

# Accuracy of Transvaginal Ultrasound in Prediction of Latency Period in Women with Preterm Premature Rupture of Membranes

# Ahmed Shrief Abd Elhamid, Ahmed Hamdi El-Sefi, Tarek Aly Raafat

Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, Cairo, Egypt Email: dr.ahmedelsefi@gmail.com

How to cite this paper: Elhamid, A.S.A., El-Sefi, A.H. and Raafat, T.A. (2020) Accuracy of Transvaginal Ultrasound in Prediction of Latency Period in Women with Preterm Premature Rupture of Membranes. *Open Journal of Obstetrics and Gynecology*, **10**, 1616-1630.

https://doi.org/10.4236/ojog.2020.10110145

Received: October 21, 2020 Accepted: November 24, 2020 Published: November 27, 2020

Copyright © 2020 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

http://creativecommons.org/licenses/by/4.0/

## Abstract

Background: Preterm prelabor rupture of membranes (PPROM) is a major cause of Pretem Birth (PTB), Pretem Birth (PTB) is the most significant cause of perinatal morbidity and mortality worldwide. Cervical length (CL), posterior uterocervical angle (PUCA) and anterior uterocervical angle (AUCA) have been postulated in several studies to have an important role in prediction of PTB. Up to our knowledge, this is the first study that combines the three cervical parameters in prediction of latency period in women with PPROM. Aim of the Work: To assess the accuracy of cervical length, posterior uterocervical angle and anterior uterocervical angle in prediction of latency period in women with Preterm prelabor rupture of membranes. Subjects and Methods: A Prospective cohort study on 205 women with PPROM was held at Ain Shams University Maternity Hospital, a transvaginal ultrasound was performed to measure cervical length, posterior uterocervical angle, anterior uterocervical angle. Results: A total of 205 pregnant women with PPROM were included in this study, the latency grade was within 2 days in 57 (27.8%) of cases while was after 2 days in 148 (72.2%) of cases. As regards cervical length cut-off value 25.0 mm, sensitivity was 78.9%, specificity was 65.5%, posterior uterocervical angle cut-off value 108.0°, sensitivity was 93.0%, specificity was 60.1%, and anterior uterocervical angle cut-off value 106.0°, sensitivity was 93.0%, specificity was 71.6%. Conclusion: The combination of cervical length (CL), posterior uterocervical angle (PUCA) and anterior uterocervical angle (AUCA) measurements greatly predicts the latency period in women with PPROM, and Anterior uterocervical angle (AUCA)  $\geq$ 106.0° had the highest diagnostic value in predicting latency period within two days.

# **Keywords**

Preterm Prelabor Rupture of Membranes, Latency Period, Transvaginal

Ultrasound, Posterior Uterocervical Angle, Anterior Uterocervical Angle, Cervical Length

## **1. Introduction**

Preterm prelabor rupture of membranes (PPROM) is defined as fetal membranes rupture prior to 37 weeks of gestation [1], It affects up to 3% of all pregnancies and accounts for about one third of all preterm births [2].

Complications of PPROMs include preterm birth (30%) as regards neonatal complications, most of them are allied to prematurity, including respiratory distress syndrome (RDS), hazards of oligohydraminos, sepsis, intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), cerebral palsy (CP) and perinatal death [2].

Also, behavioral and educational problems may persist to the school age and adulthood for those who survive [2].

Chorioamnionitis complicates approximately 30% to 40% of PROM before or at the limit of viability [3] [4], Abruption placenta is more common in pregnancies with PROM before or at the limit of viability than in the general obstetric population 2% to 44% versus 0.4% to 1.3% [5], There is a small risk of cord prolapse during conservative management of patients with PROM before or at the limit of viability reported a 1.9 percent incidence of cord prolapse [6].

The prevalence of retained placenta necessitating manual removal is increased 9% to 18% with PROM before or at the limit of viability, especially if membrane rupture occurs prior to 20 weeks of gestation [7].

Latency in PPROM is outlined as the interval between PROM and delivery [8]. It is worth noting that prediction of the time interval between the occurrence of PPROM to delivery may assist for better decision concerning in-utero transfer of neonates to better neonatal centers with advanced neonatal facilities and for administration of corticosteroids for the fetus lung maturation [9].

Cervical length measurement using transvaginal sonography (TVS) is an essential part of assessing the risk of preterm birth. At mid-gestation, it provides a useful method with which to predict the likelihood of subsequent preterm birth in asymptomatic women, short cervix (<25 mm) is significantly associated with the risk of preterm delivery and can also be used in those with cervical dilatation presenting with threatened preterm labor. The main advantage of cervical length measurement is its relatively high negative predictive value. However, the predictive accuracy of cervical length as a single measure is relatively limited [10].

Furthermore, posterior uterocervical angle (PUCA), which is defined as the angle between the posterior uterine wall and cervical canal [11], reflects a more accurate position of the cervix. This has been used as a more objective tool in the prediction of successful induction of labour or vaginal delivery within 24 hrs of labor induction [12]. Also, PUCA was shown to be associated with the interval from membrane rupture to delivery, posterior uterocervical angle of 113.0° had

a specificity of 65.5% for the delivery within 48 hrs of PPROM [9].

Anterior uterocervical angle (AUCA) is an ultrasonographic marker that is defined as the angle between the anterior uterine wall and cervical canal [13]. Several studies investigated the potential impact of AUCA for the prediction of preterm birth. A wide uterocervical angle  $\geq 95^{\circ}$  and  $\geq 105^{\circ}$  detected during the second trimester was associated with an increased risk for spontaneous preterm birth < 37 and <34 weeks, respectively [14].

#### 2. Aim of the Work

To assess the accuracy of cervical parameters measured by transvaginal sonography, that is cervical length, posterior uterocervical angle and anterior uterocervical angle in prediction of latency period in women with preterm prelabor rupture of membranes.

## 3. Materials and Methods

A Prospective cohort study was conducted at Ain Shams university maternity hospital, Cairo, Egypt during the time period from March 2019 to June 2020 after approval of the hospital Ethical Review Board (ERB).

Sample size was calculated using SPSS<sup>\*</sup> version 11 program, setting the type-1 error (*a*) at 0.05 and power at 80%. Results from a previous study [9] reported that the posterior uterocervical angle of  $113.0^{\circ}$  had a sensitivity of 80.4% and specificity of 65.5% for the delivery within 48 hrs of rupture of membranes, with the assumption of delivery within 48 hrs among 63.8% of cases, assuming same findings for anterior uterocervical angle, as it was not studied before in similar researches, calculation according to these values produced a minimal sample size of 186 cases, we included 205 cases for possible attrition.

A total of 205 eligible singleton pregnant women between 28 - 34 weeks of gestation in which PPROM was clinically confirmed by visualization of amniotic fluid through the cervical os during speculum examination presenting within 24 hrs and not in labor. Women with fetal heart rate abnormalities, vaginal bleed-ing, evidence of chorioamnionitis, cervical cerclage and women who were in labor at admission were excluded from the study.

All women were admitted, managed conservatively in the absence of signs of chorioamnionitis, advised to bed rest and counseled to stay in the hospital until delivery. Digital examination was avoided until the onset of labor (defined by the presence of regular and painful uterine contractions). All women were received antenatal corticosteroids (Dexamethasone 8 mg IM/12 hrs for 48 hrs (4 doses) and antibiotics (Azithromycin one gram orally upon admission and Ampicillin 2 g intravenously every 6 hrs for 48 hrs, followed by Amoxicillin 500 mg orally three times daily for an additional five days) which is recommended by NICHD and ACOG [15].

Abdominal and vaginal ultrasonographic examinations were performed by two investigators; using a 3.5 - 5 MHz transabdominal probe and 5 - 9 MHz transvaginal probe.

Fetal biometry, fetal presentation, fetal well-being and amniotic fluid volume (AFI) were assessed by transabdominal ultrasonography.

After voiding (The patient should have an empty bladder and the vaginal probe should be placed in the anterior fornix, minimizing pressure on the cervix in order to view the cervix adequately [16]), a vaginal scan was performed to measure the posterior uterocervical angle, anterior uterocervical angle (**Figure 1**).

In order to measure angles, the external and internal cervical os including the isthmus are identified and a line is drawn between them, a second line is then drawn parallel to the inner aspect of the posterior uterine wall (to measure PUCA) and anterior uterine wall (to measure AUCA), passing through the end of the first line in the internal cervical os (including the isthmus) and up to a distance of ideally 3 cm. The angles created by the intersection of the two lines are measured.

Cervical length which is the length of the cervical canal should be measured from the internal to the external cervical os (Figure 2).

Serial Modified Biophysical profile was done to monitor amniotic fluid volume and fetal well being. Delivery was indicated in cases if there was clinical evidence of chorioamnionitis, fetal distress determined by fetal heart monitoring, occurrence of intrauterine demise or reaching gestational age of 37 weeks.



**Figure 1.** Showing the posterior and anterior uterocervical angle in a patient on transvaginal ultrasound.



Figure 2. Transvaginal ultrasound measurement of cervical length.

Stata 13.1 (Stata Corp, TX) was used for the analysis. Continuous variables were reported as mean with standard deviation or median with range and categorical variables as frequency and percentages. Cox proportional hazards model was used to evaluate the relationship between the interval between rupture of membrane to delivery and transvaginal sonographic parameters (posterior uterocervical angle, anterior uterocervical angle and cervical length), parity, age, amniotic fluid index (AFI), total leukocyte count (TLC) at admission. Sensitivity, Specificity and Odds ratio for each parameter were measured. Observations of women who did not go into spontaneous labour because they were delivered due to maternal or fetal indications were treated as censored with the censoring time equal to the interval from rupture of membranes to delivery. A p value of  $\leq 0.05$  was considered significant.

# 4. Results

A total of 205 pregnant women with PPROM were included in this study.

The demographic characteristics such as age, body mass index (BMI) and parity were studied in addition to basal measurements such as total leucocyte count (TLC), amniotic fluid index (AFI), cervical length (CL), posterior uterocervical angle (PUCA) and anterior uterocevical angle (AUCA), as shown in **Table 1**, the demographic and the basal characteristics among the studied cases.

Mean gestational age at enrolment was  $32.9 \pm 1.8$  weeks with the range (29.3 - 35.6) weeks, mean gestational age at labor was  $34.8 \pm 1.5$  weeks with the range (29.7 - 36.3) weeks, mean birth weight was  $2.7 \pm 0.4$  kg with the range (1.8 - 3.4) kg and mean latency period was  $13.5 \pm 12.9$  days with the range (1 - 42) days.

The latency grade was within 2 days in 57 (27.8%) of cases while was after 2 days in 148 (72.2%) of cases, more than quarter of the studied cases had labor within two days.

	The Demographic and the Basal characteristics					
	Characte	eristics	Mean ± SD	Range		
	Age (y	Age (years) 26		18.0 - 41.0		
Demographic	BMI (kg/m <sup>2</sup> )		$21.4\pm3.3$	18.0 - 30.0		
			Ν	%		
	Parity	Primi	77	37.6		
		Multi	128	62.4		
	TLC (×10 <sup>3</sup> /mL)		$8.6\pm2.7$	4.0 - 18.0		
	AFI (cm)		$4.6\pm1.4$	2.0 - 8.0		
Basal	Cervical length (mm)		$25.4\pm2.9$	15.0 - 31.0		
	Posterior uterocervical angle (°)		$108.1\pm5.1$	91.8 - 119.0		
	Anterior uterocervical angle (°)		$106.5 \pm 5.3$	94.3 - 122.0		

Table 1. The Demographic and the Basal characteristics.

Labor findings among the studied cases showing that 133 (64.9%) of cases delivered by vaginal delivery while 72 (35.1) of cases delivered by a cesarean section.

In cases with latency period within 2 days, 49 (86%) of cases delivered by vaginal delivery and 8 (14%) of cases delivered by cesarean section while in cases with latency period after 2 days, 84 (56.8%) of cases delivered by vaginal delivery and 46 (43.2%) delivered by cesarean section (*p* value < 0.001). In cases with latency period within 2 days, mean birth weight was  $2.2 \pm 0.3$  kg while in cases with latency period after 2 days, mean birth weight was  $2.9 \pm 0.3$  kg (*p* value < 0.001).

Vaginal delivery was significantly more frequent among cases that had labor within two days. Birth weight was significantly lower among cases that had labor within two days.

Comparison according to latency period (two days) regarding demographic and basal characteristics showing that mean age in cases with latency period within 2 days was  $26.6 \pm 4.5$  years while in cases with latency period after 2 days was  $26.9 \pm 2.7$  years, Mean BMI in cases with latency period within 2 days was  $23.4 \pm 3.7$  while in cases with latency period after 2 days was  $20.6 \pm 2.7$ , in cases with latency period within 2 days, 16 (28.1%) of cases were primigravida while 41 (71.9%) were multipara, in cases with latency period after 2 days, 61 (41.2%) of cases were primigravida while 87 (58.8%) were multipara, Mean enrollment gestational age in cases with latency period within 2 days was  $33.0 \pm 1.5$  weeks while in cases with latency period after 2 days was  $32.8 \pm 1.9$  weeks.

Mean TLC in cases with latency period within 2 days was  $9.2 \pm 3.8$  while in cases with latency period after 2 days was  $8.4 \pm 2.2$  (*p* value < 0.049), Mean AFI in cases with latency period within 2 days was  $4.2 \pm 1.1$  cm while in cases with latency period after 2 days was  $4.8 \pm 1.4$  cm (*p* value < 0.016), Mean cervical length in cases with latency period within 2 days was  $23.6 \pm 3.5$  mm while in cases with latency period after 2 days was  $26.0 \pm 2.4$  mm (*p* value < 0.001), Mean posterior uterocervical angle in cases with latency period after 2 days was  $111.5^{\circ} \pm 3.9^{\circ}$  while in cases with latency period after 2 days was  $106.8^{\circ} \pm 4.9^{\circ}$  (*p* value < 0.001), Mean anterior uterocervical angle in cases with latency period within 2 days was  $104.6^{\circ} \pm 4.4^{\circ}$  (*p* value < 0.001).

As shown in **Table 2**, comparison according to latency period (two days) regarding demographic characteristics showing that only BMI was significantly higher among cases that had labor within two days, regarding basal measurements showing that TLC, posterior uterocervical angle and anterior uterocervical angle were significantly higher among cases that had labor within two days. AFI and cervical length were significantly lower among cases that had labor within two days.

As shown in **Table 3**, Diagnostic performance of basal measurements in prediction of latency period within two days showing that AFI and CL decreases

	comparison according to latency period (two days) regarding demographic and basal characteristics					
	Chai	racteristics	Within (N = 57)	After (N = 148)	P-value	
	Age (years)		$26.6\pm4.5$	$26.9\pm6.1$	0.753	
	BMI (kg/m <sup>2</sup> )		$23.4\pm3.7$	$20.6\pm2.7$	<0.001*	
Demographic	Devites	Primi	16 (28.1%)	61 (41.2%)	0.082	
	Parity	Multi	41 (71.9%)	87 (58.8%)		
	Enrollment GA (week)		33.0 ± 1.5	$32.8 \pm 1.9$	0.501	
	TLC (×10 <sup>3</sup> /mL)		9.2 ± 3.8	$8.4\pm2.2$	0.049*	
	AFI (cm)		$4.2\pm1.1$	$4.8\pm1.4$	0.016*	
Basal	Cervical length (mm)		23.6 ± 3.5	$26.0\pm2.4$	< 0.001*	
	Posterior ute	rocervical angle (°)	111.5 ± 3.9	$106.8\pm4.9$	< 0.001*	
	Anterior uterocervical angle (°)		$111.3\pm4.4$	$104.6\pm4.4$	<0.001*	

**Table 2.** Comparison according to latency period (two days) regarding demographic and basal characteristics.

 Table 3. Diagnostic performance of basal measurements in prediction of latency period within two days.

Factor	Diagnostic performance of basal measurements in prediction of latency period within two days					
	AUC	SE	Р	95% CI	Cut off	
TLC	0.515	0.049	0.744	0.420 - 0.610	-	
AFI	0.602	0.042	0.023*	0.520 - 0.685	-	
Celvical length	0.740	0.040	<0.001*	0.661 - 0.820	≤25 mm	
Posterior uterocervical angle	0.788	0.033	<0.001*	0.723 - 0.853	≥108.0°	
Anterior uterocervical angle	0.871	0.024	< 0.001*	0.824 - 0.918	≥106.0°	

AUC: Area under curve, SE: Standard error, CI: Confidence interval, \*significant.

significantly in patients with latency period < 2 days group (p < 0.023), (p < 0.001) respectively.

Furthermore, the PUCA and AUCA were observed to increase in patients latency period < 2 days group (p < 0.001), (p < 0.001) respectively.

Using receiver operator curve (ROC) statistics (**Figure 3**) showing that cervical length cut-off value 25.0 mm, sensitivity was 78.9%, specificity was 65.5%, posterior uterocervical angle cut-off value 108.0°, sensitivity was 93.0%, specificity was 60.1%, and anterior uterocervical angle cut-off value 106.0°, sensitivity was 93.0%, specificity was 71.6%.

Anterior uterocervical angle  $\geq 106.0^{\circ}$  had the highest diagnostic characteristics in predicting latency period within two days (Table 4).

Perinatal complications were significantly more frequent among cases that had labor within two days. In cases with latency period within 2 days, chorioam



Figure 3. ROC curve for basal measurements in prediction of latency period within two days.

 Table 4. Diagnostic characteristics of basal measures cutoff points in predicting latency period within two days.

	Diagnostic characteristics of basal measures cutoff points in predicting latency period within two days					
Characters	Cervical length $\leq$ 25.0 mm		Posterior uterocervical angle $\geq 108.0^{\circ}$		Anterior uterocervical angle ≥106.0°	
	Value	95% CI	Value	95% CI	Value	95% CI
Sensitivity	78.9%	66.1% - 88.6%	93.0%	83.0% - 98.1%	93.0%	83.0% - 98.1%
Specificity	65.5%	57.3% - 73.2%	60.1%	51.8% - 68.1%	71.6%	63.6% - 78.7%
DA	69.3%	62.5% - 75.5%	69.3%	62.5% - 75.5%	77.6%	71.2% - 83.1%
YI	44.5%	31.4% - 57.6%	53.1%	42.8% - 63.4%	64.6%	54.8% - 74.4%
PPV	46.9%	36.6% - 57.3%	47.3%	37.8% - 57.0%	55.8%	45.2% - 66.0%
NPV	89.0%	81.6% - 94.2%	95.7%	89.4% - 98.8%	96.4%	91.0% - 99.0%
LR+	2.29	1.77 - 2.97	2.33	1.89 - 2.88	3.28	2.51 - 4.27
LR-	0.32	0.19 - 0.54	0.12	0.04 - 0.30	0.10	0.04 - 0.25
LR	7.13	3.47 - 14.67	19.99	6.87 - 58.17	33.44	11.39 - 98.20
Kappa	0.368	0.249 - 0.486	0.410	0.305 - 0.514	0.536	0.427 - 0.645

CI: Confidence interval, YI: Youden's index. DA: Diagnostic accuracy, PPV: Positive Predictive value, NPV: Negative Predictive value, LR+: Positive likelihood ratio, LR-: Negative likelihood ratio, LR: Diagnostic odd ratio.

nionitis complicated 8 (14%) of cases, while in cases with latency period after 2 days, chorioamnionitis didn't complicate any of cases (p value < 0.001).

In cases with latency period within 2 days, neonatal sepsis complicated 24 (42.1%) of cases while in cases with latency period after 2 days, neonatal sepsis complicated 5 (3.4%) of cases (p value < 0.001).

In cases with latency period within 2 days, neonatal mortality complicated 24 (42.1%) of cases while in cases with latency period after 2 days, neonatal mortality complicated 10 (6.8%) of cases (p value < 0.001).



Figure 4. Perinatal complications.

Among all cases studied, chorioamnionitis complicated 8 (3.9%) of cases, neonatal sepsis complicated 29 (14.1%) of cases, neonatal mortality complicated 34 (16.6%) of cases (Figure 4).

## **5. Discussion**

### 5.1. Findings and Interpretation

Many studies had tested the usefulness of performing a cervical scan in the prediction of latency period in women with PPROM with conflicting results. Transvaginal sonographic imaging of cervix is safe. Hence, its use for the prediction of period to delivery in PPROM women is valuable [8]. It is considered the "gold standard" for the diagnosis of a short cervix throughout pregnancy as its accuracy was reported [17].

Our study assessed the entire cervical parameters (cervical length, posterior uterocervical angle and anterior uterocervical angle) measured by transvaginal ultrasound for better prediction of latency period in women with preterm prelabor rupture of membranes particularly when delivery in a hospital with advanced neonatal facilities is needed.

We found that AUCA and PUCA were significantly higher among cases that had labor within two days, on the other hand CL was significantly lower among the same cases.

Current results also have revealed that only BMI from all demographic characteristics was significantly higher among cases that had labor within two days, others like age, parity and GA were not significant in prediction of latency period.

## 5.2. Comparison with Other Studies

In our study, CL with cutoff value 25 mm sensitivity was 78.9%, specificity was 65.5% in predicting latency period within two days.

Rizzo *et al.* [18] who examined 92 singleton pregnancies with PPROM demonstrated that a CL < 20 mm was associated with shorter latency, also, Gire *et al.* [19] reported the same results. In the study by Ayad *et al.* [20] the mean CL was observed to increase in PPROM patients group with high latency period.

Mehra *et al.* [21] found a positive association between shorter CL and higher delivery rates within 7 days (when cutoff value < 20 mm with a sensitivity 44%, specificity 74%), even after adjustment for other confounding factors.

Mubarak *et al.* [22] showed that validity of CL in predicting the time of labor in women with PPROM when the cutoff value was 20 mm with a sensitivity 52.6%, specificity 69%.

In the study by Perez *et al.* [23]  $CL \le 20$  mm predicted latency  $\le 7$  days with a sensitivity of 57%, specificity 62% and latency  $\le 2$  days with a sensitivity of 80% specificity 57%.

In Contrast, Carlan *et al.* [24] and Fischer and Austin [25] found no relationship between CL and latency period using a 3 cm cutoff to characterize short CL. This may be attributed to the cutoff CL used in their studies.

Also, Kathir *et al.* [9] declared that CL at the time of admission following PPROM was not found to be correlated with latency interval.

About posterior uterocervical angle and anterior uterocervical angle, Our study revealed that both parameters are highly significant in prediction of latency period within two days in PPROM.

In the study by Kathir *et al.* [9] PUCA was shown to be associated with the interval from membrane rupture to delivery (p value = 0.003). PUCA of 113.0° had a sensitivity of 80.4% and specificity of 65.5% for the delivery within two days of PROM.

Lynch *et al.* [26] showed that in singletons, PUCA was not associated with PTB < 37 weeks, PUCA >  $105^{\circ}$  was associated with PTB < 32 weeks but their analysis suggested that an angle of >  $135^{\circ}$  might be a better cut off, overall, PUCA is superior to AUCA in prediction of PTB < 32 weeks.

Perez *et al.* [23] showed that AUCA > 105° predicted latency  $\leq$  7 days with a sensitivity of 78% (*p* value = 0.42, specificity 29%, PPV 49%, NPV 60%) and latency  $\leq$  2 days with a sensitivity of 90% (*p* value = 0.44, PPV 12%, NPV 96%). AUCA > 130° predicted latency  $\leq$  7 days with a sensitivity of 17% (*p* value = 0.12, specificity 69%, PPV 33%, NPV 49%) and latency  $\leq$  2 days with a sensitivity of 30% (*p* value = 0.7, specificity 76%, PPV 13%, NPV 91%). Unlikely, Perez *et al.* [23] suggested that AUCA measurement in a population of women with PPROM is not of clinical utility. These results might be affected by low number of cases that included in Perez' study (98 women).

Dziadosz *et al.* [14] showed that a wide AUCA  $\geq 105^{\circ}$  detected during the second trimester was associated with an increased risk for spontaneous preterm birth < 34 weeks, AUCA performed better than CL in their cohort.

In our study, Mean TLC in cases with latency period within 2 days was  $9.2 \pm 3.8$  while in cases with latency period after 2 days was  $8.4 \pm 2.2$  (*p* value < 0.049), Mean AFI in cases with latency period within 2 days was  $4.2 \pm 1.1$  cm while in cases with latency period after 2 days was  $4.8 \pm 1.4$  cm (*p* value < 0.016).

In the study by Ayad et al. [20] the mean TLC in patients with latency period

< 2 days, latency period 2 - 7 days and latency period > 7 days group were 13.449  $\pm$  2.959, 10.845  $\pm$  2.432 and 9.389  $\pm$  2.656, (10<sup>3</sup>/µL) respectively. The ANOVA test showed statistically significant difference in the mean of total leucocyte count among different PPROM groups with F = 16.755 and *p* value < 0.001.

Also, Ayad *et al.* [20] revealed that the mean levels of AFI in patients with latency period < 2 days, latency period 2 - 7 days and latency period > 7 days group were 2.36  $\pm$  0.95, 2.94  $\pm$  1.03 and 4.4  $\pm$  1.42 cm respectively. The results indicated that AFI increased significantly in patients with latency period > 7 days group (*p* value < 0.001).

Mubarak *et al.* [22] showed the validity of AFI in predicting time of labor in women with PPROM when cutoff 5cm, sensitivity was 71.1%, specificity was 50%, PPV was 56.3%, NPV was 65.6% and accuracy was 60%.

Vermillion *et al.* [27] showed that an AFI < 5 cm after PPROM between 24 and 32 weeks' gestation is associated with shorter latency preceding delivery; this finding has been supported by several authors [28] [29] [30] [31] which indicates that the presence of oligohydramnios in PPROM is related to a shorter latency compared to PPROM without oligohydramnios.

In contrast, Borna *et al.* [32] showed that AFI < 5 cm did not associate with shorter latency until delivery.

Among all the demographic characteristics studied in our study, Only BMI was significantly higher among cases that had labor within two days.

The study by Kathir *et al.* [9] did not show any significant relationship between latency to delivery and maternal age (p value = 0.504) or parity (p value = 0.124).

Also, Mubarak *et al.* [22] showed that No significant difference between latency to delivery and age or parity or GA.

Jeon *et al.* [30] reported that earlier GA at PPROM is significantly associated with longer latency duration.

Melamed *et al.* [33] reported that the duration of the latency period was inversely related to GA at admission, other authors [34] [35] [36] found that an inverse relationship between GA at the time of presentation and latency period was established.

In our study, Perinatal complications were significantly more frequent among cases that had labour within two days.

Ayad *et al.* [20] reported that longer latency period was associated with less neonatal morbidities.

Frenette *et al.* [37] mentioned that extended latency periods resulted in decreased prematurity-related morbidity without a consequent surge in life-threatening maternal or neonatal infectious morbidity.

Moreover, Nayot *et al.* [38] inspected latency stratified by gestational age at PPROM and examined outcomes at two latency periods: within 72 hrs of delivery and beyond 72 hrs of delivery, they found that serious and moderate neonatal morbidity incidence was decreased in patients with latency of greater than 72 hrs for infants born up to 34 weeks' gestation. However, after 34 weeks' gesta-

tion, their results did not display any benefit with conservative management.

# **5.3. Clinical Implications**

Clinically, The use of transvaginal ultrasonographic assessment of the cervix in cases of PPROM for better prediction of time interval between the occurrence of ROM to delivery may assist for better decision concerning in-utero transfer of neonates to better neonatal centers with advanced neonatal facilities and for administration of corticosteroids for the fetus lung maturation.

## 5.4. Weaknesses and Strengths

The small sample size is one of the limitations of our study. In addition, only women with singleton pregnancies were included as we considered that multiple pregnancy is already a risk factor for preterm birth.

Also, women who received magnesium sulfate as a clinical protocol for fetal neuro-protection or any other tocolytic agents were excluded from the study.

Despite the limitations, the major strength of our study is the objective nature of the transvaginal ultrasound technique for performing a full cervical scan in the prediction of latency period in women with PPROM, this technique has a short learning curve and is reproducible. It has the potential to reduce the variation between examiners in prediction of labor, determine the best time for corticosteroid administration and referral the cases to hospital with better neonatal facilities leading to a decrease in neonatal morbidities and mortalities.

# **6.** Conclusion

The combination of cervical length (CL), posterior uterocervical angle (PUCA) and anterior uterocervical angle (AUCA) measurements greatly predicts the latency period in women with PPROM, and Anterior uterocervical angle (AUCA)  $\geq$  106.0° had the highest diagnostic value in predicting latency period within two days.

# **Conflicts of Interest**

The authors declare no conflicts of interest regarding the publication of this paper.

## References

- Brown, R., Marchesi, J., Lee, Y.S., Smith, A., Lehne, B., Kindinger, L.M., Terzidou, V., Holmes, E., Nicholson, J.K., Bennett, P.R. and MacIntyre, D.A. (2018) Vaginal Dysbiosis Increases Risk of Preterm Fetal Membrane Rupture, Neonatal Sepsis and Is Exacerbated by Erythromycin. *BMC Medicine*, 16, Article No. 9. https://doi.org/10.1186/s12916-017-0999-x
- [2] Committee on Practice Bulletins-Obstetrics (2013) ACOG Practice Bulletin No. 139: Premature Rupture of Membranes. *Obstetrics & Gynecology*, **122**, 918-930. https://doi.org/10.1097/01.AOG.0000435415.21944.8f
- [3] Bengtson, J., VanMarter, L., Barss, V., Greene, M.F., Tuomala, R.E. and Epstein,

M.F. (1989) Pregnancy Outcome after Premature Rupture of the Membranes at or before 26 Weeks' Gestation. *Obstetrics & Gynecology*, **73**, 921-927. https://doi.org/10.1097/00006250-198906000-00002

- [4] Major, C. and Kitzmiller, J. (1990) Perinatal Survival with Expectant Management of Midtrimester Rupture of Membranes. *American Journal of Obstetrics and Gynecology*, 163, 838-844. <u>https://doi.org/10.1016/0002-9378(90)91080-V</u>
- [5] Hadi, H., Hodson, C. and Strickland, D. (1994) Premature Rupture of the Membranes between 20 and 25 Weeks' Gestation: Role of Amniotic Fluid Volume in Perinatal Outcome. *American Journal of Obstetrics and Gynecology*, **170**, 1139-1144. https://doi.org/10.1016/S0002-9378(94)70109-1
- Schucker, J. and Mercer, B. (1996) Midtrimester Premature Rupture of the Membranes. Seminars in Perinatology, 20, 389-400. https://doi.org/10.1016/S0146-0005(96)80006-1
- Beydoun, S. and Yasin, S. (1986) Premature Rupture of the Membranes before 28 Weeks: Conservative Management. *American Journal of Obstetrics and Gynecolo*gy, 155, 471-479. <u>https://doi.org/10.1016/0002-9378(86)90257-7</u>
- [8] El-Messidi, A. and Cameron, A. (2010) Diagnosis of Premature Rupture of Membranes: Inspiration from the Past and Insights for the Future. *Journal of Obstetrics* and Gynaecology Canada, 32, 561-569. https://doi.org/10.1016/S1701-2163(16)34525-X
- [9] Kathir, V., Maurya, D. and Keepanasseril, A. (2017) Transvaginal Sonographic Assessment of Cervix in Prediction of Admission to Delivery Interval in Preterm Premature Rupture of Membranes. *The Journal of Maternal-Fetal and Neonatal Medicine*, **20**, 1-4.
- [10] Hiersch, L., Ashwal, E., Melamed, N., et al. (2016) The Role of Cervical Length Measurment for Preterm Delivery Prediction in Women with Cervical Diltation Who Present with Threatened Preterm Labor. American Journal of Obstetrics and Gynecology, 214, S223. https://doi.org/10.1016/j.ajog.2015.10.446
- [11] Gokturk, U., Cavkaytar, S. and Danisman, N. (2015) Can Measurement of Cervical Length, Fetal Head Position and Posterior Cervical Angle Be an Alternative Method to Bishop Score in the Prediction of Successful Labor Induction? The Journal of Maternal-Fetal and Neonatal Medicine, 28, 1360-1365. https://doi.org/10.3109/14767058.2014.954538
- [12] Keepanasseril, A., Suri, V., Bagga, R., *et al.* (2007) Pre-Induction Sonographic Assessment of the Cervix in the Prediction of Successful Induction of Labour in Nulliparous Women. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, **47**, 389-393.
- [13] Daskalakis, G., Theodora, M., Antsaklis, P., Sindos, M., Grigoriadis, T., Antsaklis, A., Papantoniou, N., Loutradis, D. and Pergialiotis, V. (2018) Assessment of Uterocervical Angle Width as a Predictive Factor of Preterm Birth: A Systematic Review of the Literature. *BioMed Research International Volume*, **2018**, Article ID: 1837478. https://doi.org/10.1155/2018/1837478
- [14] Dziadosz, M., Bennett, T., Dolin, C., Honart, A.W., Pham, A., Lee, S.S., et al. (2016) Uterocervical Angle: A Novel Ultrasound Screening Tool to Predict Spontaneous Preterm Birth. American Journal of Obstetrics and Gynecology, 215, 376, e1-e7. <u>https://doi.org/10.1016/j.ajog.2016.03.033</u>
- [15] Committee on Practice Bulletins-Obstetrics (2018) ACOG Practice Bulletin No.
   199: Use of Prophylactic Antibiotics in Labor and Delivery. *Obstetrics & Gynecology*, 132, e103-e119. <u>https://doi.org/10.1097/AOG.0000000002833</u>

- [16] Kagan, K. and Sonek, J. (2015) How to Measure Cervical Length. Ultrasound in Obstetrics & Gynecology, 45, 358-362. <u>https://doi.org/10.1002/uog.14742</u>
- [17] Hernandez-Andrade, E., Romero, R. and Ahn, H. (2012) Transabdominal Evaluation of Uterine Cervical Length during Pregnancy Fails to Identify a Substantial Number of Women with a Short Cervix. *The Journal of Maternal-Fetal and Neonatal Medicine*, **25**, 1682-1689. <u>https://doi.org/10.3109/14767058.2012.657278</u>
- [18] Rizzo, G., Capponi, A. and Angelini, E. (1998) The Value of Transvaginal Ultrasonographic Examination of the Uterine Cervix in Predicting Preterm Delivery in Patients with Preterm Premature Rupture of Membranes. *Journal of Obstetrics and Gynaecology Canada*, **11**, 23-29. https://doi.org/10.1046/j.1469-0705.1998.11010023.x
- [19] Gire, C., Faggianelli, P. and Nicaise, C. (2002) Ultrasonographic Evaluation of Cervical Length in Pregnancies Complicated by Preterm Premature Rupture of Membranes. *Journal of Obstetrics and Gynaecology Canada*, **19**, 565-569. https://doi.org/10.1046/j.1469-0705.2002.00666.x
- [20] Ayad, O., Abd El Zaher, M. and Ismaeil, M. (2019) Prediction of Admission to Delivery Time by Transvaginal Ultrasonographic Assessment of the Cervix in Cases of Preterm Prelabour Rupture of Membranes. *The Egyptian Journal of Hospital Medicine*, **77**, 4840-4846.
- [21] Mehra, S., Amon, E., Hopkins, S., *et al.* (2015) Transvaginal Cervical Length and Amniotic Fluid Index: Can It Predict Delivery Latency Following Preterm Premature Rupture of Membranes? *American Journal of Obstetrics and Gynecology*, 212, 400. e1-400e9. <u>https://doi.org/10.1016/j.ajog.2015.01.022</u>
- [22] Mubarak, A. (2018) Transvaginal Cervical Length and Amniotic Fluid Index: Can it Predict Delivery Latency Following Preterm Premature Rupture of Membrane? *Medical Journal of Babylon*, 15, 78-82. <u>https://doi.org/10.4103/MJBL\_MJBL\_20\_18</u>
- [23] Perez, W., Vricella, L., Miller, C. and Mehra, S. (2018) Uterocervical Angle as a Predictor of Latency in Preterm Premature Rupture of Membranes. *American Journal* of Obstetrics and Gynecology, **218**, S259-S260. https://doi.org/10.1016/j.ajog.2017.10.363
- [24] Carlan, S., Richmond, L. and O'Brien, W. (1997) Randomized Trial of Endovaginal Ultrasound in Preterm Premature Rupture of Membranes. *Obstetrics & Gynecolo*gy, 89, 458-461. <u>https://doi.org/10.1016/S0029-7844(97)00002-1</u>
- [25] Fischer, R. and Austin, J. (2008) Cervical Length Measurement by Trans-Labial Sonography in Women with Preterm Premature Rupture of Membranes: Can It Be Used to Predict the Latency Period or Peripartum Maternal Infection? *The Journal* of Maternal-Fetal & Neonatal Medicine, 21, 105-109. https://doi.org/10.1080/14767050701866955
- [26] Lynch, T., Nicasio, E., et al. (2019) Posterior Uterocervical Angle for Predicting Spontaneous Preterm Birth. American Journal of Obstetrics and Gynecology, 220, S678. https://doi.org/10.1016/j.ajog.2018.11.1081
- [27] Vermillion, S., Kooba, A. and Soper, D. (2000) Amniotic Fluid Index Values after Preterm Premature Rupture of the Membranes and Subsequent Perinatal Infection. *American Journal of Obstetrics and Gynecology*, 183, 271-276. https://doi.org/10.1067/mob.2000.107653
- [28] Park, J., Yoon, B., Romero, R., Moon, J., Oh, S., Kim, J., et al. (2001) The Relationship between Oligohydramnios and the Onset of Preterm Labor in Preterm Premature Rupture of Membranes. American Journal of Obstetrics and Gynecology, 184, 459-462. <u>https://doi.org/10.1067/mob.2001.109398</u>

- [29] Mercer, B., Rabello, Y., Thurnau, G., Miodovnik, M., Goldenberg, R., Das, A., et al. (2006) The NICHD-MFMU Antibiotic Treatment of Preterm PROM Study: Impact of Initial Amniotic Fluid Volume on Pregnancy Outcome. American Journal of Obstetrics and Gynecology, **194**, 438-445. https://doi.org/10.1016/j.ajog.2005.07.097
- [30] Piazze, J., Anceschi, M., Cerekja, A., Brunelli, R., Meloni, P., Marzano, S., et al. (2007) Validity of Amniotic Fluid Index in Preterm Rupture of Membranes. *Journal of Perinatal Medicine*, 35, 394-398. <u>https://doi.org/10.1515/JPM.2007.077</u>
- [31] Jeon, S., Kwon, J., Kim, W. and Park, Y. (2009) Prognostic Factors Associated with Prediction of Longer Latency in PPROM. *American Journal of Obstetrics and Gynecology*, 201, S190. <u>https://doi.org/10.1016/j.ajog.2009.10.676</u>
- [32] Borna, S., Borna, H. and Hantoushzadeh, S. (2004) Perinatal Outcome in Preterm Premature Rupture of Membranes with Amniotic Fluid Index < 5 (AFI < 5). BMC Pregnancy and Childbirth, 4, Article No. 15. https://doi.org/10.1186/1471-2393-4-15
- [33] Melamed, N., Hadar, E., Ben Haroush, A., Kaplan, B. and Yogev, Y. (2009) Factors Affecting the Duration of the Latency Period in Preterm Premature Rupture of Membranes. *The Journal of Maternal-Fetal & Neonatal Medicine*, 22, 1051-1056. https://doi.org/10.3109/14767050903019650
- [34] Singhal, S., Puri, M. and Gami, N. (2012) An Analysis of Factors Affecting the Duration of Latency Period and Its Impact on Neonatal Outcome in Patients with PPROM. *International Journal of Infertility and Fetal Medicine*, 3, 87-91. https://doi.org/10.5005/jp-journals-10016-1048
- [35] Aziz, N., Cheng, Y. and Caughey, A. (2008) Factors and Outcomes Associated with Longer Latency in Preterm Premature Rupture of Membranes. *The Journal of Maternal-Fetal & Neonatal Medicine*, 21, 821-825. https://doi.org/10.1080/14767050802251255
- [36] Levy, A., Test, G., Wiznitzer, A. Holcberg, G., Zlotnik, A., Sheiner, E. and Mazor, M. (2011) Factors Affecting the Latency Period in Patients with Preterm Premature Rupture of Membranes. *Archives of Gynecology and Obstetrics*, 283, 707-710. https://doi.org/10.1007/s00404-010-1448-7
- [37] Frenette, P., Dodds, L. and Armson, B. (2013) Preterm Prelabour Rupture of Membranes: Effect of Latency on Neonatal and Maternal Outcomes. *Journal of Obstetrics and Gynaecology Canada*, 35, 710-717. https://doi.org/10.1016/S1701-2163(15)30861-6
- [38] Nayot, D., Penava, D. and Da Silva, O. (2012) Neonatal Outcomes Are Associated with Latency after Preterm Premature Rupture of Membranes. *Journal of Perinatology*, **32**, 970-977. <u>https://doi.org/10.1038/jp.2012.15</u>