Transvaginal Cervical Length and Amniotic Fluid Index to Predict Delivery Latency following Preterm Premature Rupture of Membranes

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Introduction

'Preterm Prelabour rupture of membranes' (PPROM) is defined as rupture of foetal membranes before 37 weeks of gestation.[1] It affects almost 3% of all pregnancies and is responsible for about one-third of all premature births.[2] PPROM is amongst the commonest causes of preterm birth, and it can cause significant perinatal morbidity and mortality.[3] As per Statistics PPROM birth costs are eight times more than that of uncomplicated births.[4]

Preterm births accounted for 12% of all births in 2006, a 36% rise since 1981. For an individual patient, forecasting the timing of birth (latency) is challenging, resulting in uncertainty about the same for both the patient and the health care provider. Thus the ability to predict the timing of delivery is beneficial for both the patient and the physician. Interventions such as steroid administration, magnesium sulphate for neuroprotection, or the in-utero transfer to a tertiary centre can be optimized with the help of this information.[5] Thus it could be especially useful in counselling women who refuse hospital care or leave against medical advice. In women with PPROM, expectant management improves neonatal survival rate by about 2% for each additional day of intrauterine maturation, with the greatest benefit between 28 and 36 weeks.

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Prediction of Delivery Latency in PPROM

Prediction of the latency period is crucial when delivery is planned in a hospital with tertiary-level facilities. Few studies have been conducted to identify factors that predict the latency from membrane rupture to delivery. Gestational age, cervical length or dilatation at admission, amniotic fluid index, and parity are some of the suggested influencing factors. PPROM patients are frequently admitted to the hospital for intensive monitoring. Foetal heart rate, uterine contractions, ultrasonography (for estimating foetal growth and obtaining biophysical profile), and any signs of infection are monitored.

The methods employed for sonographic cervical assessment are: transabdominal (TAUS), trans-perineal (TPUS, also known as trans-labial), and Transvaginal ultrasound (TVU). The cervix can be imaged with Transvaginal sonography, which is a safe procedure.[6] In both singleton and twin pregnancies, it has been found helpful to predict the probability of premature delivery with intact membranes.[7,8,9,10] TVUS-measured cervical length (CL) predicts preterm birth (PTB) better than other methods. As a result, its application in predicting the time to delivery in PPROM women is valuable.[6] The sensitivity of TAUS in detecting a short cervix ≤25 mm (confirmed by TVU) ranges from 44.7 percent

to 96.1 percent.[11,12] Because of its high accuracy, it is regarded as the "gold standard" for the detection of a short cervix during pregnancy.[11] Serial TVU has been found to be safe in women with PPROM, with no increased risk of endometritis, chorioamnionitis, or newborn infection.[13,14] Previously TVU was avoided in the presence of ruptured membranes, therefore its use in the management of PPROM has been studied infrequently. Studies by Carlan et al[13] showed the safety of transvaginal sonography (TVS) and proved that there was no increase in peripartum infection or reduction in latency period when compared to women who did not undergo TVS. According to some studies15 either TAUS or Trans - labial ultrasound cannot reliably reproduce accurate CL measurements. The latency period following PPROM was not found to be associated with CL by trans-labial ultrasound.16 TVS can be safely performed with a low interobserver variance rate of 5-10% when performed by trained operators.[17,18]

Compared to TAUS , TVS is less affected by maternal obesity, position of cervix, and shadowing from the foetal presenting part[19,20,21,22] American college of obstetricians and Gynaecologists(ACOG) and Society for maternal-fetal medicine consult series(SMFM) recommend routine transvaginal ultrasound screening for women with a history of prior preterm birth with a singleton pregnancy currently (GRADE1A).[23]

Throughout the pregnancy, TVS has been used extensively to document the appearance of the cervix. The cervical length has a bell-shaped distribution in a normal pregnancy, with a majority of women maintaining a cervical length between 30 and 40mm throughout the pregnancy. PTB is more likely in pregnancies with a cervical length less than 20 mm, according to sonographic measurements. A mid-pregnancy cervical length is a useful tool for identifying women who are at high risk of PTB.[9,24,25] According to various studies;[19] a short cervix can be used to predict preterm birth. It has been recommended as a valuable tool in predicting intra-amniotic infections or inflammation in preterm labour.[26,27] Increased bacterial ascent into the lower pole of the uterus is associated with the shorter cervical length and maternal and foetal response to the release of inflammatory mediators, resulting in preterm parturition.[27]

Although it has been shown that sonographic measurement of cervical length in patients with PPROM does not increase the risk of infection, it is not routinely performed, and the importance of a short cervix in PPROM is not well understood in asymptomatic women or women in preterm labour.[13,14] According to some studies, a short cervix has been a predictor of an impending delivery in PPROM.[14,28,29,30]

Short cervix and Intra-amniotic infection/ inflammation are associated with an increased risk of preterm delivery in PPROM, but there is a paucity of data on the relationship between this inflammatory process and short cervix. Furthermore, it is unknown whether the increased risk of impending preterm delivery in PPROM, associated with a short cervix, is a result of these inflammatory processes or not. These issues are crucial since assessing cervical length with a non-invasive and quick method allows for early detection of such conditions during the initial evaluation of PPROM patients.[31]

Many studies[9,29,32] have showed that a short CL is significantly associated with premature delivery after PPROM, by using TVS to assess the posterior cervical angle. This is a useful tool in determining the latency period in women with PPROM. These findings were supported by Kathir et al.[33] This could aid in patient counselling and planning their prompt referrals to centres with neonatal facilities.

Several studies postulated a relationship between cervical length and delivery latency. Cervical length ≤ 2cms is associated with delivery within 7days among 60% of pregnancies between 24 -32 weeks of gestation in several studies.[28,29,34] A similar study done by Kathir et al[33] found a relationship between the posterior angle of the cervix but not with the length of the cervix. Some studies showed no relationship between them. The main benefit of measuring the cervical length is its significant negative predictive value. On the other hand, the prognostic value of cervical length as a single measure is relative low.[35]

In a study[36] conducted in 80 singleton pregnancies with PPROM between 24-32 weeks of gestation, it was found that when the cut-off value was 2 cm, the sensitivity was 52.6%, specificity was 69%, positive predictive value (PPV) was 60.6%, negative predictive value (NPV) was 61.7%, and the accuracy

was 61.25%. In 33 of the 80 pregnancies, the CL was 2cm, and delivery occurred in 20 of the pregnancies within 7 days, accounting for 60% of the pregnancies.

In a prediction study conducted by Suwan Mehra et al,[28] a cervical length of 2 cm was found in 40% of women in women with PPROM with gestational age ranging from 23weeks +5days to 33weeks +6 days. The predictive value was 62% for delivery within 7 days for a cervical length of 2cm. The study's sensitivity was 51%, specificity was 71% and negative predictive value was 61%.

Another study[34] was conducted on pregnant women between 24 and 32 weeks of gestation with PPROM. In 58/101 cases, pregnant women delivered within 7 days of presentation (57%). Logistic regression analysis revealed that cervical length (odds ratio (OR) = 0.91, 95 percent CI 0.86-0.96, P = 0.001), gestation at presentation (OR = 1.35, 95 percent CI 1.14-1.59, P = 0.001), and the presence of contractions (OR = 3.07, 95 percent CI 1.05-8.92, P = 0.039) made significant independent contributions in the prediction of delivery within 7 days without any significant independent contributions from ethnicity, maternal age, BMI, parity, previous history of preterm delivery, cigarette smoking, vaginal bleeding, or the use of tocolytics, antibiotics, or steroids.

Another study conducted by Rizzo et al[29] found that TVS evaluation of the cervical length (CL) is predictive of PTB in women between 24 and 32 weeks of gestation with PPROM, with a value of 15 mm identifying approximately 70% of symptomatic women who will deliver within one week. Biomarkers in the cervico-vaginal fluids (fetal fibronectin, phosphorylated insulin-like growth factor protein-1, placental alpha-microglobulin-1, and cytokines) and other ultrasonographic cervical variables (posterior cervical angle, elastography) aid in identifying women at risk with a CL between 15 and 30 mm, presence of a short cervical length.[37]

In a study conducted by Kathir et al[33] between 28 and 32 weeks of gestation, the mean time interval was 96.9 hours between membrane rupture and delivery. The majority of the women (63.8% (n = 51)) gave birth within 48 hours. TVCL was not found to be related to the latency period (p =.559). The latency interval was found to be significantly associated with the posterior cervical angle (hazard ratio 1.03, 95 percent CI: 1.01–1.06; p =.003).

The mean gestational age presenting with PPROM was 29.7 +/- 2.8 weeks in a study conducted by Fischer et al16. The median latency period was 10 days, and the mean trans-labial cervical length was 2.8 +/- 1.1 cm (interquartile range 4-15 days). Cervical length and latency period had no statistically significant relationship (r=0.15, p=0.28). Furthermore, cervical length cut-offs of 2.5 cm or 1.5 cm, as well as the presence of cervical funnelling, was not associated with latency periods spanning less than seven days. Similarly, neither chorioamnionitis nor postpartum endometritis was associated with the development of these criteria.

There were no significant differences in the incidences of chorioamnionitis (28% and 20%), endometritis (6% and 9%), or neonatal infections in a randomized study conducted by Carlan[13] (17% and 20%). The average latency period in women who went into spontaneous labour and had an initial cervical length of 3.0 cm or less was 9.4 days, as compared to 11.0 days if the cervix was longer than 3.0 cm, showing a non-significant difference.

The amniotic fluid index is another important factor in determining delivery latency. Most examiners use an AFI <5 cm as the threshold for oligohydramnios.[37] Intrauterine Growth Restriction (IUGR) was found to be more common in women, whose AFI was close to the cut-off point. Also, they have more prenatal consequences.[38] The cut-off-point of the amniotic fluid index has been defined in different ways. Luo et al.[39] defined it to be between 5-8 cm; Banks and Miller[40] stated it to be between 5.1 and 9.9 cm; Phelan et al.41 defined it in the range of 5-8 cm in their research.

In PPROM amniotic fluid index (AFI) ≤ 5cm has been associated with a shorter latency period and higher rates of delivery within 7 days in comparison to women with normal AFI.[28] Amniotic fluid volumes have been suggested as useful adjuncts in identifying patients at risk of PPROM, Studies have noted increased perinatal morbidity and mortality in presence of oligohydramnios.[37,42,43] Several studies[44,45] have linked oligohydramnios to perinatal infection, fetal distress, caesarean delivery, and neonatal death in patients with preterm premature rupture of

membranes. Oligohydramnios has been associated with a reduction in latency period. There could be several reasons for this but the most widely accepted is that there is a redistribution of blood flow in these foetuses because of inflammatory response syndrome in the foetus.[44]

In a study done by Raina et al,[46] an analysis was made of the factors affecting the duration of latency period in patients with preterm premature rupture of membranes in a tertiary care centre. Among 51 pregnancies, AFI ≤5 was observed in 21 pregnancies and 14 pregnancies delivered within 48 hours. In this study, Oligohydramnios was significantly more common in subjects with latency less than 48 hours compared to subjects with latency more than > 48 hours (p-value = 0.040). In another study by Borna et al,[47] after PPROM, AFI ≤ 5 was significantly associated with an increased risk of chorioamnionitis; on the other hand, the patients in the AFI ≤ 5 groups did not have a shorter latency period. Hence no evidence was found between the association between the development of chorioamnionitis and latency interval in patients with ruptured membranes (P=0/783) in this study as the latency period was not significantly different between the two groups.

In the Park et al study,[48] patients having an amniotic fluid index of ≤ 5 cm had a significantly shorter latency interval-to-delivery when compared to patients with an amniotic fluid index of ≥ 5 cm (median, 38 hours; range, 0.2-1310 hours; vs median, 100 hours; range, 0.1-2917 hours; P.01). A Cox proportional hazards model analysis revealed that an amniotic fluid index of ≤ 5 cm was a significant predictor of pregnancy duration (odds ratio, 2.4; 95 percent confidence interval, 1.4-3.9; P.001).

Vermillion et al.[49] demonstrated that an AFI of ≤5 cm after PPROM between 24 and 32 weeks of gestation was associated with a shorter latency period before delivery. This finding has been supported by several authors,[48,50] who showed that the presence of oligohydramnios in PPROM is associated with a shorter latency period when compared to PPROM without oligohydramnios.

The latency period in days from PPROM was significantly lower in women in the group with AFI ≤5 cm (P0.05) in a study of 114 pregnancies conducted by JuanPiazze.[50] AFI ≤5 cm was found to be associated with 66% of pregnancies complicated by chorioamnionitis (8/12) and in 70% of neonates with RDS (19/27) at birth).

Several studies[48,49,50] hypothesized a relationship between AFI and delivery latency in PPROM and found a significant relationship between AFI ≤5 cm and delivery latency. In the above studies, in cases where the amniotic fluid index was less than or equal to 5, delivery occurred within 48 hours in the majority of cases, which is statistically significant. Along with delivery latency, low AFI explained the association with chorioamnionitis, neonatal death, and RDS.

According to Morris et al.,[44] AFI of ≤ 5 was positively correlated with asphyxia, Caesarean section, low Apgar score, and a pH 7 of the umbilical cord blood and found a positive correlation between AFI of ≤5 and prolonged latency. Therefore they suggested AFI for predicting prenatal problems.

Other factors that can predict the delivery latency, in addition to the cervical length and amniotic fluid index, are gestational age, parity, and associated chorioamnionitis. Lower delivery latency is associated with Elderly females and higher parity. Chorioamnionitis is a common indication for labour induction in PPROM patients. Specific signs of chorioamnionitis, such as fever, maternal or foetal tachycardia, abdominal pain, or an offensive odour of the amniotic fluid, indicating that the baby should be delivered right away.[51]

Prediction of Latency with Combined Cervical Length and Amniotic Fluid Index (AFI):

Many Studies[50,52,53,54] found there is a shorter latency interval and high rate of delivery within 7 days, with AFI of ≤5 cm in PPROM when compared to women with a normal AFI. Many studies[55] reported that combining both AFI and TVCL was more accurate in predicting delivery latency than using single parameters. Megha et al[6] in their study found an increase in Positive predictive value (PPV) when AFI <5 cms and CL <2 cms were combined, with a 78.98 % risk of delivery within 7 days after PPROM. Mubarak et al36found an increase in PPV to 86.4 % when combined AFI <5 cms, and TVCL <2 cms were used to predict delivery latency within 7days. Lee et al.[55] concluded in their study that by

combining the sum of AFI and TVCL to 8.57, the latency period is reduced to 1.6 days. Mehra et al[28] found that a combination of TVCL >2 cm and AFI >5 cm increased the likelihood of remaining undelivered 7 days after PPROM.

Conclusion

Prediction of the latency period is crucial when delivery is planned in a hospital with tertiary-level facilities. Serial TVU has been found to be safe in women with PPROM, with no increased risk of endometritis, chorioamnionitis, or newborn infection. Previously TVU was avoided in the presence of ruptured membranes; therefore its use in the management of PPROM has been studied infrequently. Compared to transabdominal ultrasonography, transvaginal ultrasonography is less affected by maternal obesity, position of cervix, and shadowing from the foetal presenting part.

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