ARTICLE

Uterocervical angle as a second trimester screening method for the prediction of preterm birth in a Filipino population in a tertiary government hospital

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ABSTRACT

In the Philippines, universal screening in the second trimester for predicting preterm birth (PTB) has not been universally adopted and there is a lack of studies on screening locally. Recently, the uterocervical angle (UCA) has been introduced as another prediction tool for preterm labor hence it is important to validate its reliability and clinical utility.

Objectives: To correlate UCA and CL measurement and perinatal outcomes among Filipino women seen at the Philippine General Hospital from March – May 2023.

Methods: This is a prospective cohort study **(computed sample size = 144)** where both the UCA and cervical length (CL) were sonographically measured in singleton **pregnancies between 16 and 24 weeks age of gestation**. All participants were followed up until delivery. **Clinical, imaging and perinatal outcomes were collected from patient records and subsequently analyzed (Figure 4).**

Results: This prospective study included a total of 144 participants where 60% (n=87) delivered at term and 40% (n=57) delivered preterm. Among those that delivered prematurely, 70% (n=40) had spontaneous PTB between 34 to <37 weeks and 29% (n=17) at < 34 weeks. There was a significant association between the gravidity, interpregnancy interval, and history of previous PTB with spontaneous PTB ($p<0.05$). Receiver operating curves (ROC) for UCA had areas under the curve of 0.54 (95% CI 0.43-0.64, p= 0.43) and 0.55 (95% CI 0.45-64, p= 0.33) for patients who had spontaneous PTB at < 34 weeks and between 34 to < 37 weeks, respectively, showing that contrary to other publications, the UCA alone at the recommended cut-offs was not useful in predicting spontaneous PTB. A UCA of >105 degrees had very low sensitivity in predicting preterm birth at <34 (23.53 %) and between 34 to < 37 weeks (35.09%) in our population. It also had low specificities of 63.78% and 65.52%, and low diagnostic accuracy rates of 59.03% and 53.47% for predicting PTB at <34 and between 34 to <37 weeks, respectively. In this population, cervical length alone at the recommended cut-off of 25 mm was an even poorer screening tool with ROC area under the curves

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Preterm labor, uterocervical angle, cervical length, interobserver agreement

of 0.34 (95% CI 0.17-0.52, p= 0.08) for predicting PTB at <34 and 0.47 (95% CI 0.38-0.57, p= 0.58) between 34 to <37 weeks.

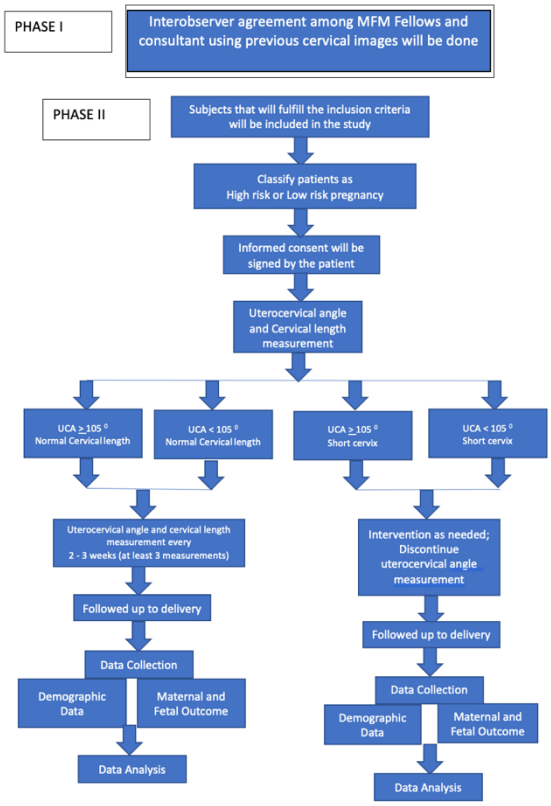

Figure 4: Complete flow chart of the study.

Conclusion: In the second trimester, both the UCA and CL were found to be poor predictors of spontaneous PTB in our study population. Our findings do not preclude the utility of these tests in assessments where a combination of risk factors such as a history of previous PTB, positive biochemical studies, and the presence of clinical indicators are included. Further research is recommended to evaluate and customize the predictive cut-offs of these tools in various populations. A correlation with the actual etiology of PTB in these cases would be more informative in designing better prediction tools.

INTRODUCTION

In perinatal medicine, preterm birth remains an unresolved issue (Greene et al, 2019). According to the United Nations International Children's Emergency Fund (UNICEF), approximately 15 million premature births occur each year. Preterm birth rates among African American women were 14.4% in 2020, this was 50% higher than rates among white or Hispanic women, which were 9.1% and 9.8%, respectively (Villasmil et al, 2020). According to local clinical practice guidelines, the Philippines has had a variable preterm birth rate ranging from 7 to 24 % in the last five years (Guinto et al, 2019).

Preterm birth is defined as a delivery occuring less than 245 days after conception. It may also occur before 37 weeks (259 days) of gestation from the first day of the last menstrual period (Resnik et al, 2019).

Preterm birth is classified based on clinical presentation as either indicated or spontaneous PTB. Indicated preterm births are induced due to a medical condition and are actively undertaken as a response to maternal or fetal compromise (Greene et al, 2019). Causes of spontaneous PTB include preterm labor, preterm spontaneous rupture of membranes, and cervical incompetence. The pathophysiologic process that triggers spontaneous PTB is still unknown but may be attributable to the following: activation of the hypothalamic-pituitary-adrenal axis, inflammation and infection, decidual hemorrhage, pathologic uterine distention, vascular disorders, progesterone insufficiency in pregnancy, stress, breakdown of maternal-fetal tolerance, and cervical disease (Guinto et al, 2019).

Despite various factors triggering spontaneous PTB, the final pathway entails premature remodeling, softening, and shortening of the cervix, which leads to cervical dilation and delivery of the fetus. The mechanical strength of the cervix relies on its collagen network. Therefore, it has been proposed that early decrease in collagen concentration and increase in smooth muscle cells may cause cervical shortening or softening leading to preterm labor (Ressel 2002).

Preterm delivery causes serious impairment to the newborn, which is a significant global health issue. Over 1.1 million newborns are lost annually due to prematurity. Preterm birth complications that cause infant mortality include pulmonary hypertension, respiratory distress syndrome, necrotizing enterocolitis, perinatal infection, and central nervous system (CNS) issues such as intraventricular hemorrhage. The Philippines has a premature neonatal mortality rate ranging from 12 to 81 percent, according to clinical practice guidelines on preterm labor (Guinto et al, 2019).

Due to the high prevalence of neonatal mortality, many interventions have been devised to prevent PTB and to improve the outcomes of preterm infants. Recommended prenatal screening tests to identify patients who are at high risk for PTB have been widely available but not routinely practiced. There are three (3) broad categories of preterm labor prediction tests: risk factor assessment, biochemical marker assessment, and cervical assessment.

Cervical assessment has been performed in a variety of ways, including digital cervical examination, transvaginal sonography, cervical elastography, quantification of cervical apparent diffusion coefficient (ADC), sonoelastography, acoustic radiation force impulse or shear wave velocity, and fetal adrenal gland biometry. However, the latter techniques call for advanced technologies and are not suitable for widespread use. Internal examination typically underestimates cervical length by 12 mm in more than 80% of women in the second and third trimesters (Singh et al, 2022). Transvaginal cervical length measurement, a powerful predictor of preterm labor, has been recommended by the American College of Obstetrics and Gynecology (ACOG) as a necessary component of preterm labor management. But recent studies have introduced the uterocervical angle (UCA) measurement as a novel way of evaluating the cervix in the second trimester. Like cervical length, the UCA is a sonographic marker that determines the angle between the cervical canal and the lower uterine segment.

Some investigations have shown that sonographic UCA can better predict PTB as compared to cervical length. A cross sectional analytical study by Khamees, R., et al in 2021 stated that having a UCA greater than 105° increased the risk for PTB as compared to cervical length measurement with a sensitivity of 86% and 27%, respectively (Singh et al, 2022). Another landmark study done by Singh, et al. in 2022, also favored UCA measurement as a better predictor of spontaneous PTB (Singh et al, 2022).

Hence, this investigation will try to evaluate UCA as a predictor of spontaneous preterm birth.

MATERIAL AND METHODS

This is an analytical prospective cohort study to evaluate the uterocervical angle measurement as a predictor of preterm birth and labor. This study involved all women at any age who had a routine second trimester scan at the University of the Philippines – Philippine General Hospital between March to May 2023 and were recruited based on the inclusion criteria: singleton pregnancies between 16-24 weeks with proven accurate dating; and exclusion criteria: multiple gestation, patients with a sonographically short cervix prior to recruitment, patients with a cerclage or pessary prior to recruitment, and patients who will require indicated preterm delivery.

All Maternal Fetal Medicine (MFM) fellowship trainees in our institution underwent didactics and hands on training to properly measure both the UCA and cervical length using an HS60 High-End Ultrasound System (Samsung, Republic of Korea). **Transvaginal measurements were performed using a high-frequency endovaginal probe. Pregnant women were instructed to empty their bladder and were placed in dorsal lithotomy position. The vaginal probe was placed in the anterior fornix without undue pressure. The sagittal view of the cervix and anterior uterine wall were then obtained with optimal magnification. The echogenic endocervical canal and surrounding hypoechoic zone of cervical mucosa were identified. The external os was visualized as the point where both anterior and posterior lips of the cervix met in the vaginal canal and the internal os as the point at the end of the endocervical canal. To measure the UCA, the first ray was determined by placing calipers along the external os to the internal os, while a second ray was drawn to delineate the lower uterine segment. The latter ray was traced along the anterior uterine segment to the lower uterine segment for at least 3 cm. (Figure 3).**

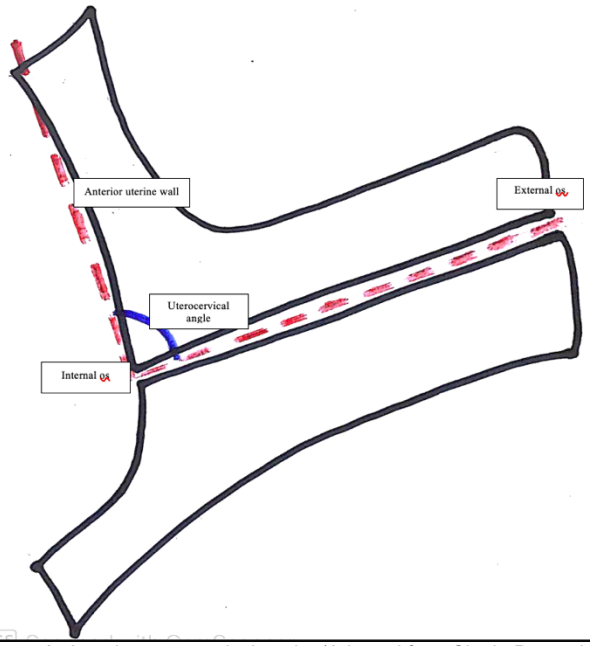

Figure 3: Anterior uterocervical angle. (Adapted from Singh, Pramod, et al. : Evaluation of Uterocervical Angle and Cervical Length as Predictors of Spontaneous Preterm Birth; Department of Radiodiagnosis and Imaging, IMS, Banaras Hindu University, Varanasi, Uttar Pradesh, Indian J Radiol Imaging 2022;32:10)

Sample size was calculated as follows:

A. Outcome accessors and interobserver agreement:
   A random sampling of images (n=30) used to determine interobserver agreement among the outcome accessors (eleven fellows-in-training and one consultant)

B. Calculation of sample population for the prospective cohort study:
   A sample size (n=144) was calculated using the following formula:

$$n = [DEFF*Np(1-p)]/ [d^2/Z^2_{1-\alpha/2}* (N-1) +p* (1-p)]$$

(CI 95% ; Alpha cut off 0.05)

Considering an attrition rate of 20%, 173 pregnant patients were to be recruited.

Statistical analysis of data including demographic details, sonographic UCA and cervical length measurements, clinical and delivery outcomes were described using mean and standard deviation (SD) for continuous variables. Categorical variables were described using frequencies and percentages.

Comparison of the outcome was performed using the Student's t test for continuous variables and the Chi- square test for categorical variables with a $p<0.05$ considered significant. A receiver operating curve (ROC) was used to determine the sensitivity and specificity of the different uterocervical angle measurements. SPSS version 20 was used to determine the sensitivity and specificity of the UCA in predicting spontaneous preterm birth outcomes. The MEDCALC calculator was used to determine the sensitivity, specificity, accuracy, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of the UCA measurements in predicting spontaneous PTB.

Validaiton of Khamees et al.'s UCA threshold cut off > 105 degrees was determined by calculating its ROC, and determination of sensitivity and specificity in a Filipino population (Khamees et al, 2021).

The correlation of the UCA measurements and cervical length were determined using Pearson's correlation.

All statistical procedures used a level of significance with p-value less than 0.05, adjusting for multiple comparisons in the analysis of variance performed.

Method Proper

After approval of our protocol by the University of the Philipines – Manila Research Ethics Board, a consultant trained MFM fellows to meet standard procedures as seen in appendix A based on the study of Singh et al. (Singh et al, 2022) Uterocervical angle measurements were classified into either of two (2) categories (>105 degrees or <105 degress) as per Khamees et al. (Khamees et al, 2021). Interobserver agreements were evaluated between "fellow versus fellow" and "fellow versus consultant." There was moderate agreement among fellows and the single consultant. We then prospectively measured the UCA and cervical length for each of the 144 participants and correlated their maternal and fetal outcomes with PTB as the primary outcome.

RESULTS

A total of 177 participants were recruited from which 144 patients were included in this prospective cohort study. Excluded patients did not complete the study or delivered elsewhere. Among the participants, 87 (60%) delivered at term and 57 (39.58%) delivered preterm. Among those who delivered prematurely, 40 (70%) had spontaneous PTB at less than 37 weeks while 17 (29%) were delivered at less than 34 weeks. Among those who delivered at less than 34 weeks, 11 had spontaneous PTB, 2 had medically indicated preterm delivery at

less than 34 weeks, and 3 had underwent ultrasound indicated cerclage.

Demographic evaluation of the 144 participants showed statistically significant differences in the following parameters: gravidity, interpregnancy interval, and history of previous PTB across both categories of early (<34 weeks) and late (>34 weeks) PTB as seen in Appendix C.

Sensitivity and specificity were not statistically significant nor discriminatory in determining spontaneous PTB in less than 34 weeks and less than 37 weeks as seen in the ROC (see Figure 1 and 2).

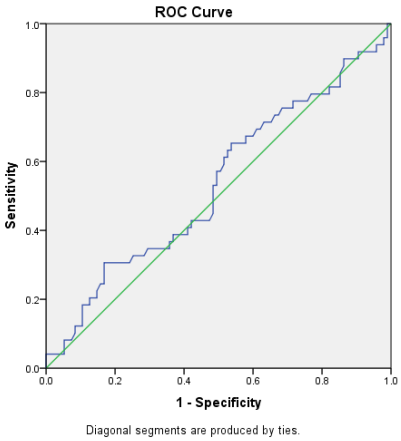

Figure 1: Receiver operating curve showing sensitivity of UCA degrees in predicting spontaneous PTB at <34 weeks in patients recruited at the outpatient department of the UP - Philippine General Hospital between March 2023 – May 2023.

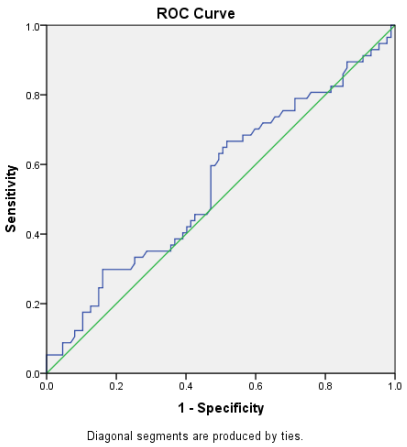

Figure 2: Receiver operating curve showing sensitivity of UCA degrees in predicting spontaneous PTB at <37 weeks in patients recruited at the outpatient department of UP- Philippine General Hospital between March 2023 – May 2023.

Using Pearson's correlation, no significant linear correlations were reported for both UCA and PTB, and cervical length and PTB. (see Table I)

Table 1: Correlation of UCA measurement with the risk of spontaneous PTB among patients seen at the outpatient department of the UP - Philippine General Hospital between March 2023 – May 2023.

	r	p-value
Cervical length	-0.002	0.983
Uterocervical angle	0.112	0.182

Furthermore, there was not enough evidence to evaluate the correlation between UCA and cervical length measurements.

From the sample population, there were 140 (97.2%) with cervical length of >25 mm and 50 (34.7%) had UCA more than 105 degrees. Analyses showed that the association between cervical length and UCA degrees with the different patient outcomes were not significant. (Table 2).

Table 2: Cervical assessment and outcomes according to term, early and late preterm.

Cervical assessment and outcome	Birth at term n=87	spontaneous PTB <37 weeks n=40	spontaneous PTB <34 weeks n=17	Total n=144	p-value
Cervical length, mm:					0.26
Cervical length < 25mm	4 (4.6%)	0 (0%)	0 (0%)	4 (2.8%)	
Cervical length > 25mm	83 (95.4%)	40 (100%)	17 (100%)	140 (97.2%)	
UCA, degrees:					0.488
UCA < 105 degrees	57 (65.5%)	24 (60%)	13 (76.5%)	94 (65.3%)	
UCA >150 degrees	30 (34.5%)	16 (40%)	4 (23.5%)	50 (34.7%)	

For the maternal and fetal outcomes: mean gestational age at delivery, birthweight, Ballard score, those with signs of preterm labor, and those who did not receive any intervention to arrest preterm labor were significantly associated with spontaneous PTB at $p < 0.05$. (see Table 3)

Table 3: Maternal and Fetal birth outcomes according to term, late and early preterm birth.

Maternal and Fetal outcome	Birth at term n=87	spontaneous PTB <37 weeks n=40	spontaneous PTB <34 weeks n=17	Total n=144	p-value
Gestational age at deliver	38.05 (.93)	35.79 (.92)	29.34 (4.62)	36.39 (3.29)	.001*

Preterm labor	4 (4.6%)	32 (80%)	9 (52.9%)	45 (31.2%)	.001*
Intervention to arrest preterm birth					.003*
None	83 (95.4%)	39 (97.5%)	12 (70.6%)	134 (93.1%)	0.0005*
Cerclage	1 (1.1%)	1 (2.5%)	1(5.9%)	3 (2.1%)	
Nifedipine	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Progesterone	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Birthweight	2963.09 (410.2)	2478.73 (383.77)	1536.0 (803.3)	2675.90 (638.45)	.001*
Ballard score	37.85 (.88)	35.73 (.99)	31.42 (3.12)	36.68 (2.25)	.001*
APGAR score >7	84 (96%)	43 (97%)	17 (72%)	143 (100%)	0.0323

DISCUSSION

One of the challenges in perinatal medicine is preterm labor. Due to the high prevalence of neonatal mortality secondary to PTB, many interventions have been devised to prevent such an event and thereby improve outcomes. Prenatal screening is recommended to identify patients who are at high risk for having preterm labor, and this includes cervical assessment.

Cervical assessment may be performed in a variety of ways. Cervical length measurement in particular is known to be a powerful predictor of preterm labor and is recommended by the American College of Obstetrics and Gynecology (ACOG) as a component of preterm labor management. But recent studies have introduced the uterocervical angle (UCA). This sonographic marker represents the angle between the cervical canal and the lower uterine segment. While international studies have shown promising results, it is important to emphasize that the use of the UCA as a standalone predictor for PTB has not been firmly established. More research using different populations are needed prior to its universal acceptance. Introducing a new predictor necessitates rigorous scientific research and validation to establish its efficacy and reliability.

In this prospective study, demographic analysis of the local population involved showed a significant association between the gravidity, interpregnancy interval and history of previous PTB with the occurrence of spontaneous PTB ($p<0.05$). Most of those who delivered preterm where multigravid and multiparous which was consistent with the study of Koullali, B. et al that also showed increased gravity and parity contributed to higher risks of spontaneous PTB (Koullali, 2020). As for the interpregnancy interval, it was noted that those who had spontaneous preterm births had a longer interval compared to those who delivered at term. This was in contrast to the study of Schummers, L. et al., where shorter interpregnancy intervals increased the risk for preterm labor due to several factors such as poor uterine recovery, nutrient depletion, increased stress and lack of preconceptional care (Schummers, 2018). As for the history of previous PTB, this was the strongest predictor for preterm labor and delivery.

For neonatal outcomes, the mean gestational age at delivery was 36.39 weeks (within the late preterm period), mean birthweight was 2675.90 grams, and mean Ballard score was 36.68 weeks. This was in contrast to studies where most preterm deliveries reported poorer neonatal outcomes. In this study, deliveries during the late preterm period were mostly due to participants spontaneously reaching active labor (cervical dilatation of at least 5-6 cm with regular contractions) where interventions to arrest labor were no longer effective.

For maternal post-delivery outcomes, mean gestational age at delivery, birthweight, Ballard score, and those with signs of preterm labor and who did not receive any intervention to arrest preterm labor, were significantly associated with spontaneous PTB ($p< 0.05$). These further emphasize the need for early detection, proper management, and specialized neonatal care to reduce materno-fetal morbidity and mortality.

On the other hand, although cervical length measurement was thought to be one of the best predictors of spontaneous preterm labor, according to a prospective study by Singh, et al (Singh et al, 2022), this parameter had a sensitivity of only 12.5%. Our study similarly showed its poor predictive ability. In both phases of this investigation, a cut off of <25 mm to establish a short cervix was not associated with spontaneous PTB. Alternatively, a number of publications did suggest that the sonographic UCA could yield better results in PTB prediction. But as seen in our study sample population, **the UCA was also a poor predictor of PTB**. Most likely, the wide range of populations included among the studies compared was a factor that lead to the current conflicting results.

CONCLUSION AND RECOMMENDATION

In the second trimester, both the UCA and cervical length were found to be poor predictors of spontaneous PTB. Our findings do not preclude the utility of these tests in assessments where they are combined with risk factors such as a history of previous PTB, positive biochemical studies, and the presence of clinical indicators for concurrent preterm labor. Further research is recommended to evaluate the predictive cut-offs of these tools in various populations. A correlation with the actual etiology of PTB in these cases would be more informative in designing better prediction tools. Studies in our Filipino population will allow us to customize cut-offs which can be used in future universal screening programs for preterm birth locally.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

CONTRIBUTIONS OF INDIVIDUAL AUTHORS

DRVR is the sole first author and corresponding author. Conceptualization, Methodology, Conduction, Analysis and Original Draft Writing of the Research were contributed by DRVR. Conceptualization, Methodology, Analysis, Manuscript Revision and Editing, and overall Supervision of the research were contributed by CLV.

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