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Ultrasonographic assessment of the uterocervical angle in the second trimester of pregnancy as a predictor of spontaneous preterm birth

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AIM: To evaluate the uterocervical angle in the second trimester in singleton pregnancies as a predictor of spontaneous preterm labour.

MATERIAL AND METHODS: An observational cohort study was carried out from March 2022 to May 2023, including consecutively selected patients with singleton pregnancies who underwent routine examinations between 18.0 and 23.6 weeks to analyse the risk of prematurity. The uterocervical angle (UCA) measurement was added to the transvaginal ultrasonographic analysis of the cervix. Birth-related outcomes were prospectively collected.

RESULTS: patients were evaluated. The occurrence of spontaneous preterm birth (sPTB) before 37 weeks was 12%, with 50 patients. An association was observed between a more obtuse uterocervical angle and the occurrence of birth before 37 weeks, with the area under the curve of 0.636 (p=0.003; 95% CI: 0.546–0.726). The cutoff point of 77.2 degrees demonstrated a sensitivity of 80% and specificity of 29.4% (p=0.003), a positive predictive value of 13.6%, and a negative predictive value of 91.3%, with a positive likelihood ratio of 1.13 and negative 0.88.

CONCLUSION: The measurement of UCA in the second trimester of pregnancy is associated with the occurrence of sPTB. The result corroborates recent literature conclusions that UCA is a relatively recent predictor of sPTB. New evidence in different populations may contribute to its possible incorporation into prematurity risk assessment.

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Introduction

Prematurity is the main dilemma in paediatrics and represents the largest cause of mortality and morbidity.[1,2] Despite advances in therapies and structure achieved mainly at the end of the last century, more than 900.000 deaths worldwide occurred because of complications associated with premature births in 2022.[3] Short-term events such as bronchopulmonary dysplasia, necrotising enterocolitis, intraventricular haemorrhage, and septicaemia are causes of exhaustion in intensive care units (ICUs). In the medium and long term, changes in neuropsychomotor development, susceptibility to infections, and cardiovascular diseases represent important obstacles to the functionality of these individuals.[2,4,5]

Worldwide, premature births—defined by the World Health Organization as birth before 37 weeks of gestation—occur in 9.9% of all pregnancies.[6] Although factors such as maternal diseases or foetal development disorders often cause early therapeutic termination of pregnancy, in 40%–45% of cases, there is no defined aetiology, and are called spontaneous premature labour (PTB). The mechanisms involved are complex and not fully understood.[7–11]

In recent years, studies have sought methods for early detection of patients at risk for spontaneous preterm birth (sPTB) through clinical history, biochemical tests, and ultrasound predictors. However, the multifactorial pathophysiology that involves sPTB and the heterogeneity of populations did not allow the implementation of universal methodologies capable of identifying situations subject to intervention until now.[8,12]

In this context, the analysis of cervical remodelling and shortening using transvaginal ultrasound (TVUS) has been the most applied method, with the best cost-benefit for predicting prematurity.[13–15] Despite being the most widely used technique for predicting sPTB today, universal screening by measuring cervical length (CL) using TVUS is still subject to questioning, and new markers have been studied.[16–18]

The uterocervical angle (UCA), a triangular segment formed between the longitudinal axis of the cervix and the lower portion of the anterior wall of the uterus, has been proposed as a new predictor of sPTB in the general population, with promising results and good reproducibility. The hypothesis is based on remodelling promoted by changes linked to pregnancy, with tension forces on the cervical canal. The less obtuse UCA acts as a containment mechanism, reducing direct tension on the cervical canal.[19–26]

This study aims to evaluate the measurement of UCA by TVUS in the second trimester of pregnancy as a universal screener for sPTB in asymptomatic pregnant women with a singleton foetus.

Methods

An observational cohort study was carried out between March 2022 and May 2023, inviting all pregnant women with a single foetus during this period who underwent routine TVUS in the second trimester (between 18 and 24 weeks) to investigate the risk of prematurity.

Pregnant women over 18 years of age, asymptomatic, with a single foetus and submitted to transvaginal analysis of the cervix in the second trimester were included in the study consecutively. The exclusion criteria were the absence of a compatible image for adequate measurement during the examination, loss of follow-up with the impossibility of collecting data related to the evolution of pregnancy, therapeutic premature termination of pregnancy, multiple pregnancies, and patients undergoing pessary or cerclage prior to analysis. The study was approved by the local ethics committee and all invited patients signed the informed consent form.

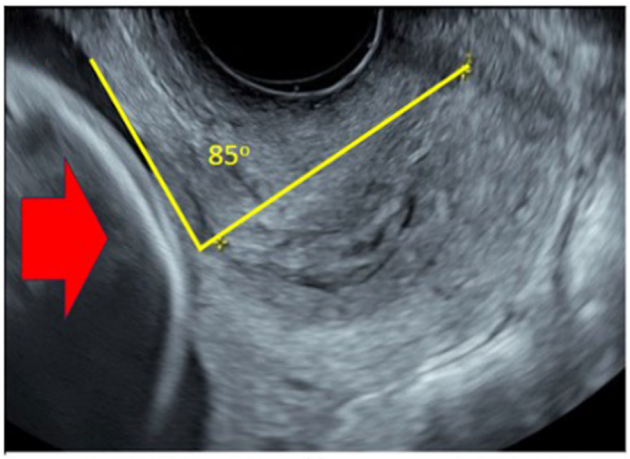
The data were collected by a professional with experience in ultrasound and four devices: one GE Voluson S8, two GE Voluson S6, and one Samsung HS 40, with the devices having similar settings and features. The measurement of ultrasound parameters was carried out using a standardised exam to measure the cervix: after bladder emptying, in lithotomy position, with the introduction of the transvaginal probe into the anterior fornix, without exerting pressure on the cervix, obtaining a sagittal cut of the uterine cervix and at least three centimetres of the lower portion of the anterior myometrial wall.

The UCA is defined as the area bounded by the cervical canal and the lower portion of the anterior wall of the uterus. The line of the cervical canal is drawn between the internal and external OS, being considered the straight distance even in curved cervical canals. The second line was drawn parallel to the lowest segment of the myometrial wall, outlining it in a straight line, intersecting with the first line. The resulting angle between the two lines is the anatomical representation of the UCA (Figure 1).

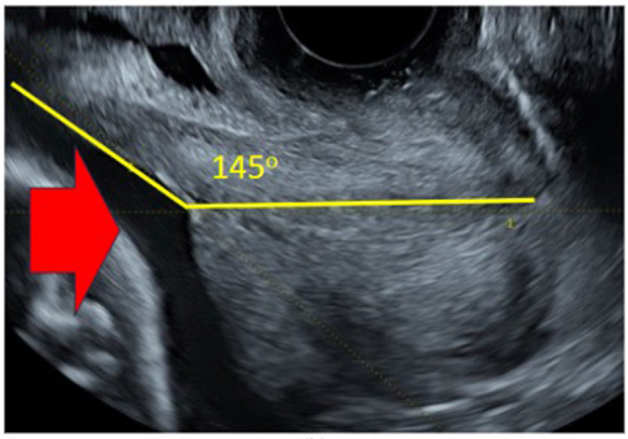
The measurement of UCA was added to the routine assessment of the cervix, already usually carried out during the second trimester examination. After the standard CL measurement, the UCA was obtained through three measurements, with the most obtuse UCA being considered among the technically appropriate measurements.

Demographic data and ultrasound findings obtained in the cervix analysis were collected for comparison, such as the presence of funnelling, cervical gland area, and amniotic fluid sludge. Data related to pregnancy evolution and childbirth follow-up were collected later via telephone contact. Subsequent analysis of the images and completion of the data instrument were carried out without the examiner having information about the case.

For statistical analysis, a descriptive evaluation was carried out for all variables with a comparison between the groups of patients delivering before 37 weeks and pregnant women delivering at term. Quantitative variables were expressed as median and interquartile range, using the Mann–Whitney U test for comparison between the groups. For qualitative variables, the chi-square test (with Yates correction) or Fisher's exact test was applied, with values expressed as a percentage. The receiver operating characteristic (ROC) curve was used to analyse performance with the area under the curve and determine the UCA cutoff



(a)



(b)

Figure 1 – Uterocervical angle and tension forces of the pregnant uterus. (a) less obtuse angle, constituting a natural barrier to tension forces on the cervical canal (red arrow). (b) more obtuse angle, with tension forces exerted directly on the cervical canal (red arrow).

value for predicting prematurity. The software used was SPSS software (version 26, IBM Corporation, Armonk, NY, United States), with a significance level of 5%.

Results

Of the 451 consecutive eligible patients, 10 patients (2.2%) were excluded from the study due to premature therapeutic termination of pregnancy. These include patients with systemic diseases such as diabetes or severe pre-eclampsia and 1 patient with premature rupture of membranes with associated infection. Sixteen patients (3.5%) were excluded due to loss of follow-up and 15 (3.4%) due to photographic images that would not allow adequate measurement of the UCA. The result was obtained from 410 patients. The general characteristics of the studied population are listed in Table 1.

Prematurity was found in 50 cases (12.1%), with 40 patients (9.7%) progressing to delivery between 34 and 37 weeks of gestation and 10 (2.4%) to delivery before 34 weeks. The median gestational age at birth in the group delivering before 37 weeks was 35.1 weeks (IQR 34.1 – 36.2) and in the group delivering at term was 39.1 weeks (IQR 38.1 – 40.1). There was a significant difference in caesarean delivery rates, with 18 patients (36%) in the premature birth group and 220 patients (61.1%) in the group that delivered at term (p=0.001). Among infants born before 37 weeks of gestation, higher rates of admission to ICUs were observed with 27 cases (54%) when compared to infants born at term, with 8 patients (2.2%) (p<0.001). The neonatal outcomes are listed in Table 2.

Maternal age, ethnicity, smoking percentages, preconception body mass index, presence of arterial hypertension

Table 1
Maternal characteristics and comparison between groups (sPTB and birth at term). Data presented as median (interquartile range) or absolute number (percentage).

Maternal characteristics		Groups		*p* value
		sPTB (<37 weeks) n=50	Birth at term (≥37 weeks) n=360	
Age (years)		34.4 (27.4–41.5)	34.2 (28.9–39.7)	0.573 (a)
Ethnicity	White	43 [86%]	310 [86,1%]	0.704 (b)
	Black	1 [2%]	16 [4.4%]	
	Mixed	6 [7%]	34 [9.2%]	
Nulliparous		31 [62%]	220 [61.1%]	0.184 (b)
Natural conception		46 [92%]	327 [90.8%]	1.000 (b)
Prior sPTB		4 [8%]	18 [5.0%]	0.409 (b)
Prior cervical conization		1 [2%]	7 [1.9%]	1.000 (b)
Prior curettage		5 [10%]	17 [4.7%]	0.168 (b)
Tobacco use		3 [6%]	17 [4.7%]	0.723 (b)
Body mass index at conception (kg/m^2)		22.2 (16.8 – 27.7)	22.9 (19.0 – 26.9)	0.585 (a)
Hypertensive disorder		1 [2%]	6 [1.7%]	0.601 (b)
Diabetes		2 [4%]	2 [0.6%]	0.075 (b)
Gestational age at TVUS (weeks)		22.1 (21.0 – 23.1)	22.3 (21.3 – 23.3)	0.093 (a)
Cervical length (mm)		36.0 (25–47)	37.0 (29–45)	0.651 (a)
Cervical length ≤ 25mm		3 [6%]	7 [1.9%]	0.110 (b)
Uterocervical angle (degrees)		99.0 (57.5 – 140.6)	89.0 (59.8 – 118.2)	0.002 (a)
Funnelling		2 [4%]	8 [2.2%]	0.350 (b)
Sludge		5 [10%]	13 [3.6%]	0.055 (b)
Cervical gland area		1 [2%]	2 [0.6%]	0.324 (b)

Note: sPTB: spontaneous Preterm Birth; TVUS: transvaginal ultrasound. (a)Mann–Whitney U test; (b) Fisher's exact test.

Table 2
– Perinatal outcomes and comparison between groups (sPTB and birth at term). Data presented as median (interquartile range) or absolute number (percentage).

Perinatal outcome	Groups		*p* value
	sPTB (<37 weeks) n=50	Birth at term (≥37 weeks) n=360	
Gestational age at delivery (weeks)	35.1 (34.1 – 36.2)	39.1 (38.1 – 40.1)	< 0.001 (a)
Caesarean	18 [36%]	220 [61.1%]	0.001 (c)
Female neonate	28 [56%]	168 [46.7%]	0.277 (c)
ICU admission	27 [54%]	8 [2.2%]	< 0.001 (b)

Note: sPTB: spontaneous Preterm Birth; ICU: intensive care unit. (a) Mann–Whitney U test; (b) Fisher's exact test (c) Yates test.

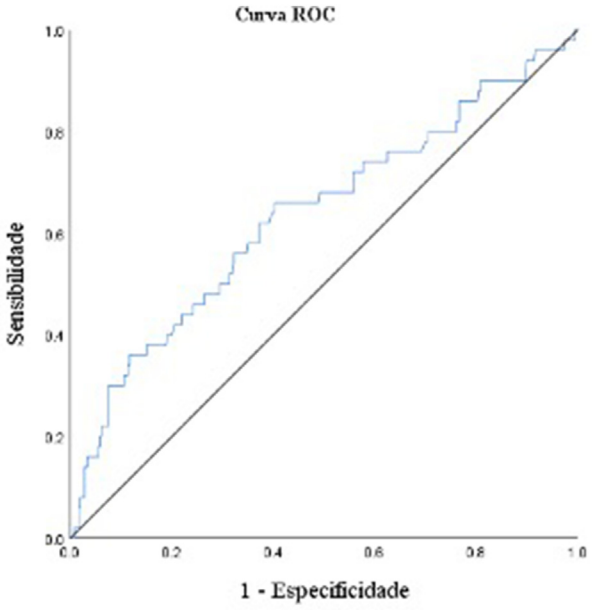


Figure 2 ROC curve – Prematurity < 37 weeks. ROC, receiver operating characteristic.

or diabetes, previous premature birth, antecedents related to previous surgical manipulation of the cervix, parity, and percentage of natural conception method did not show a statistically significant association with the occurrence of sPTB, with similarities between groups (Table 1).

The UCA showed a statistically significant association with the occurrence of prematurity. The median obtained in patients delivering before 37 weeks was 99 degrees (IQR 57.5 – 140.6), while in patients delivering at term, it was 89 degrees (IQR 59.8 – 118.2) (p=0.002). ROC curves were generated to evaluate the association between UCA and sPTB (Figure 2). The area under the curve was 0.63 (p=0.003; SE = 0.046; 95% CI: 0.54–0.72). A cutoff point of 77.2 degrees was chosen to obtain good sensitivity with the highest possible specificity.

The cutoff point corresponding to the UCA of 77.2 degrees demonstrated a sensitivity of 80%, specificity of 29.4%, positive predictive value of 13.6%, negative predictive value of 91.3%, positive likelihood ratio of 1.13 and negative of 0.88 (Table 3). In a subsequent analysis, the cutoff point of 95 degrees was applied, which demonstrated sensitivity of 58%, specificity of 64.2%, positive predictive value of 18.3%, negative predictive value of 91.7%, positive likelihood ratio of 1.62, and negative likelihood ratio of 0.62 (Table 3).

Performance calculations from false positives were realised. The percentage of false positives for the cutoff point of 77.2 degrees was 86%. When using the cutoff point of 95 degrees, the false positive rate was 82%. The cutoff point with the lowest false positive rate was 137.8 degrees, with a detection rate of 14% and 59% of false positive (Table 4).

Table 4
– Uterocervical angle cutoff points and spontaneous preterm birth prediction comparing false positive rate.

Parameters	Detection rate (%)	False-positive rate (%)
UCA > 77,2°	80	86
UCA > 95,1°	58	82
UCA > 137,8°	14	59

UCA: uterocervical angle.

The CL showed no significant difference between the two groups. The median CL was 36 mm (20–59) in the prematurity group and 37 mm (14–70) in the group with a term birth (p=0.651) (Table 1). During the study, 10 patients with CL less than or equal to 25 mm were observed. All of them received progesterone to prevent sPTB. Seven patients (70%) progressed to at-term birth and three (30%) to premature birth, requiring ICU in one case (10%).

The other ultrasound predictors presented similarities between the two groups (Table 1). Membrane funnelling was observed in two patients (4%) with premature birth and in eight patients (2.2%) with at-term birth (p=0.350). The absence of cervical gland area was observed in one patient (2%) with sPTB and in two patients (0.6%) without sPTB (p=0.324). Amniotic fluid 'sludge' was observed in five patients (10%) who delivered before 37 weeks and in 13 (3.6%) who delivered after 37 weeks (p=0.055). Patients with 'sludge' received antibiotic therapy according to the service's protocol, with 14 (77.7%) progressing to delivery after 37 weeks and four (22.3%) to sPTB, with two newborns (11.2%) requiring ICU.

Discussion

This is the first study about the performance of the UCA as a predictor of sPTB in the Brazilian population. In our sample, an association between a more obtuse UCA and the occurrence of prematurity was observed. However, this association proved to be poor, with an area under the curve of 0.63 and without a cutoff point with good sensitivity that does not generate high rates of false positives. Similar results were observed by Farràs Llobet *et al.* (2020), with an area under the curve of 0.58 for detecting birth before 37 weeks, and Sawaddisan *et al.* (2020), with an area under the curve of 0.70 in patients with CL > 25 mm.[24,25] These results partially agree with the strong association obtained by

Table 3
– Performance of UCA cutoff points for predicting prematurity (<37 weeks).

UCA	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio
> 95.1°	58.0%	64.2%	18.3%	91.7%	1.62	0.62
> 77.2°	80.0%	29.4%	13.6%	91.3%	1.13	0.88

UCA: Uterocervical angle.

Dziadosz *et al.* (2016), with an area under the curve of 0.78.[22]

In our study, the cutoff point used to obtain a sensitivity of 80% with the best specificity (29.4%) was 77.3 degrees. The cutoff point of 95 degrees presented a sensitivity of 58% and a specificity of 64.2% in our population. Dziadosz *et al.* (2016) obtained a sensitivity of 80% and specificity of 53%, and later Singh *et al.* (2022) obtained a sensitivity of 86% and specificity of 93%.[21,22] In a meta-analysis involving 15 studies, Goldstein, Bailer, and Gonzalez-Brown (2023) obtained a sensitivity of 70% (95% CI, 66%–73%; I2 = 90%) and specificity of 67% (95% CI, 66%–68%; I2 = 97%) in detecting sPTB.[19]

The reduced sample of patients with prematurity, especially with a gestational age of less than 34 weeks, was a limitation in this study. Another important point is that patients considered to be at high risk for sPTB with CL $\leq$ 25 mm had received prophylactic treatment with progesterone or tocolysis according to the adopted protocol, modifying the result. There is consistent scientific evidence of the good performance of progesterone as an intervention for patients with short cervix.[18] Patients with other ultrasound markers in TVUS evaluation, including cervical gland area, funnelling and amniotic fluid 'sludge' also underwent treatments to prevent prematurity, modifying the outcome of the pregnancy. This is an inevitable limitation to all studies that compare screening methods because these patients must receive the most appropriate assistance possible.

Considering the strength of this study due to its use of a single examiner and the adoption of rigorous evaluation criteria, it did not aim to evaluate the variation between intra-observer measurements, which has already been reported in previous studies. Dziadosz *et al.* obtained in 2016, a Kappa coefficient of 0.94 for masked interobserver variability and 0.90 for masked intra-observer variability, showing good agreement. In 2018, Farràs Llobet *et al.* also observed good reproducibility, with an intraclass correlation coefficient of 0.82 (95% CI: 0.74 – 0.97) for masked interobserver variability.[22,27]

Regarding the characteristics of the studied population, peculiarities were observed in relation to other studies related to UCA, mainly regarding ethnicity with 86% of white patients and BMI with median of 22.9 kg/m2, with low rates of obesity. Diversity between populations is one of the most important limitations reported in review and meta-analysis studies on UCA, with significant heterogeneity.[19,23] In this context, our study brings more evidence to be added in research on the association between UCA and sPTB.

In recent years, questions about the applicability of CL as a universal screening for the risk of sPTB have stimulated research into possible new markers for predicting prematurity.[16,28] In this context, UCA has been approached as an option to be used alone or in conjunction with CL for risk analysis for sPTB. However, evidence shows that, although a more obtuse UCA is associated with the occurrence of sPTB, it does not increase risk detection rates, whether isolated or in association with CL until this moment. Further studies are needed, especially with comparative analysis between UCA and CL.[19]

Considering the association between UCA and sPTB, patients with this finding might be classified as a higher-risk group in relation to the general population and should be kept under surveillance. Together with other markers, it can be part of risk scores in the future, as cervical remodelling has several associated elements, some quantitative, and others qualitative.[8]

Prematurity is the main cause of infant morbidity and mortality in public health, and its prevalence has been maintained over the years.[3] The detection of risk cases for the administration of preventive therapies, especially in cases of spontaneous prematurity, is limited by the multifactorial pathophysiology and heterogeneity of populations. The TVUS in the second trimester of pregnancy continues to be a promising form of screening, but with still limited results in detection and universal applicability.

Conclusion

Considering the results of this study, measuring UCA in the second trimester of pregnancy is associated with the occurrence of sPTB. The result corroborates recent literature conclusions that UCA is a relatively recent predictor of sPTB, and new evidence in different populations may contribute to its possible incorporation into prematurity risk assessment.

Ethics approval and consent to participate

The Pontifical Catholic University of Campinas (PUC-Campinas) research ethics committee approved the protocol number 5.503.023.

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Authors' contributions

1. Guarantor of Integrity of the Entire Study: Nicolau EG
2. Study Concepts and Design: Reis LO
3. Literature Research: Nicolau EG
4. Clinical Studies: Nicolau EG
5. Experimental Studies / Data Analysis: Nicolau EG
6. Statistical Analysis: Nicolau EG
7. Manuscript Preparation: Nicolau EG
8. Manuscript Editing: Reis LO
9. Funding Acquisition, Project Development, Supervision: Reis LO

Conflict of Interest

The authors declare no conflict of interest.

Availability of data and materials

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

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