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Role of cervical gland area as a predictor of preterm labor

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Abstract

Cervical gland area (CGA) is a relatively recent ultrasonographic measure proposed for the prediction of preterm birth. During an ultrasonography examination, the cervical mucosa is often characterised by a hyperechoic or hypoechoic segment, which may or may not correspond to the presence of mucosal glands in the cervical canal. Preterm birth may be predicted by determining whether or not these glands have developed by the end of the second trimester. As a result, the primary purpose of this research was to assess the validity of transvaginal ultrasonography for predicting cervical gland area and, by extension, premature labour. Methods: Benha University Hospitals' Obstetrics and Gynecology Departments recruited 160 pregnant women for this prospective cohort research. Women who tested positive for CGA during pregnancy were placed in Group A, whereas those who did not were placed in Group B. (pregnant women with absent CGA by TVUS). As a result, 78.1% of individuals had CGA and 21.9% did not. With a sensitivity of 64.6%, a specificity of 96.4%, and an accuracy of 86.9%, the presence of CGA is a strong predictor of premature labour. Because of the requirement for specialised prenatal care, it is crucial to accurately predict preterm and extremely preterm birth (gestational age 32 weeks). It would seem that CGA detection is a useful signal for this. CGA should be studied in conjunction with other markers to see which ones are most useful for predicting the likelihood of a premature birth.

Key words: cervical gland area, predictor, preterm labor.

1. Introduction

Intact membranes and cervical dilatation of 2cm or greater over the course of 2 hours are diagnostic of preterm labour. The leading cause of prenatal morbidity and death, preterm birth (PTL) also puts premature infants at higher risk for complications such RDS, IVH, septicemia, necrotizing enterocolitis, and developmental delays [1].

Not only is premature birth a leading cause of infant death, but it is also associated with behavioural issues in later childhood and adolescence. Preterm birth affects around 12.8% of pregnancies in the United States, with 3.6% of them occurring before 34 weeks. Predicting preterm labour (PTL) is crucial since it affects 6–10% of births in industrialised nations. Ultrasound has been used in obstetrics for over 20 years, and several studies have identified sonographic indicators that may be used to predict premature labour [2].

Because cervical change is so crucial to labour starting, assessing it is a key aspect of PTL forecasting. The two most common measurements are cervical length and cervical funnelling. Recent research has shown a correlation between longer cervical length during the second trimester and an increased risk of preterm delivery [3].

While a shorter cervical length is a helpful indicator of cervical maturity and hence a relevant PTL criteria, it is not the only criterion. Cervical maturation is characterised by a number of symptoms, not the least of which is a reduction in cervical length. Since the rate of preterm delivery remains high despite the large number of studies on cervical length, it seems that more research into other cervical alterations is warranted. An further change in cervical maturation is the atrophy and eventual removal of the cervical gland region (CGA). Changes in collagen and proteoglycan composition are linked to cervical ripening as a normal physiological process [4].

During an ultrasonography examination, the cervical mucosa is often characterised by a hyperechoic or hypoechoic segment, which may or may not correspond to the presence of mucosal glands in the cervical canal. Preterm delivery is a risk factor that may be predicted if these glands are not present by the end of the second trimester [3].

Collagen degeneration, reduced collagen concentration, and increased water content are all signs of cervical maturation [5].

The loss of CGA in ultrasound imaging is attributable to a number of factors, including a rise in water content and metabolic changes. Most women, pregnant and not, have this region. On the other hand, it goes away later in pregnancy or sooner in PTL. There is a clear need for more research on the CGA, since earlier efforts have clearly fallen short [4].

The goal of this study was to determine whether transvaginal ultrasonography measurements of the cervical gland region are useful for predicting when a woman may go into labour prematurely.

2. Patients and Methods

This is a prospective, cohort study conducted on one hundred and sixty (160) pregnant women attending for antenatal care at outpatient clinics of obstetrics and gynecology departments of Benha university hospital.

2.1. Sample size justification

The sample size was equal to 146 subjects. Assuming a drop-out ratio of 10%, the total sample size was160 women.

2.2. Inclusion criteria

All women under the study were fulfilling the selection criteria of being:

- Pregnant women aged 20-40 years.
- Singleton pregnancy.
- Gestational age less than 34 weeks at the initial antenatal care visit.
- Uncomplicated pregnancy.

- Women free from medical diseases.

2.3Exclusion criteria

Cases with the following criteria were excluded from the study:

- Age less than 20 years and more than 40 years.
- Gestational age more than 34 weeks at the initial antenatal care visit.
- Women having risk factors for preterm delivery (PTD), such as multiple pregnancy, polyhydramnios, oligohydramnios, fetal macrosomia, intra uterine fetal death, mullerian malformation, intra uterine growth restriction (IUGR), premature rupture of membrane, vaginal bleeding, placental abruption, placenta previa, history of cerclage or other surgical procedures on cervical canal.
- Women with preterm delivery due to a known cause, such as iatrogenic or preeclampsia.
- Women with cervical length (CL) <25 mm was conducted to cerclage and excluded from the study.
- Women who had medical disorders with pregnancy, such as maternal diabetes mellitus, cardiovascular, renal, or liver disorders.

All participants had provided informed written consent following a discussion on the nature of the study as well as the expected value and outcome.

Obstetric abdominal ultrasound scan was done via gray scale real time ultrasound machine. (SONOACE X8 diagnostic ultrasound system ,MEDISON CO., LTD. SAMSUNG, MEDISON), using transabdominal curved probe with frequency range (2MHz~5MHz).

Fig. (1) SONOACE X8 diagnostic ultrasound system**.**

The Scan include

a. Viability.
b. Single or multiple gestations.
c. Fetal biometric measures: Biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL).
d. Expected fetal weight.
e. Exclusion of fetal congenital anomalies.
f. Amniotic fluid index (AFI).
g. Placental location.

Transvaginal ultrasound: vaginal sonography was performed via (SONOACE X8 diagnostic ultrasound system, MEDISON CO., LTD. SAMSUNG, MEDISON), using 7.5 MHz transvaginal probe.

Participants was examined by trans-vaginal ultrasonography (TVUS) between 16th and 19th weeks of gestation to assess cervical length, cervical funneling and cervical gland area (CGA). Gestational age was determined according to last menstrual period (LMP) and ultrasonographic findings.

Guidelines were followed to obtain reproducible cervical assessment. Each sonographic examination was performed according to a defined protocol: the patient was asked to empty her bladder and then was placed in a dorsal lithotomy position. The transvaginal probe was inserted and advanced along the vaginal canal until the sagittal image of the cervix was visualized. The probe was withdrawn slowly and stopped when an adequate image was obtained. An adequate image was defined as presence of external cervical axis, endocervical canal and internal cervical axis, which is the cranial end of the cervical canal adjacent to the intrauterine cavity.

Cervical length (CL) was measured from internal to external os in the sagittal view after visualizing the internal and external orifice in the same plane, women with cervical length (CL) < 25 mm have been conducted to cerclage and were excluded from the study. Presence of cervical gland area (CGA) was examined by US as a hyper- or hypoechoic area just next to the endocervical canal. If the cervix seen iso-echoic, it was considered as absence of CGA.

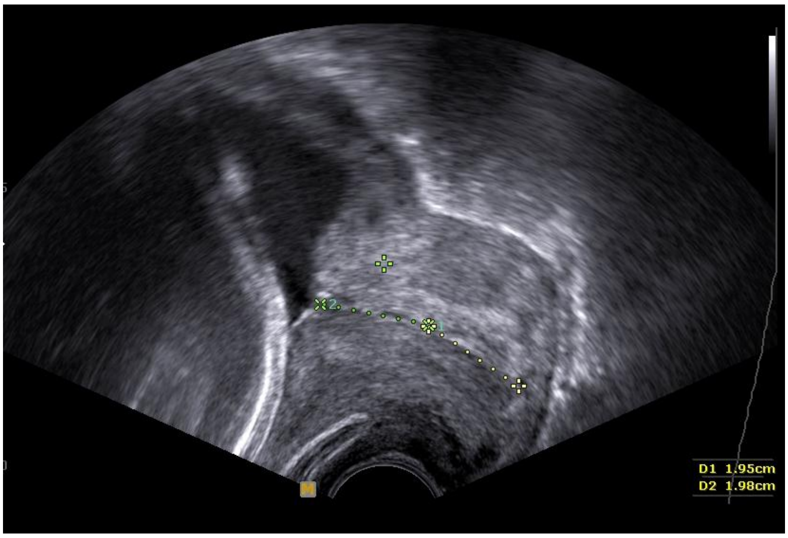

Fig. (2) Transvaginal sonography showing sagittal view of the cervix.

The scan include:

a. Closed cervical length which is the most accurate parameter.

➢ Cervical length was measured with electronic calipers as the linear distance between the external os and the functional internal os along a closed endocervical canal **(6)**.

Fig. (3) Transvaginal cervical assessment and measurement of cervical length.

b. Cervical funneling: defined as the opening of the internal cervical os on ultrasound **(6)**.
c. Cervical gland area [CGA]. Presence of CGA was examined by TVUS as a hyper- or hypoechoic area just next to the endocervical canal. If the cervix was seen iso-echoic, it was considered as absence of CGA.

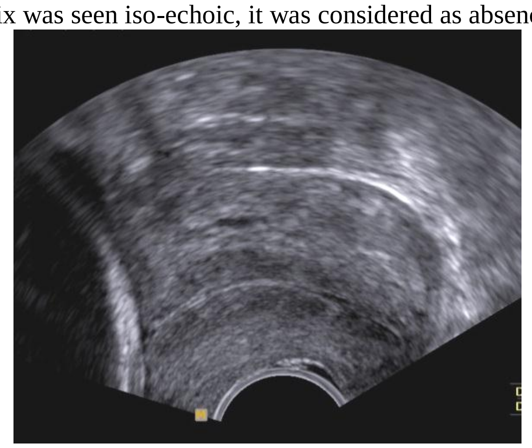

Fig. (4) Transvaginal cervical assessment of cervical gland area (shown here as hypoechoic band surrounding the cervical canal)

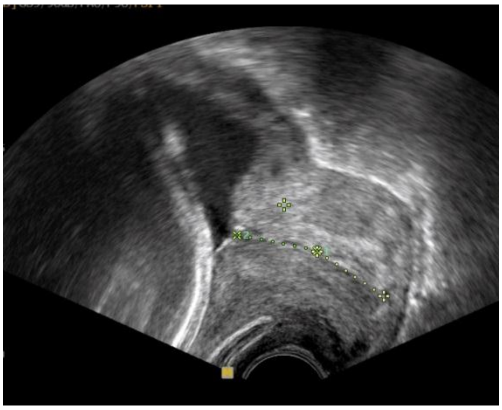

Fig. (5) Transvaginal cervical assessment of cervical gland area (shown here as hyperechoic band surrounding the cervical canal)

Fig. (6) Transvaginal cervical assessment of cervical gland area (shown here as isoechoic band so considered as absent.)

According to this view, the pregnant women were divided into two groups based on presence or absence of CGA:

Group A:

Pregnant women with present cervical gland area (CGA) by trans-vaginal ultrasonography (TVUS).

Group B:

Pregnant women with absent cervical gland area (CGA) by trans-vaginal ultrasonography (TVUS).

Then pregnant women were followed up until delivery time by ultrasound scanning and digital examinations that was performed once every 4 weeks between 16th and 27thweeks of gestation; once every 2 weeks between 28th and 35th weeks of gestation; and once a week from 36th weeks of gestation.

The date of delivery was recorded according to medical reports. According to gestational age at the time of delivery, the mothers were further subdivided into two subgroups: the term group with gestational age equal or more than 37 weeks and preterm group with gestational age<37 weeks.

A full medical history was obtained from all participants. The maternal age, number of pregnancies and history of previous preterm deliveries were recorded. Obstetric ultrasonography and basic laboratory tests were performed, including, complete blood count, urine analysis and liver and kidney function tests. Maternal body weight and vital signs (heart rate, blood pressure, and respiratory rate) were checked.

2.3. Statistical analysis

Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows (Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test while Fischer exact test and Monte Carlo test were used when expected cell count less than 5. Continuous variables were presented as mean ± SD (standard deviation) for parametric data and median (min-max) for non-parametric data. The two groups were compared by student t- test (parametric) and Mann Whitney test (non-parametric). Sensitivity and specificity at different cut off points were tested by ROC curve.

For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level.The results was considered significant when $p \leq 0.05$. The smaller the p-value obtained, the more significant are the results

4. Results

Table (1) Menstrual history and Contraception use of the studied participants:

All participants (n= 160)		Mean & SD	Median	Range	IQR
Age of menarche (years)		11.09 ± 1.918	11.00	8.0, 14.0	9.00, 13.00
Cycles regularity		127		79.4%	
Dysmenorrhea		43		26.9%	
	None	51		31.9%	
Contraception	**IUD**	85		53.1%	
	COC	24		15.0%	

Data is expressed as mean and standard deviation, median, range and interquartile range or as percentage and frequency.

Table) shows that the age of menarche ranged from 8 to 14 years old with (mean ± SD = 11.09 ± 1.918 years). Regarding the menstrual history, 79.4% of the participants had regular cycles and 26.9% had dysmenorrhea. Regarding the contraception, 53.1% were on IUD, 15% were on COC and 31.9% hadn't used any method of contraception.

Table (2) Menstrual history and Contraception use of the studied participants according to presence of CGA:

		Group A (n= 125)	Group B (n= 35)	95% CI	P
Age of menarche (years)		11.02 ± 2.000	11.34 ± 1.589	-1.05, 0.40	0.374
Cycles regularity		100 (80.0%)	27 (77.1%)	-	0.712
Dysmenorrhea		27 (21.6%)	12 (34.3%)	-	0.122
	None	39 (31.2%)	12 (34.3%)		
Contraception	**IUD**	70 (56.0%)	15 (42.9%)	-	0.245
	COC	16 (12.8%)	8 (22.9%)		

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

ed any method of contraception.

Table shows that there were non-significant differences between both groups regarding the age of menarche, cycles regularity, dysmenorrhea, and contraception method (P = 0.374, 0.712, 0.122 and 0.245 respectively).

Table (3) Gestational age at delivery, neonatal APGAR score, Maturity, Mode of Delivery, and type of Anesthesia of the studied participants:

All participants (n= 160)		Mean & SD	Median	Range	IQR
GA at delivery		37.48 ± 2.003	38.00	33.0, 40.0	36.00, 39.00
APGAR 1 min		8.59 ± 1.123	9.00	6.0, 10.0	8.00, 10.00
APGAR 5 min		9.10 ± 1.023	9.00	6.0, 10.0	8.00, 10.00
Maturity	**Preterm**	48		30.0%	
	Full term	112		70.0%	
Mode of Delivery	**CS**	71		44.4%	
	VD	89		55.6%	
	Local	89		55.6%	
Anesthesia	**Spinal**	70		43.8%	
	GA	1		0.6%	

Data is expressed as mean and standard deviation, median, range and interquartile range or as percentage and frequency.

Table) shows that the gestational age at delivery ranged from 33 to 40 weeks with (mean ± SD = 37.48 ± 2.003 weeks), the neonatal APGAR 1 min ranged from 6 to 10 with (mean ± SD = 8.59 ± 1.123) and the neonatal APGAR 5 min ranged from 6 to 10 with (mean ± SD = 9.10 ± 1.023). 30% of the participants had preterm labor, 55.6% had vaginal delivery and 44.4% delivered by CS. 55.6% had local anesthesia, 43.8 had spinal anesthesia and 0.6% had general anesthesia.

Table (4) Gestational age at delivery, neonatal APGAR score, Maturity, Mode of Delivery, and type of Anesthesia of the studied participants according to presence of CGA:

		Group A (n= 125)	Group B (n= 35)	95% CI	P
GA at delivery		38.17 ± 1.590	35.00 ± 1.213	2.60, 3.74	**< 0.001**
APGAR 1 min		8.87 ± 0.984	7.60 ± 1.035	0.90, 1.65	**< 0.001**
APGAR 5 min		9.25 ± 0.913	8.57 ± 1.220	0.30, 1.05	**< 0.001**
Maturity	**Preterm**	17 (13.6%)	31 (88.6%)	-	**< 0.001**
	Full term	108 (86.4%)	4 (11.4%)		
Mode of Delivery	**CS**	56 (44.8%)	15 (42.9%)	-	0.838
	VD	69 (55.2%)	20 (57.1%)		
Anesthesia	**Local**	69 (55.2%)	20 (57.1%)	-	0.858
	Spinal	55 (44.0%)	15 (42.9%)		
	GA	1 (0.8%)	0 (0.0%)		

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table ( ) shows that there were statistically significant differences between both groups regarding the gestational age at delivery, neonatal APGAR score 1, 5 min and maturity (P < 0.001). There were non-significant differences between both groups regarding the mode of delivery and anesthesia (P = 0.838 and 0.858 respectively).

Table (5) Cervical canal length, Internal OS Diameter and Shape of the studied participants**:**

All participants (n= 160)		Mean & SD	Median	Range	IQR
Cervical canal length		32.67 ± 2.762	33.00	28.0, 37.0	30.00, 35.00
Internal OS Diameter		10.52 ± 1.690	10.00	8.0, 13.0	9.00, 12.00
Internal OS Shape	**T**	147		91.9%	
	Y	13		8.1%	

Data is expressed as mean and standard deviation, median, range and interquartile range or as percentage and frequency.

Table) shows that the cervical canal length ranged from 28 to 37 with (mean ± SD = 32.67 ± 2.762) and the internal OS diameter ranged from 8 to 13 with (mean ± SD = 10.52 ± 1.690). Regarding the internal OS shape, 91.9% had T shape and 8.1% had Y shape.

Table (1) cervical canal length, Internal OS Diameter and Shape of the studied participants according to presence of CGA:

		Group A (n= 125)	Group B (n= 35)	95% CI	P
Cervical canal length		32.86 ± 2.787	32.03 ± 2.606	-0.21, 1.87	0.118
Internal OS Diameter		10.50 ± 1.669	10.57 ± 1.787	-0.71, 0.57	0.835
Internal OS Shape	**T**	114 (91.2%)	33 (94.3%)	-	0.555
	Y	11 (8.8%)	2 (5.7%)		

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (1) shows that there were non-significant differences between both groups regarding the cervical canal length, internal OS diameter and internal OS shape (P = 0.118, 0.835 and 0.555 respectively).

Table (7) Frequency of CGA and non CGA among the studied participants:

All participants (n= 160)		Frequency	Percentage
CGA	**Present**	125	78.1%
	Absent	35	21.9%

Data is expressed as percentage and frequency.

Table) shows that 78.1% of the participants had cervical gland area (CGA) while it was absent in 21.9%.

Table (2) Diagnostic profile of CGA in detection of preterm labor in the current study:

Parameter	Value
AUC	0.805
P	**< 0.001**
Sensitivity	64.6%
Specificity	96.4%
PPV	88.6%
NPV	86.4%
Accuracy	86.9%
P is significant when < 0.05.	

Table (2) shows that presence of CGA is a significant predictor of preterm labor (P < 0.001) with sensitivity of 64.6%, specificity of 96.4% and accuracy of 86.9%.

4. Discussion

According to the results of the present investigation, the average age of menarche was 8.4 years (SD = 3.1). In terms of menstrual history, 26.9% of the women reported having dysmenorrhea, whereas 79.4% reported having regular periods. In terms of birth control, 53.1% were using an IUD, 15% were using COC, and 31.9% had never used birth control.

Age at menarche, cycle regularity, dysmenorrhea, and method of contraception were all comparable across the two sets of participants (P = 0.374, 0.712, 0.122, and 0.245, respectively).

Results from the present research demonstrate that the newborn APGAR scores varied from 6 to 10 at both the 1- and 5-minute marks, that 30% of participants had preterm labour, that 55.6% gave birth vaginally, and that 44.4% gave birth through CS. The anaesthetic methods used were as follows: 55.6% local, 43.8% spinal, and 0.6% general.

Maternal age, newborn APGAR score at 1, 5, and maturity all differed significantly between the two groups (P 0.001). Delivery method and anaesthetic choice did not vary significantly between the two groups (P = 0.838 and 0.858, respectively).

The median 5-minute Apgar score increased from 7 for pregnancies less than 28 weeks to 8 for pregnancies between 28 and 30 weeks, and from 9 for pregnancies between 29 and 30 weeks to 10 for pregnancies 31 weeks and beyond (P 0.001).

A similar pattern was seen by Lee et al. [8], who discovered that low Apgar scores were more prevalent at earlier gestational ages. Between 24 and 36 weeks of pregnancy, the median Apgar score increased from 6 to 9. The relative risk of mortality was highest for Apgar scores of 0-3 compared to 7-10, and this was true even at the earliest gestational ages, ranging from 3.1 (95% confidence range 2.9, 3.4) at 24 weeks to 18.5 (95% confidence interval 15.7, 21.8) at 28 weeks.

The length of the cervical canal in the present research varied from 28 to 37 mm, while the internal diameter of the OS was between 8 and 13 mm. When looking at the OS from the inside, 91.9% were T-shaped, whereas 8.1% were Y-shaped.

Length of the cervical canal, internal OS diameter, and internal OS shape did not change significantly between the two groups (P = 0.118, 0.835, and 0.555, respectively).

Afzali et al. [9] also looked at the significance of CGA absence in predicting preterm birth, and they observed a similar range of CL across 600 women (26-45 mm). There was no significant difference between the two groups for CL (P value = 0.874), with the term group having a mean CL of 35.4 4.11 mm and the preterm group having a mean CL of 35.6 4.48 mm.

According to the results of this research, CGA was present in 78.1% of subjects and missing in 21.9%.

With a sensitivity of 64.6%, a specificity of 96.4%, and an accuracy of 86.9%, the present research demonstrates that the presence of CGA is a strong predictor of preterm labour (P 0.001).

Marsoosi et al. [4] also discovered that CGA was present in 189 out of 190 patients (94.5%), which is consistent with our findings. Eleven women, or 5.5% of the sample, did not have CGA. Of these, four had SPTL before 35 weeks gestation and six had it before 37 weeks. When CGA was absent between weeks 37 and 35 of pregnancy, SPTL was significantly higher. Before 35 weeks gestation, the test had a sensitivity of 25%, specificity of 99%, a PPV of 33%, and an NPV of 99%. For a gestational age of 37 weeks, the results were a sensitivity of 14.3%, specificity of 99.0%, PPV of 33.3%, and NPV of 97.0%. Women who lacked CGA were shown to have shorter cervical lengths than females who did (p0.001).

Afzali et al. [9] also observed that CGA was present in 75.7% of all moms; their total number was 454, with 432 belonging to the term group and 22 to the preterm group. The percentage of instances without CGA was substantially lower in the term group (22.9% vs. 45%) than in the preterm group (P value 0.002).

In a similar vein, Asakura et al. [5] observed that the majority of patients who gave birth at 34 weeks had a short cervix (75%), an absence of CGA (68.8%), a combination finding of a short CL without CGA (62.5%), or findings of short CL without CGA (43.8%). These occurrences occurred at considerably greater rates than in individuals who gave birth at a gestational age of 34 weeks or less (p 0.04).

Not only that, but Pires et al. [10] discovered that there was a significant correlation between CGA not being detected with SPTD before 37 weeks' (p 0.001; OR = 194.5) and before 35 weeks' gestation (p 0.001; OR = 129.6).

5. Conclusion

Because of the requirement for specialised perinatal care, accurately predicting preterm and extremely preterm birth (gestational age before 32 weeks) is a significant difficulty. It would seem that CGA detection is a useful signal for this. CGA should be studied in conjunction with other markers to see which ones are most useful for predicting the likelihood of a premature birth.

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