Correlation between Amniotic Fluid Volume in Women with Forewater Preterm Premature Rupture of Membranes and Perinatal Outcomes

Original Article

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ABSTRACT

Objectives: Preterm premature rupture of membranes (PPROM), which occurs before 37 weeks of gestation, is a significant pregnancy complication. This study aimed to investigate the correlation between the amniotic fluid index (AFI) and neonatal respiratory distress in (PPROM) cases.

Patients and Methods: We studied 100 females, aged 19-45, with singleton pregnancies between 24 and 37 weeks, confirmed PPROM via amniotic fluid, and presented within 24 hours before labor began. All patients underwent abdominal ultrasounds.

Results: AFI was negatively correlated with total leukocytic count (r=-0.248, *P*=0.013), neonatal mortality (r=-0.258, *P*=0.01), occurrence of respiratory distress syndrome (RDS) (r=- 0.309, *P*=0.002), occurrence of necrotizing enterocolitis (NEC) (r=-0.202, *P*=0.044) and five minutes of APGAR (appearance, pulse, grimace, activity, and respiration) scores (r=-0.254, *P*=0.011). AFI had significantly diagnostic accuracy for predicting outcome of pregnancy in patient group at cut off 4.1 for identifying unfavourable results in the patient group with a 51.5% specificity and a 77.6% sensitivity. Compared to AFI≥5, the following outcomes were substantially higher: infant death, birth weight < 2.000 g, neonatal sepsis, hospitalisation to the neonatal intensive care unit for more than two weeks, RDS, 5-minute APGAR score<7, and NEC.

Conclusions: Adverse newborn outcomes are a result of low residual amniotic fluid levels in individuals with postpartum haemorrhage. AFI<5 cm was linked to poor newborn outcomes overall and respiratory distress specifically, according to our findings.

Key Words: Amniotic fluid volume, forewater, preterm premature rupture of membranes, perinatal outcomes, women.

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INTRODUCTION

Preterm premature rupture of membranes (PPROM), defined as membrane rupture before 37 weeks of gestation, is a major pregnancy complication[1,2].

PPROM is linked to various complications for both the fetus and the mother, including umbilical cord compression and prolapse, oligohydramnios, placental abruption, necrotizing enterocolitis, respiratory distress syndrome, fetal death, and risks for maternal intra-amniotic and postpartum infections. Preterm infants who develop chorioamnionitis are at risk for neurodevelopmental handicaps, early-onset sepsis, and severe intraventricular hemorrhage[3].

The cause of PPROM is complex and involves multiple factors. An infection triggers the production and release of proinflammatory cytokines from the decidua and amniotic membranes, leading to PPROM[4].

Multiple factors increase the risk of PPROM, which ranges from 16% to 32% and include black race, low socioeconomic status, smoking, history of antepartum hemorrhage, cervical incompetence, and previous operations involving the uterine cervix. These invasive prenatal tests- amniocentesis, chorionic villus sampling, fetoscopy, and cervical cerclage - are uncommon causes of PPROM[5].

Amniotic fluid safeguards fetal growth. Amniotic fluid volume is crucial for fetal health assessment. When Amniotic Fluid Index (AFI) by ultrasound measures less than 5 cm in cases of oligohydramnios or below 3 cm for severe oligohydramnios[6], the AF index ultrasound method is applied.

Ultrasound determines AFI. An ultrasound examination is conducted for most PPROM cases to assess fetal position, wellbeing, and residual amniotic fluid volume. The limited

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interpretation of studies depends on their small sample size, inconsistent gestational ages, insufficient adjustment for confounding variables, and diverse definitions of respiratory morbidity[7].

AFV significantly influences fetal lung development. Severe oligohydramnios during pregnancy's critical periods can result in pulmonary hypoplasia for the fetus. The link between fluid loss and pulmonary hypoplasia during late second and early third trimesters of pregnancy requires further investigation[8].

The study aimed to investigate the relationship between AFI and neonatal respiratory distress in preterm births due to PPROM.

PATIENTS AND METHODS

This study included 100 females, aged 19 to 45, with singleton pregnancies between 24- and 37-weeks GA, as confirmed by menstrual history and ultrasound before 15 weeks, and who had clinically diagnosed preterm prelabor rupture of membranes (PPROM) with amniotic fluid visible through the cervical os during speculum exam within 24 hours of PPROM and not in labor. The study was carried out between March 2020 and March 2022, following ethical approval from Tanta University Hospitals, Tanta, Egypt. Patients gave their informed consent in writing.

Women not eligible were before 24 or after 37 weeks, electing labor induction, multifetal pregnancies, missing data, vaginal bleeding, chromosomal anomalies, intrauterine growth restriction, fetal infections, or fetal heart rate abnormalities.

Patients underwent comprehensive diagnostic workup including CBC, CRP, kidney and liver function tests, viral markers and urine analysis as part of their history taking and clinical examination, as well as radiological investigations.

Abdominal ultrasonographic examinations

The obstetrics and gynaecology department of Tanta University Hospitals, Egypt used MINDRAY DC-N2, China, ultrasound equipment with a 3.5–5 MHz transabdominal probe for assessing foetal viability, foetal biometry, biparietal diameter (BPD), foetal length (FL), abdominal circumference (AC), head circumference (HC), placental (site and placental grade and excluding placental separation), detection of any foetal gross anomalies, liquor (amount reported as AFI and turbidity), foetal presentation, and fetal well-being.

Follow up

Patients were admitted to the antenatal care unit to wait 24 hours, undergo necessary investigations except for chorioamnionitis, placental separation, and fetal compromise. Regular and painful uterine contractions marked the beginning of labour, delaying digital examination until then. Resting in bed is commonly advised. Women with PPROM were given a single course of 6 mg dexamethasone, 4 doses, every 12 hours, up until 36w+6D of gestation. 2g/day Sulbactam-ampicillin was initiated intravenously for 2-5 days followed by azithromycin 500mg orally. Patients at risk for intrapartum GBS infection receive one of the following regimens: 5 million IV initial doses and 2.5 million units iv every 4 hours until delivery for penicillin G, 2g IV initial dose and 1g / 4 hours until delivery for ampicillin, 2g IV initial dose followed by 1g iv / 8 hours until delivery for cefazolin, or 1g IV / 12 hour until delivery for vancomycin, depending on their penicillin allergy. Magnesium sulfate, with a loading dose of 4g given slowly IV over 15-20 minutes and a continuous infusion of 1g/hr for 24 hours, is administered for fetal neuroprotection in women delivering before 32 weeks. Managing underlying risks includes treating urinary tract and vaginal infections. We closely monitored maternal and fetal health for signs of chorioamnionitis or fetal compromise until labor began or maturity was reached through daily pulse and temperature checks, CRP levels, CBCs, fetal heart rate counts, biophysical profiles, and ultrasound examinations for amniotic fluid index and fetus growth. If a mother displayed clinical evidence of chorioamnionitis (elevated temperature of 38oC with no extrauterine cause, accompanied by fetal tachycardia, maternal tachycardia, leukocytosis, uterine tenderness, or new-onset foul-smelling vaginal discharge), inpatient delivery was recommended; otherwise, she was monitored as an outpatient for 48-72 hours before being discharged and advised to seek medical help if symptoms worsened.

Selected cases for outpatient monitoring

Hospitalized patients diagnosed with PPROM (premature rupture of membranes) between 24+0 and 33+6 weeks of gestation, with a singleton fetus, no abnormalities, lack of maternal infection (fever >38°C or uterine tenderness), and normal fetal heart rate below 160 beats/min, should not be delivered within 48 hours. No foul odor of amniotic fluid, no signs of labour (regular contractions, cervical dilation), and no tachycardiotocography, lab samples, or weekly examinations were required.

Maternal complications resulted from PPROM, including chorioamnionitis, placental separation, and cord prolapse. The assessed outcomes included a normal live birth, birth weight, APGAR score, NICU admissions, RDS, NEC, and neonatal sepsis, without any instances of intra uterine growth restriction (IUFD), stillbirth, neonatal death, or IUGR.

Neonatal morbidity and mortality were recorded using neonate data sheets and neonatologist diagnoses. Neonatal sepsis was diagnosed based on positive culturing results from blood, cerebrospinal fluid or urine, in conjunction with clinical indicators of cardiovascular collapse.

Based on clinical symptoms of intolerance to oral feeding, frequent vomiting, abdominal distension, and radiologic findings, NEC was diagnosed.

Statistical analysis

IBM Inc., Chicago, IL, USA used SPSS v26 for statistical analysis. The statistical variables were denoted by their mean and standard deviation (SD), and the unpaired Student's t-test was employed to compare them between the two groups. Frequency and percentage (%) were used to represent qualitative variables, and the Chi-square or Fisher's exact test were used for analysis as necessary. Assessment of the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of diagnostic performance. A statistically significant result was defined as a two-tailed *P value* less than 0.05.

RESULTS

Demographic characteristics, risk factors of PPROM, mode of delivery and mean GA at PPROM and delivery of pregnant women were enumerated in this table (Table 1).

Table 1: Demographic characteristics, risk factors of PPROM, mode of delivery and mean GA at PPROM and delivery of pregnant women

		N=100
Age (years)		26.86 ± 3.84
<20		1(1.0%)
20-30		82(82.0%)
>30		17(17.0%)
BMI (kg/m^2)		27.01± 4.02
<18.5		0(0.0%)
18.5–24.9		24(24.0%)
25.0–29.9		49(49.0%)
>30		27(27.0%)
Parity		1.34 ± 1.15
Zero		29(29.0%)
Only 1 parity		30(30%)
2 to 3 parity		22(22%)
Over 3 birth		19(19%)
PPROM		17(17.0%)
Previous Preterm labour	1-2	36(36.0%)
	3	6(6.0%)
Vaginal infection	Mixed infections	28(28.0%)
	G.B. S	14(14.0%)
UTI during pregnancy		25(25.0%)
History of abortion	1-2	37(37.0%)
	3-4	2(2.0%)
Mode of current delivery	Vaginal	29(29.0%)
	CS	71(71.0%)
GA at PPROM (weeks)		32.75 ±1.86
GA at delivery (weeks)		34.19 ±1.76

Data are presented as mean ± SD or frequency (%). BMI: Body mass index, PPROM: Previous preterm prelabour rupture of membrane, UTI: urinary tract infection, GBS: group B streptococcus, CS: Cesarean section, GA: gestational age.

The mean of CRP was 26.7± 28.6 mg/dl, TLC was 11.174±3.439103/µL, AFI was 3.85±1.8, biophysical profile was 1.5±3.4 and EFW was 2.4±3.8. Regarding latency period, 71% of women were delivered within 24 hours of the onset of PPROM, whereas only 13% of patients were delivered after 72 hours and the remaining 16% were delivered between 25 and 72 hours with the meantime interval of onset of membrane rupture and delivery was 2.88±12.95 days. Symptoms and signs of chorioamnionitis can developed in 7(7.0%) cases (Table 2).

Table 2: CRP, TLC, AFI, biophysical profile, EFW, latency period between PPROM and delivery and maternal morbidity in PPROMM cases at admission

	N=100
CRP (mg/dl)	26.7±28.6
TLC (103/µL)	11.174±3.439
AFI	3.85±1.8
Biophysical profile	1.5±3.4
EFW	2.4±3.8
Latency period (hours)	2.88±12.95
<24	71(71.0%)
>24–≤72	16(16.0%)
>72	13(13.0%)
Symptoms and signs of chorioamnionitis	7(7.0%)

Data are presented as mean ± SD or frequency (%). CRP: Serum C-reactive protein, TLC: total leucocytic count, AFI: Amniotic fluid index, EFW: estimated fetal weight, PPROM: Previous preterm prelabour rupture of membrane.

Distribution of birth weight of newborns to PPROM mothers, morbidity and mortality of newly born babies were enumerated in this table (Table 3).

Table 3: Distribution of birth weight at of newborns to PPROM mothers, morbidity and mortality of newly born babies

	N=100
Birth Weight (g)	2414±382.35
1000-1499	1(1.0%)
1500-2000	22(22.0%)
≥2000	77(77.0%)
Neonatal Mortality	14(14.0%)
Neonatal Sepsis	12(12.0%)
NICU admission more 2 weeks	52(52.0%)
RDS	35(35.0%)
5 min APGAR score<7	39(39.0%)
NEC	2(2.0%)

Data are presented as mean ± SD or frequency (%). NICU: neonatal intensive care unit, NEC: necrotizing enterocolitis, RDS: Respiratory distress syndrome, APGAR: Appearance, pulse, grimace, activity and respiration.

All babies [2 (2%)] born at a lower GA of 28-30 weeks at delivery. In the 16 cases whose GA was slightly better 30-32 weeks; morbidity was 12(75%) and mortality was 4(25%) percent. Furthermore, in the 53 cases born at GA 32-35 week the morbidity was 35(66.03%) and mortality was 6(11.3%) percent. Additionally, in the 18 cases with GA more than 35 weeks and less than 37 the morbidity was 5(27.78%) and the mortality was 2(11.11%). While no mortality and only 2(18.18%) cases showed morbidity in the full-term group (≥37 weeks of gestation. The mean AFI in cases without neonatal morbidity and mortality risks was 4.48 ±1.9 while it was 2.7±0.78 in cases whose babies died, 3.77±1.7 in cases whose neonates displayed various morbidity and 3.03±1.1 in cases whose neonates showed RDS and 2.89±0.86 in cases whose neonates intubated because of RDS (Table 4).

Table 4: Distribution of morbidity and mortality based on GA, AFI in cases with and without neonatal morbidity and mortality

	Mortality	Morbidity
28-30	2(100%)	0(0%)
30.1-32	4(25%)	12(75%)
32.1-35	6(11.3%)	35(66.03%)
>35-<37	2(11.11%)	5(27.78%)
≥37	0(0%)	2(18.18%)

	Cases with no morbidity and mortality risks	Cases with overall morbidity risks	Cases with mortality risks	RDS cases (n=35)	RDS with intubation (n=15)
AF I	4.48±1.9	3.77±1.7	2.7±0.78	3.03±1.1	2.89±0.86

Data are presented as frequency (%). AFI: amniotic fluid index, RDS: Respiratory distress syndrome, GA: gestational age.

Neonatal mortality, birth weight: < 2.000 g, neonatal sepsis, NICU admission more 2 weeks, RDS, 5 min APGAR score<7 and NEC was significantly higher when AFI <5 than AFI≥5 (Table 5).

Table 5: AFI in cases with neonatal morbidity and mortality

	AFI <5	AFI≥5	*P*
Neonatal Mortality	11(78.57%)	3(21.42%)	<0.001*
Birth weight: < 2.000 g	15 (65.21%)	8(34.78%)	<0.001*
Neonatal Sepsis	8 (66.67%)	4(33.33%)	<0.001*
NICU admission more 2 weeks	37(71.15%)	15(28.85%)	<0.001*
RDS	21(60%)	14(40%)	0.009*
5 min APGAR score<7	27(69.33%)	12(30.77%)	<0.001*
NEC	2(100%)	0 (0%)	<0.001*

Data are presented as frequency (%). AFI: amniotic fluid index, RDS: Respiratory distress syndrome; NEC: necrotiinng enterocolitis, NICU: neonatal intensive care unit, APGAR: Appearance, pulse, grimace, activity and respiration.

The ROC curve analysis demonstrated that an AFI threshold of 5.05 served as the optimum cutoff for detecting RDS in the patient group, yielding a sensitivity of 94.3% and a specificity of 38.5% (AUC=0.687, 95% CI: 0.585-0.789, *P*=0.002). For predicting adverse outcomes, the ROC curve indicated an optimal AFI threshold of 4.1 with a sensitivity of 77.6% and a specificity of 51.5% (AUC=0.637, 95% CI: 0.519-0.756, P=0.026) (Figure 1).

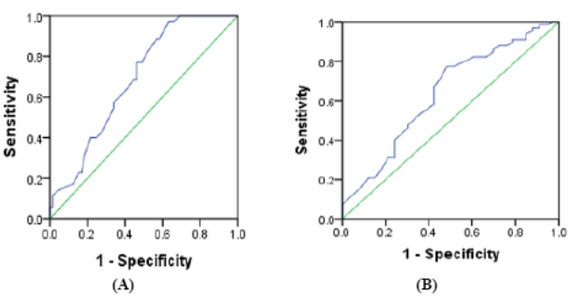

Fig. 1: ROC curve of amniotic fluid index for predicting (A) respiratory distress syndrome and (B) adverse outcome in neonates of preterm prelabour rupture of membranes cases

AFI was negatively correlated with TLC (103/µL) (r=-0.248, *P*=0.013), Neonatal Mortality (r=-0.258, *P*=0.01), occurrence of RDS (r=- 0.309, P=0.002)., occurrence of NEC (r=-0.202, *P*=0.044) and 5 min Apgar score (r=-0.254, *P*=0.011) (Table 6).

Tale 6: Correlation between AFI and other parameters

	AFI	
	r	*P*
Age (Years)	-0.050	0.620
BMI (Kg/m^2)	0.021	0.8
Parity	-0.094	0.352
GA at hospitalization (weeks)	-0.045	0.657
GA at delivery (weeks)	0.121	0.230
Previous preterm PROM	-0.065	0.520
Preterm labour	-0.085	0.402
history of abortion	-0.003	0.979
Predisposing infection	-0.173	0.085
UTI during pregnancy	-0.136	0.176
Mode of delivery	0.042	0.681
Birth weight	0.067	0.507
CRP (mg/dl)	-0.033	0.748
TLC (10^3/µL)	-0.248	0.013*
Symptoms and signs of chorioamnionitis	0.005	0.957
Neonatal Mortality	-0.258	0.01*
Neonatal Sepsis	-0.155	0.124
NICU more 2 weeks	-0.142	0.160
RDS	-0.309	0.002*
NEC	-0.202	0.044*
5 min APGAR score	-0.254	0.011*

r: Pearson coefficients, * Significant *p value* <0.05, BMI: Body mass index, PPROM: Previous preterm prelabour rupture of membrane, UTI: urinary tract infection, CRP: Serum C-reactive protein, TLC: total leucocytic count, RDS: Respiratory distress syndrome, NEC: necrotiinng enterocolitis, NICU: neonatal intensive care unit, APGAR: Appearance, pulse, grimace, activity and respiration, GA: gestational age.

DISCUSSION

Perinatal morbidity and death are still mostly caused by preterm birth, defined as birth occurring before 37 weeks of gestation. Thirty percent of premature deliveries occur after PPROM, with the majority of preterm births occurring spontaneously. Assessing and treating women with PPROM has proven to be difficult[9].

As regard inflammatory markers, our results revealed that the mean of CRP at admission was 26.7± 28.6 ranged between 1.5-100 (mg/dl), whereas the mean TLC was 11174±3439 103/µL ranged between 1.099-20.986 (103/µL). Our results were in concordance with Hosseinian Kandsar *et al*.[10] found that out of 418 pregnant women 11 (2.6 percent) had PPROM and their CRP level was 22.5 ±2.8 mg/dl. Horasanlı *et al*.[11] reported that the mean TLC was 11.79± 3.59 103/µL and the mean CRP was 9.02 ± 14.97 mg/dl. Abd El-Fattah *et al*.[12] reported a mean TLC was 8.1±1.66 103/µL.

In terms of the method of birth for the current pregnancy, our findings showed that 29 (29%) of the PPROM women had a vaginal delivery, whereas 71% (n=71) of the women had a CS delivery. The prevalence of CS among PPROM cases was in agreement with prior studies that showed increased CS in PPROM cases. It was 69% in Fahmy *et al*.[13],75.4% in Abdel Maaboud *et al*.[14], 81.8% in Abd El-Fattah *et al*.[12] and 65.2% in Kahramanoglu *et al*.[15] research.

Regarding maternal morbidities in the current work, our results displayed that 7% of PPROM cases developed symptoms and signs of chorioamnionitis. Our results were comparable to Fahmy *et al*.[13] observed that in 7 % of cases chorioamnionitis was diagnosed. Abouseif *et al*.[16] agreed with us in that women presented with PPROM women developed chorioamnionitis were 4.3% While Shweta and Patil[17] reported 3 %.

Our results about neonatal birth weight and morbidity and mortality of newly born babies were nearer to that reported by Fahmy *et al*.[13] showed that prematurity accounted for 53% of all newborn complications in their work (compared to 89% in our sample), followed by RDS (52%), neonatal sepsis (16%), and necrotising enterocolitis (3%). However, they recorded an overall 8% newborn death rate. 54.79% of infants that were born had an Apgar score of 6.

A deeper look at our data revealed that congenital pneumonia (n=18, 9.3%), sepsis (n=33, 17.1%), and RDS (n=88, 45.8%) were the most frequent newborn morbidities. The rate of neonatal death was 6.7% as in Kahramanoglu *et al*.[18] study that is in agreement with our results.

As regards our aim to correlate AFI to neonatal morbidity as whole and to respiratory morbidity in particular, we found that the mean of AFI was 3.85±1.8. Most cases with neonatal mortality and morbidity had AFI less than 5 as: 11(78.57%) of the mortality cases, 15 (65.21%) of the neonates with birth weight: < 2.000 g, 8 (66.67%) of the neonatal sepsis cases, 37(71.15%) of the neonates admitted to NICU more than15 days, 21(60%) of the RDS cases, 27(69.33%) of the neonates with 5 min APGAR score<7 and all NEC cases [2(100%)] had AFI less than 5. The mean AFI in cases without neonatal morbidity and mortality risks was 4.48 ±1.9 while it was 2.7±0.78 in cases whose babies died, 3.77±1.7 in cases whose neonates displayed various morbidity and 3.03±1.1 in cases whose neonates showed RDS and 2.89±0.86 in cases whose neonates intubated because of RDS. According to the ROC curve, the best cutoff value for AFI to identify RDS in the

patient group was 5.05, with a sensitivity of 94.3% and a specificity of 38.5%; the AUC was 0.687 (95% CI: 0.585-0.789). Furthermore, the ROC curve demonstrated that the best cutoff for AFI was 4.1 with a sensitivity of 77.6%, specificity of 51.5%, and an AUC of 0.637 (95% CI: 0.519-0.756) for identifying bad outcomes in the patient group.

Moreover, AFI was negatively correlated with TLC (103/µL) (r=-0.248, *P*=0.013), Neonatal Mortality (r=-0.258, *P*=0.01), occurrence of RDS (r=- 0.309, *P*=0.002), occurrence of NEC (r=-0.202, *P*=0.044) and 5 min Apgar score (r=-0.254, *P*=0.011). Mousavi *et al*.[19] found no statistically significant differences among cases with AFI <5 and those with AFI ≥ 5 regarding GA at birth, RDS, NEC rates in PPROM pregnancies but they reported significant increase in neonatal sepsis and death in AFI <5 group like our findings. Ladella *et al*.[20] discovered notable variations in the newborn outcomes, with the oligohydramnios group (AFI<5) having shorter NICU stays and worse Apgar scores at 1 and 5 minutes, respectively.

One of the study's limitations was the very small sample size. There was just one centre for the study. Therefore, we suggested that a patient's first amniotic fluid evaluation may be used as a predictor of poor newborn outcomes if the patient had PPROM. In particular, when PPROM develops at extremely preterm GA, the residual AFI can be employed as a significant predictive marker for perinatal outcomes in PPROM patients and assist guide the care counselling and treatment measures for the PPROM patients.

CONCLUSIONS

Adverse newborn outcomes are a result of low residual amniotic fluid levels in individuals with postpartum haemorrhage. AFI<5 cm was shown to be associated with poor newborn outcomes overall and respiratory distress specifically. With a sensitivity of 94.3% and a specificity of 38.5% for RDS detection in the patient group, the optimal AFI cutoff was 5.05; for the detection of overall unfavourable outcome in the patient group, it was 4.1, with a sensitivity of 77.6% and a specificity of 51.5%.

ABBREVIATIONS

PPROM: Preterm Premature Rupture of Membranes; **AFI:** Amniotic Fluid Index; **NEC:** Necrotizing Enterocolitis; **RDS:** Respiratory Distress Syndrome; **APGAR:** Appearance, Pulse, Grimace, Activity, and Respiration; **BPD:** Biparietal Diameter; **FL:** Foetal Length; **AC:** abdominal circumference; **HC:** head circumference; **IUGR:** Intra Uterine Growth Restriction; **NPV:** Negative Predictive Value; PPV: positive predictive value

CONFLICT OF INTERESTS

There are no conflicts of interest.

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