with history of preterm birth; it

was found that there were non-statistical significant difference between preterm and term delivery regarding age, parity, and gravidity while there is statistical significant difference as regard BMI, Moreover, there is a significant difference between preterm and term delivery in term of preterm labor history, and short cervix.

This comes in agreement with the study of *Mabrouk et al. (2020)* which reported that there were non-statistical significant differences between preterm and term groups as regard each of age, BMI, parity, gravidity, DM, and HTN, while there were statistical significant differences between them as regard abortion and preterm.

In addition to above findings, we compared US findings between preterm and term delivery among group A, and found that cervical length was significantly lower in preterm group compared to term group.

In *Dalili et al. (2013)* study, 12% of spontaneous preterm birth women had positive funneling. Duration of pregnancy and cervical length significantly differed between women with and without funneling.

Yost et al. (2010) found that cervical canal dilation of 2–4 mm was a significant predictor of spontaneous preterm birth of less than 35 weeks in univariate analyses. Regarding the cervical position, 10 out of 13 women in high risk group who had horizontal position of the cervix between 20-24 weeks had a preterm birth. This incidence was statistically insignificant. In literature there are conflicting results, *Chhabra and Varma (2010)* found that the incidence of preterm birth was significantly higher in women with vertical position of cervix (80%) than that with horizontal position (20%). However *Yost et al. (2010)* reported that horizontal position of the cervix was found in 59% and it was insignificant in prediction of preterm birth.

Similar to our findings, the study of *Mabrouk et al. (2020)* reported that there were statistical significant difference between term and preterm groups as regard each of cervical length, low anterior thickness, mid anterior thickness, fundal thickness and posterior thickness which were lower among preterm group.

In our study, the predictive role of cervical length measurement in mm was evaluated by ROC curve between 20 to 24 weeks cervical length ≤25mm has sensitivity 100%, specificity 64%, PPV 52.4% and the NPV 100%.

The sensitivity and specificity of cervical length measurement of 25 mm in low risk women was calculated in *Dalili et al. (2013)* study, they were 55.5% and 93.6% respectively.

Barber et al. (2010) found that a cervical length of ≤25mm at 24 weeks had a sensitivity of 37%, a specificity of 92%,a positive predictive value 18%, and a negative predictive value 97 % in the prediction of spontaneous preterm labor at less than 35 weeks gestation.

Arisoy and Yayla (2012) concluded that, although low sensitivity and low positive predictive value of cervical length measurement, it has high negative predictive values so it can be used in screening of preterm labor in pregnant women.

Cervical length is a better predictor of preterm birth in women at increased risk,

such as those with a history of spontaneous preterm birth, than in asymptomatic women at low risk *(Crane and Hutchens, 2012)*. In study of *Durnwald et al. (2010)* on women with a history of preterm birth, using a cervical length cut-off of 25 to 30 mm to predict preterm birth 37 weeks of gestation, sensitivity is 60% to 80%, positive predictive value is 55% to 70%, and negative predictive value is 89% to 94%. Thus, a long cervix (at least 25 to 30 mm) is reassuring and can help to reduce unnecessary and costly interventions, such as activity restriction, maternal transfer, steroids, and tocolytics.

A study *Szychowski et al. (2013)* found that the gestational age at which the prior preterm delivery occurred affects the frequency and rate of cervical shortening in the current pregnancy. A prior spontaneous early preterm birth less than 24 weeks) puts women at a higher risk of cervical shortening. Women in this group also have a higher rate of cervical decline that begins at an earlier gestational age than women with a history of a later preterm birth (24 to 32 weeks).

In the current study, cervical length was found to be significant predictor of preterm delivery.

In a prospective study of *Gürsoy Erzincan et al. (2019)* The optimal cutoff values for CL, fundal MT-to-CL and mid-anterior MT-to-CL ratios in predicting PTB were calculated as 31.1 mm, 0.19 and 0.20, respectively. Fundal MT-to-CL ratio predicted preterm delivery with 71% sensitivity, 72% specificity, 68% positive and 75% negative predictive values. For mid-anterior MT-to-CL ratio, respective values were 76, 76, 73 and 79%.

Myometrial thickness has undergone sonographic evaluation during normal pregnancy, labor and postpartum and in certain situations such as twin pregnancy, polyhydramnios and PPROM *(Romero et al., 2013)*. Some studies showed the decrease of myometrial thickness in the 2^{nd} and 3^{rd} trimesters compared with the 1st trimester and also in specific pregnancies which are associated with preterm labor such as twin pregnancy and polyhydramnios *(Kalantari et al., 2010)*, this can explained that in our study fundal thickness is found to be significant predictors of preterm delivery.

CONCLUSION

The role of ultrasound in the prediction of preterm birth, cervical length, low anterior thickness, fundal thickness and posterior thickness were significant predictors of preterm delivery. Cervical length measured in transvaginal sonography has acceptable consistency for screening and early diagnosis of spontaneous preterm deliveries in low risk women.

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تقييم خصائص عنق الرحم عن طريق الموجات فوق الصوتية والتشخيص الاكلينيكى للتنبوء بحدوث ولادة مبكرة

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خلفية البحث: الولادة المبكرة العفوية هي السبب الرئيسي لوفيات الولدان. وأصبح التقييم الصحيح والمناسب لحالة عنق الرحم مهمًا في التنبوء بالبدء التلقائي للولادة مع الاستخدام الواسع النطاق للتصوير بالموجات فوق الصوتية في ممارسة التوليد، وقد بدأ الباحثون في دراسة التغيرات في مورفولوجيا عنق الرحم عن طريق المسح بالموجات فوق الصوتية ودعوا إلى أن التصوير بالموجات فوق الصوتية عبر المهبل طريقة موثوقة لتقييم عنق الرحم والجزء السفلي من الرحم.

الهدف من البحث: تقييم عنق الرحم سريريًا والتصوير بالموجات فوق الصوتية أثناء الحمل كمنبئ للولادة المبكرة.

المريضات وطرق البحث: كانت هذه دراسة قائمة على الملاحظة شملت مائة وأربع وعشرين إمرأة من الحوامل، وتم تقسيم المشاركات إلى مجموعتين: **المجموعة (أ):** 82 من النساء الحوامل كان لديهن تاريخ سابق للولادة المبكرة مع أو بدون عامل خطر آخر، **والمجموعة (ب):** 42 من النساء الحوامل ليس لديهن عوامل خطر للولادة المبكرة مع الولادة الطبيعية السابقة. وقد تم إختيار جميع الحالات من التوليد وقسم أمراض النساء بمستشفى الأزهر الجامعي (الحسين) خلال الفترة من يناير 2021 إلى يوليو 2021.

نتائج البحث: هناك فرق كبير بين المجموعات من حيث تاريخ المخاض قبل الأوان، وقصر عنق الرحم، والإجهاض المهدد، والفاصل الزمني 18 شهرًا، والإفرازات المهبلية، حيث كانت أكثر تكرارا في المجموعة أ. وتم تقييم الدور التنبئي لقياس طول عنق الرحم بالمليمتر من خلال منحنى الروك بين 20 إلى 24 أسبوعًا، وطول عنق الرحم 25مم ملم لديه حساسية 100٪، ونوعية 64٪، و القيمة التنبؤية الموجبة 4.52٪، و القيمة التنبؤية السالبة 100٪. و كان طول عنق

الـــرحم أقـــل بشـــكل معتـــد بـــه فـــي المجموعـــة (أ) مقارنـــة بالمجموعـــة (ب). هنـــاك فـــرق معتـــد بـــه بـــين الـــولادة الطبيعـــة والـــولادة المبكـــرة مـــن حيـــث تـــاريخ المخـــاض المبكـــر، وقصر عنق الرحم.

الاســـتنتاج: هنـــاك دور للموجـــات فـــوق الصـــوتية فـــي التنبـــوء بـــالولادة المبكـــرة، حيـــث وجـــد أن طـــول عنـــق الـــرحم، والســـماكة الأماميـــة المنخفضـــة، وســـمك قـــاع الـــرحم والســـمك الخلفـــي تنبـــئ بشـــكل كبيـــر بـــالولادة المبكـــرة. وكـــان طـــول عنـــق الـــرحم المقـــاس فـــي التصـــوير بالموجـــات فـــوق الصـــوتية عبـــر المهبـــل لـــه إتســـاق مقبـــول للفحـــص والتشخيص المبكر للولادات المبكرة العفوية في النساء منخفضة الاخطار.

الكلمات الدالة: الولادة المبكرة، طول عنق الرحم، الموجات فوق الصوتية.