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Prediction of Admission to Delivery Time by Transvaginal Ultrasonographic Assessment of the Cervix in Cases of Preterm Prelabour Rupture of Membranes

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ABSTRACT

Background: Preterm Premature Rupture of Membranes (PPROM) heralds about 30% of cases with spontaneous preterm births. Latency in PPROM is delineated as the time interval between PROM and delivery**.** It might be beneficial to predict this latency period as it may help to make a decision concerning in-utero transfer of fetus to better neonatal centers with advanced facilities and to administer corticosteroids in favor of fetal lung maturity.

Objective: The aim of the current study was to assess the usefulness of measuring the cervical parameters by transvaginal sonography mainly cervical length and posterior cervical angle, in predicting the interval from admission to delivery in women with (PPROM). **Subjects and methods:** This study was conducted at Kafr El- Shiekh General Hospital and Al-Azhar University Hospitals and included 100 pregnant women with a singleton pregnancy of gestational age between 28-34 weeks and PPROM presenting within 24 hours and not in labour.

Results: showed non-significant differences between the mean of PCA among different groups (P>0.05). Nevertheless, the results indicated that amniotic fluid index (AFI) increased significantly in patients with latency period >7days group (P<0.001). Furthermore, the mean Cervical length (CL) was observed to increase in PPROM patients' group with high latency period. The latency period had significant positive correlation with AFI and cervical length (p<0.05). Also, it had significant negative correlation with birth weight, gestational age at hospitalization, CRP, and TLC, and neonatal sepsis (p<0.05).

Conclusion: It could be concluded that assessment of Cervical length via transvaginal sonography is a valuable tool in the evaluating the interval between rupture of membranes and delivery in women with PPROM.

Keywords: PPROM, TVS, Cervical length, posterior cervical angle, latency period.

INTRODUCTION

Preterm Prelabour rupture of membranes (PPROM) is delineated as fetal membranes rupture prior to 37 weeks of gestation. It has an incidence of 2.7-7% in China and 5 -15% in America. Moreover, it precedes 30% of cases with spontaneous preterm births **(1).** Statistics propose that PPROM birth costs are eight folds more than that of uncomplicated births **(2).** Serious sequels of PPROM include Chorioamnionitis, postpartum infection, and maternal mortality owing to sepsis. Furthermore, placental abruption is frequent in PPROM cases especially if infection is present. As regard 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. Also, behavioral and educational problems may persist to the school age and adulthood for those who survive **(2).**

Clinical consequences and management of PPROM remains an area of controversy **(3).** Digital vaginal examination should be evaded as it upsurges the infection risk and reduce the latency period of entering into labour **(4).**

Latency in PPROM is outlined as the interval between PROM and delivery **(5).** 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 **(4).**

Transvaginal sonographic imaging of cervix is assumed to be safe. Hence, its use for the prediction of period to delivery in PPROM women may be valuable **(5).** It is considered the "gold standard" for the diagnosis of a short cervix throughout pregnancy as its accuracy was reported **(6).** Moreover, cervical length as determined by transvaginal ultrasound has emerged as a powerful means of predicting spontaneous preterm delivery in both women with intact membranes, and in women with PPROM **(6).** Furthermore, Posterior cervical angle (PCA) which defined as the angle between the posterior uterine wall and cervical canal **(8),** may reflect more accurate position of the cervix **(4).**

The aim of the current study was to assess the usefulness of measuring the cervical parameters by transvaginal sonography mainly cervical length and posterior cervical angle, in predicting the interval from admission to delivery in women with (PPROM).

SUBJECTS AND METHODS

This prospective study included a total of 100 pregnant women, attending at Kafr El-Shiekh General Hospital and Al-Azhar University Hospitals. This study was conducted between February 2018 to December 2018.

Ethical approval:

Approval of the research was taken from quality education assurance unit, Al-Azhar university faculty of medicine, Egypt (approval code:

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Gyn._153 Med. Research.PPROM.Cervical.Assess.TVUS._00000153). Each individual participated in the present study was fully informed concerning the nature of the disease and the diagnostic procedures.Informed consent: Informed verebal consent was obtained from all participants included in the study.

Inclusion Criteria:

The included subjects matched the following three criteria: 1) A singleton pregnancy of gestational age between 28-34 weeks. (2) PPROM clinically confirmed by visualization of amniotic fluid through the cervical os during sterile speculum examination. (3) And presenting within 24 hours of PPROM and not in labour.

Exclusion Criteria:

Pregnant ladies who were before 28th or after 34th week of gestation, with vaginal bleeding, with fetal heart rate abnormalities, with clinical or biochemical evidence of chorioamnionitis, with cervical cerclage , in labour at admission, or with history of cervical surgery as conization or trachelectomy were excluded from the study.

Complete history taking and physical examination were done at admission. Local examination and sterile speculum examination to confirm PPROM with no digital vaginal examination was performed. Then, all cases were subjected to Routine laboratory investigations including complete blood count (CBC), blood grouping, Rh typing, C-reactive protein (CRP) and urine analysis. BMI was calculated.

Ultrasound Examination:

All cases underwent: Transabdominal ultrasound examination at admission for assessment of: Fetal viability, number, fetal biometry [biparietal diameter (BPD) - fetal length (FL) - abdominal circumference (AC)], placental (site and maturity), Liquor (amount described as amniotic fluid index (AFI) and turbidity).

Transvaginal ultrasound examination was used for measuring the cervical length and posterior cervical angle by the same operator. The ultrasound equipment used was (MINDRAY DC-N2, China) using a 3.5- 5-MHz transabdominal probe and 5-9 MHz transvaginal probe.

Technique of ultrasound examination:

1) Cervical length (CL) measurement:

Patients were requested to empty their bladder before vaginal sonography. Ultrasound examination of the cervix was performed along with standard techniques in the dorsal lithotomy position; a transvaginal probe was inserted in the anterior fornix. The cervical canal was equidistant from the anterior to posterior cervical walls. A sagittal view of the cervix was attained, for visualization of the total cervical canal calipers were used to estimate the distance between the triangular area at the external os and the V-shaped notch at the internal os**.** The images of cervical length measurements were shown in **Figure 1**. No fundal pressure was done to avoid contraction the womb. Three measurements were taken, and the shortest one was noted down.

2) Posterior cervical angle (PCA) measurement:

PCA was estimated with a protractor applied to the hard copy images taken in the sagittal plane, at the internal OS level. It was the angle between an imagined track across the cervical canal and the tangential to the posterior uterine wall at its intersection with the internal os. In cases of an excessively curved cervix, the angle was determined at the junction between the line of the cervical length and the posterior uterine wall (**figure 1**).

Then, all women were admitted at the hospital, managed expectantly in the absence of signs of chorioamnionitis, restricted to bed rest and received antenatal corticosteroids (Dexamethasone 6mg twice daily for 48 hours) and antibiotics (Amoxicillin/ Sulbactam "Unictam" 3 gram per day in two divided doses intravenously for 48 hours). Subsequently it was changed to oral therapy in form of Erythromycin 250mg, four times daily for 10 days and counseled to stay in the hospital until delivery.

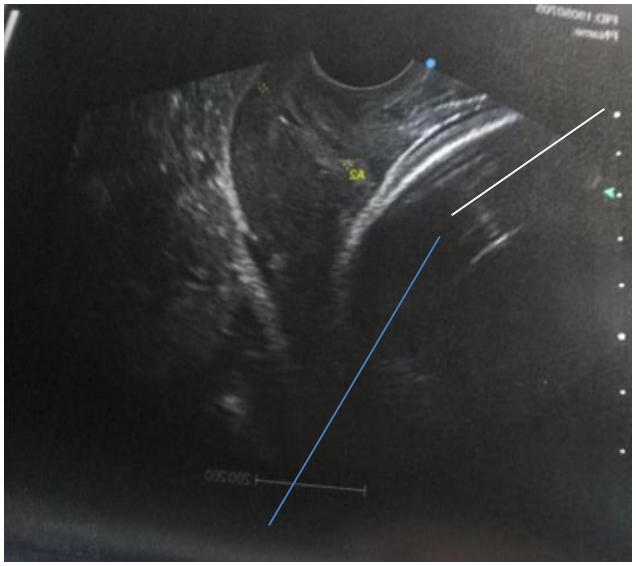

Figure 1: Transvaginal ultrasound of the cervix showing cervical length and posterior cervical angle.

Latency periods between PROM at admission and delivery were recorded to be correlated with demographic, clinical and investigational data and ultrasonographic results of CL and PCA at admission.

In the present study, statistical analyses of data were carried out using SPSS version 23.

RESULTS

PPROM patients' were divided into 3 groups according to latency period which was calculated from PPROM to delivery; (latency period <2 days, latency period 2-7 days, and latency period > 7 days). The means of age were 25.57 ± 3.64, 24.95 ± 2.75 and 25.14 ± 3.56 years and the means of BMI were 27± 4.65, 27.13 ± 4.77 and 25.7 ± 4.85 kg/m^2 for patients with latency period <2 days, latency period 2-7 days and latency period > 7 days group, respectively (Table 1).

The ANOVA test showed non-significant differences between the mean of age and BMI among different groups (F=0.259, P=0.772 and F=0.974, P=0.381, respectively). In contrast the ANOVA test showed significant differences between the means of gestational age at both admission and delivery as well as the birth weight among different groups (F=11.358, P<0.001, F=3.154, P=0.047 and F=6.197, P=0.003, respectively), where the means of gestational age at both admission was 31.6 ± 1.97, 32 ± 1.49 and 30.38 ± 1.29 weeks, respectively and that at delivery was 31.6 ± 1.97, 32.55 ± 1.32 and 32.05 ± 1.22 weeks, respectively as well as the mean birth weight was 2101.1 ± 383.1, 2288.12 ± 323.8 and 2030.4 ± 299.4 days, respectively in latency period <2 days, latency period 2-7 days and latency period > 7 days group (Table 1). Among pregnancies complicated by PPROM, women with a latency period more than 7 days had a lower gestational age at admission than other groups (P=0.005 and 0.001; respectively). The results revealed that there was significantly increased in the mean gestational age at delivery from patients with latency period (2-7 days) to latency period <2 days group (P=0.049). As for birth weight, the weight increased significantly from patients with latency period <2 days to those with latency period 2-7 days group (P=0.043) whereas, there was a significant decrease in birth weight in patients with latency period >7 days compared to those with latency period (2-7 days) (P>=0.001) (Table 1).

Table (1): Age, BMI, gestational age at admission and delivery, and birth weight of patients with PPROM based on latency period (N =100).

Groups / Parameters		Latency Period (days)		
		<2 days (N=23)	**2-7 days (N=40)**	**>7 days (N=37)**
Age (years)	**Mean ± SD**	25.57 ± 3.64	24.95 ± 2.75	25.14 ± 3.56
P-value		_	NS	NS
BMI(Kg/m^2)	**Mean ± SD**	27± 4.65	27.13 ± 4.77	25.7 ± 4.85
P-value		_	NS	NS
Gestational age at hospitalization (weeks)	**Mean ± SD**	31.6 ± 1.97	32 ± 1.49	30.38 ± 1.29
P-value		_	NS	▼<0.005[a**] ▼<0.001[b***]
Gestational age at delivery (weeks)	**Mean ± SD**	31.6 ± 1.97	32.55 ± 1.32	32.05 ± 1.22
P-value		-	0.049[a*]	NS
Birth weight (g)	**Mean ± SD**	2101.1 ± 383.1	2288.12 ± 323.8	2030.4 ± 299.4
P-value		-	▲0.043[a*]	▼0.001[b***]

- [a]: significant difference from Latency Period < 2days, [b]: significant difference from Latency Period 2-7days,
- *: P ≤0.05, **: P ≤0.01, ***: P ≤ 0.001. ▲Increased ▼ decreased, - NS = Non significant

Moreover, The results (Table 2) showed markedly decrease in the mean level of CRP in PPROM patients' groups with high latency period P<0.001, where, the mean levels of CRP in patients with latency period <2 days, latency period 2-7 days and latency period > 7 days group were 62 ± 29.37, 18.8 ± 17.44 and 7.44 ± 4.69, mg/dl respectively. The results indicated that serum CRP concentration decreased significantly from patients with latency period <2days to patients with latency period >7days group (P<0.001).

Table (2): Mean levels of serum CRP and mean TLC among PPROM patients' groups.

Groups / Parameters		Latency Period (days)		
		<2 days (N=23)	**2-7 days (N=40)**	**>7 days (N=37)**
CRP (mg/dl)	**Mean ± SD**	62 ± 9.37	18.8 ± 1.44	7.44 ± 1.69
P-value		-	▼<0.001[a***]	▼<0.001[a.b***]
TLC (10^3/µL)	**Mean ± SD**	13.449 ± 2.959	10.845 ± 2.432	9.389 ± 2.656
P-value		_	▼<0.001[a***]	▼<0.001[a***]
				▼<0.018[b*]

- [a]: significant difference from Latency Period < 2days, [b]: significant difference from Latency Period 2-7days,
- *: P ≤0.05, **: P ≤0.01, ***: P ≤ 0.001.
▲Increased ▼ decreased, - NS = Non significant

Furthermore, the mean TLC in patients with latency period <2 days, latency period 2-7 days and latency period > 7 days group were 13.449 ± 2.959, 10.845 ± 2.432 and 9.389 ± 2.656, (10^3/µL) respectively. The ANOVA test showed statistically significant difference in the mean count of total leucocytes among different PPROM groups with F=16.755 and P<0.001.

The ANOVA test showed non-significant differences between the mean of PCA among different groups (P>0.05).

Nevertheless, 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 ± 0.95, 2.94 ± 1.03 and 4.4 ± 1.42 cm respectively. The results indicated that AFI increased significantly in patients with latency period >7days group (P<0.001). Furthermore, the mean CL was observed to increase in PPROM patients' group with high latency period. The means CL in patients with latency period <2 days, latency period 2-7 days and latency period > 7 days group were 23.35 ± 3.7, 25.3 ± 3.8, and 25.73 ± 2.72 mm respectively(Table 3).

Table (3): Sonographic data for PPROM patients' groups.

Groups / Parameters		Latency Period (days)		
		<2 days (N=23)	**2-7 days (N=40)**	**>7 days (N=37)**
PCA	**Mean ± SD**	118.522 ± 10.73	117.03 ± 8.1	116.16 ± 9.92
P-value		-	NS	NS-
AFI	**Mean ± SD**	2.36 ± 0.95	2.94 ± 1.03	4.4 ± 1.42
P-value		-	NS	▲<0.001[a,b***]
Cervical length (mm)	**Mean ± SD**	23.35 ± 3.7	25.3 ± 3.8	25.73 ± 2.72
P-value		-	▲0.05[a*]	▲0.01[a**]

- [a]: significant difference from Latency Period < 2days, [b]: significant difference from Latency Period 2-7days, - *: P ≤0.05, **: P ≤0.01, ***: P ≤ 0.001. ▲Increased ▼ decreased. - NS = Non significant

In the studied subjects the latency period had significant positive correlation with AFI and cervical length (p<0.05). Also, it had significant negative correlation with birth weight, gestational age at hospitalization, CRP, and TLC, and neonatal sepsis (p<0.05) (figure 2).

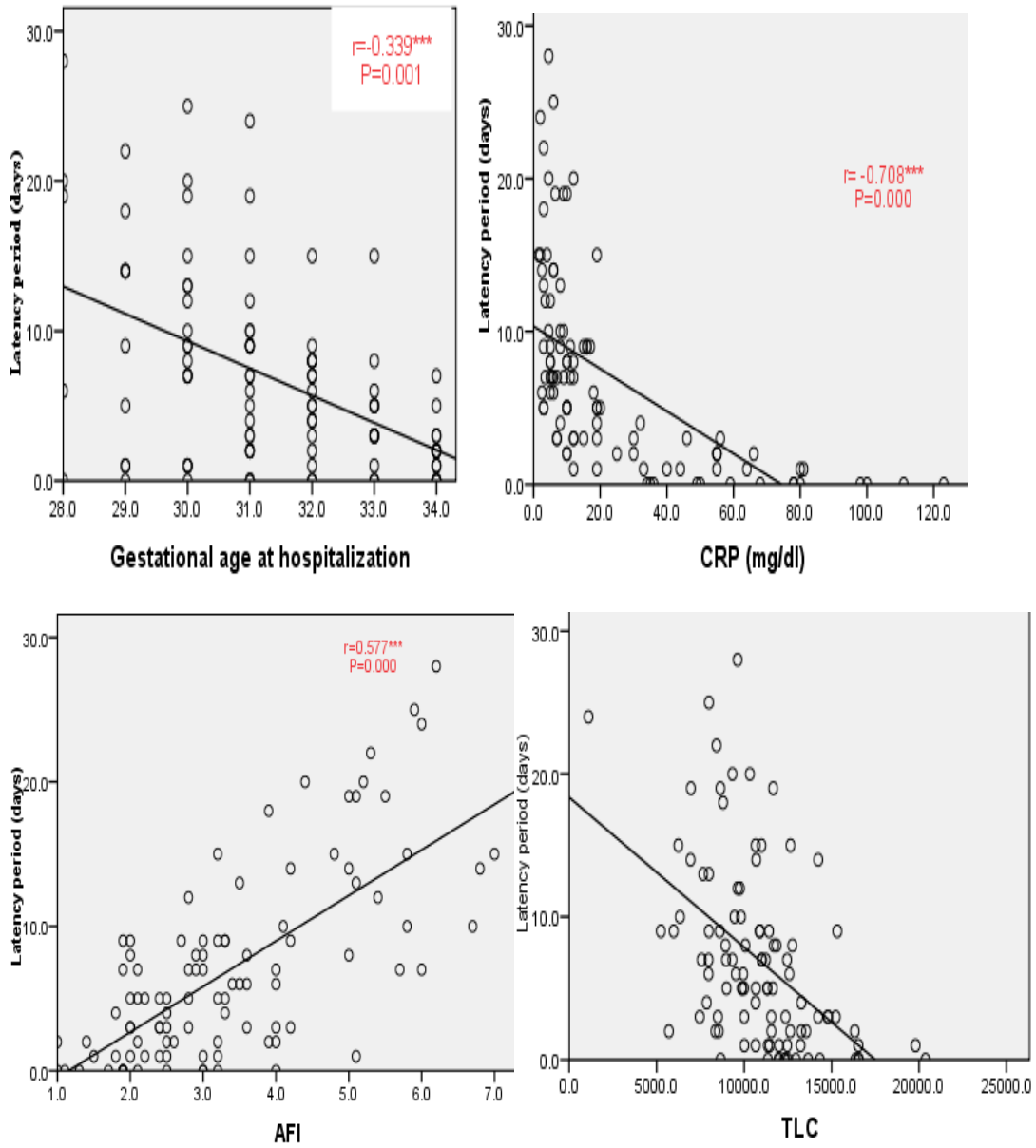

Figure (2): Correlation between latency period, and Other Parameters including Gestational age at hospitalization, CRP, AFI, and TLC.

At last but not least, The ROC curve declared that at a cervical length cutoff value of 23.5 cm cervical length had a sensitivity, specificity, 52.2%, 78.4% respectively (Figure 3).

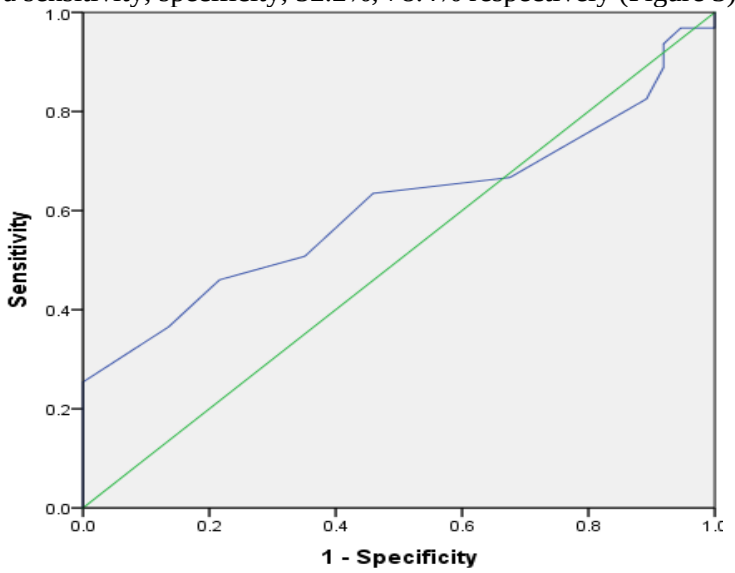

Figure (3): Receiver operating characteristic (ROC) curve of cervical length.

DISCUSSION

The competence to expect the usual sequence and duration of the latency period is still limited, and numerous literatures that attempted to clarify the factors affecting it were conducted in the absence of conventional care [9].

Our findings that longer latency period was associated with less neonatal morbidities agreed with **Frenette *et al.*** [10] who 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.*** [11] who inspected latency stratified by gestational age at PPOMM and examined outcomes at two latency periods: within 72 hours of delivery and beyond 72 hours of delivery. They found that serious and moderate neonatal morbidity incidence was decreased in patients with latency of greater than 72 hours for infants born up to 34 weeks' gestation however, after 34 weeks' gestation, their results did not display any benefit with expectant management.

Current results also have revealed that there was no statistically significant difference between the three groups as regard age and BMI. Similarly, **Kathir *et al.*** [4] didn't find any momentous association between latency to delivery and maternal age or parity. Furthermore, Length of latency until delivery appeared to be inversely correlated with the gestational age at which PPROM occurs.

This was in correspondence with **Peaceman *et al.*** [12] research on the interval from time of PPROM to delivery. They observed that median latency between 24-28 weeks was analogous at around 9 days, but it was significantly shorter with PPROM at 29, 30, and 31 weeks ($p<0.001$).

In addition, **Frenette *et al.*** [10] found that the mainstream of later gestational age women were had latency periods of less than 48 hours, while the majority of women in the earlier gestational age group were associated with latency greater than 48 hours.

Several studies have outlined the fact that in cases with PPROM, the latency period is inversely correlated with gestational age such as, **Nayot *et al.*** [11] who reported that extension before delivery for 72 h as a minimum was detected in 67% of gestations between 25 and 28 weeks, but in only 10% of pregnancies between 33 and 36 weeks.

Melamed *et al.* [9] also demonstrated a significant association between early gestation and latency period.

Also, the results of the present work indicated markedly decline in the mean level of CRP in PPROM patients' groups with high latency period ($P<0.001$). Furthermore, a marked decrease in the mean total leucocytic count (TLC) was observed in PPROM patients' group with high latency period

However, **Çetin *et al.*** [13] found that there was no significant correlation between the mean C-reactive protein (CRP), sedimentation rate, and leukocyte counts at the time of PPROM diagnosis and the latency period in groups.

Musilova *et al.* [14] stated that maternal WBC count at the admission point in time cannot aid as a non-invasive screening means for identifying complications in PPROM ladies.

As regard sonographic parameters for prediction of length of latency period, TVS of cervical length has professionally served to predict spontaneous preterm delivery in women without PROM in a plenty of former studies [15].

Carlan *et al.* [15] has confirmed the safety of transvaginal sonography (TVS) without upsurge in peri-partum infection or diminution in latency period compared to those who did not undergo TVS.

The ANOVA test showed non-significant differences between the mean of PCA among different groups ($P>0.05$). Nevertheless, the results showed progressively increase in the mean of AFI in PPROM patients' groups with high latency period ($P<0.001$). Furthermore, the mean CL was observed to be increased in PPROM patients' group with high latency period.

Many studies revealed that short cervix was notably concomitant with premature delivery after PPROM [13].

Moreover, our results were in line with a recent study conducted by **Mubarak** [16], who found a significant difference in AFI which was lesser and a highly significant difference in CL which was shorter in women delivered within 7 days.

Unlikely, **Fischer and Austin** [17] proclaimed that although cervical length is a crucial prognostic parameter in the preterm labour, it did not correlate with the latency period. However, with subdivision of cervical into two sections with the cut-off of 25 mm, they found significantly shorter latency periods in patients with less than 25 mm.

This can be elucidated as the shorter the cervix, the more the microbial ascent into the lower pole of the uterus, with concurrent release of pro-inflammatory mediators heading to preterm parturition. Additionally, weakness of the cervix might trigger herniation of the amniotic sac and shortening the barrier and also promoting bacterial ascent and its consequences [18].

In contrast, **Borna *et al.*** [19] showed that AFI <5 cm were not associated with shorter latency until delivery.

Also in contrary to the presenting study, a recent study done by **Kathir *et al.*** [4] declared that cervical length at the time of admission following PPROM was not found to be correlated with latency interval. However their outcomes showed that posterior cervical angle assessment using TVS was a beneficial tool in predicting the latency interval in women with PPROM.

As regard the best cut off value for cervical length it was found that at cutoff of 23.50 mm the sensitivity was 52.5% and specificity 78.4%. Between interval delivery <2 days and >2days.

Many studies have reported cervical length to be useful in the prediction of latency period and a cut off 2 cm was found to be associated with shorter interval from membrane rupture to delivery.

Mubarak [16] stated that the validity of CL in predicting labor in women with PPROM when cutoff = 2 cm, with a sensitivity = 52.6%, specificity = 69%, PPV = 60.6%, negative predictive value (NPV) = 61.7%, and accuracy = 61.25%.

CONCLUSION

It could be concluded that cervical length via transvaginal sonography, amniotic fluid index can be used as predictors of length of latency period in PPROM which need a further research work.

CONFLICT OF INTERESTS

The authors declare that they have no conflicts of interest.

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