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Maternal and perinatal outcomes in pregnancies after preterm premature rupture of membranes determined by single deepest vertical pocket

Abstract

Objective: To evaluate maternal and perinatal outcomes in cases with oligohydramnios after preterm premature rupture of membranes (PPROM) using single deepest pocket (SDP) at the time of diagnosis

Methods: We performed a retrospective cohort study of perinatal outcomes based on SDP measurement at the time of PPROM during the study period 2011 to 2015 at a single institution. The SDP was determined by reviewing archived ultrasound images and reports at the time PPROM was diagnosed. Patients were subsequently divided into two groups, SDP <2cm (n=24) and SDP ≥ 2cm (n=54). Maternal and perinatal outcomes were subsequently compared according to single deepest vertical pocket. The Student's t-test and Chi-squared test were used to compare variables. All p values were expressed as exact values against the null hypothesis.

Results: We identified 78 patients with PPROM between 24 and 34 weeks of pregnancy. A SDP <2cm in the setting of PPROM was associated with earlier gestational age at time of membrane rupture, earlier delivery, increased respiratory distress syndrome (RDS), lower Apgar score at one minute, and decreased birth weight. We believe that this association is the result of gestational age itself rather than a smaller single deepest vertical pocket.

Conclusion: The presence of a SDP <2cm in the setting of PPROM is not associated with adverse maternal and perinatal outcomes. SDP was not shown to be a good predictive marker of composite perinatal morbidity. Larger prospective studies, however, should be performed to allow for a multivariate analysis.

Keywords: Oligohydramnios, Outcomes, PPROM, SDP

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Abbreviations:

PPROM, Preterm Premature Rupture of Membranes; AFI, Amniotic Fluid Index; SDP, Single Deepest Vertical Pocket; BPP, Bi-Weekly Biophysical Profile; NST, Non-Stress Testing

Introduction

Preterm premature rupture of membranes (PPROM) is defined as spontaneous rupture of the fetal membranes prior to 37 weeks of gestation in the absence of labor. PPROM complicates 2-3% of all pregnancies and is associated with 30-40% of preterm deliveries. This condition, therefore, is a major cause of perinatal morbidity and mortality.[1,2] Amniotic fluid has a number of functions that are essential for normal growth and development of the fetus. It has been hypothesized that amniotic fluid possesses certain bacteriostatic properties that protect against infectious processes while *in utero*. In addition, it plays an important role in the development of the fetal thorax as it allows for normal lung development. Appropriate levels of amniotic fluid decrease the incidence of cord compression and fetal heart decelerations that may lead to an emergent cesarean delivery.[3]

Amniotic fluid volume is an essential component in the assessment of overall fetal well being.[4] Low residual amniotic fluid after PPROM has been associated with complications such as short latency period, chorioamnionitis, neonatal sepsis, respiratory distress syndrome, low Apgar scores, cesarean deliveries, and neonatal death.[1-13]

Ultrasound assessment of amniotic fluid estimation is performed by either the four quadrant amniotic fluid index (AFI) or the single deepest vertical pocket (SDP) technique.[4] The majority of studies in the current literature use AFI to determine the perinatal outcomes of oligohydramnios secondary to PPROM.[1-13] Only two studies[6,7] were identified that assessed perinatal outcomes after PPROM using the SDP and both of these studies were noted to have conflicting results. A recent Cochrane meta-analysis determined that SDP measurement is superior for the assessment of amniotic fluid volume as AFI increases the rate of diagnosis of oligohydramnios and subsequent interventions without improving perinatal outcome.[4,5] The aim of this study is to evaluate the association between oligohydramnios and maternal and perinatal outcomes in cases of PPROM between 24 to 34 weeks of gestation determined by the measurement of the residual amniotic fluid using the single deepest pocket technique.

Materials and methods

This retrospective cohort study was performed using an obstetric database at our single tertiary care center between January 2011 and January 2015. This study was approved by the Institutional Review Board at our facility. We hypothesized that cases with oligohydramnios (SDP <2cm) after PPROM were associated with higher rates of composite maternal and perinatal morbidity.

Maternal demographic information including age and race, gestational age at time of PPROM, parity, antepartum history, and maternal and neonatal outcomes were extracted from patient charts. Composite maternal and perinatal morbidity outcomes were subsequently compared according to single deepest vertical pocket.

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We included singleton pregnancies with a confirmed diagnosis of PPROM as indicated by one or more of the following: gross pooling of amniotic fluid in the vagina, positive Nitrazine paper test, or a positive placental alpha macroglobulin-1 protein assay (Amnisure) by sterile speculum exam technique. Bimanual exams were not performed due to potential risk for chorioamnionitis. Only cases of PPROM between 24 and 34 weeks were included for review. PPROM was defined as spontaneous rupture of membranes prior to 37 weeks of gestation in the absence of active labor. Oligohydramnios after PPROM was defined as a SDP <2cm.

We excluded patients with signs of active labor, chorioamnionitis, or non-reassuring fetal heart tracing at admission. In addition, patients with multiple gestations, intrauterine growth restriction, chromosomal abnormalities or malformations, and those with a history of cerclage or short cervix were excluded. We also excluded cases with incomplete or insufficient information in the medical record such as those missing a SDP measurement or those without readily available perinatal data.

Patients included in the study were admitted to our facility for conservative management and received antenatal corticosteroids for lung maturation (2 doses of betamethasone 12 mg IM at 24 hours interval) and antibiotic prophylaxis according to the Mercer protocol.[6] Magnesium sulfate was administered for neuroprotection (4 gram loading dose over 20 minutes followed by 1 gram per hour maintenance) if gestational age was between 24 and 32 weeks. Urine and cervical cultures were collected and treatment was employed accordingly. An ultrasound was obtained on admission and single deepest pocket measurement was obtained by measuring the vertical diameter of the largest amniotic fluid pocket. All patients remained hospitalized until delivery and were followed with daily non-stress testing (NST) and bi-weekly biophysical profile (BPP). Indications for delivery included active labor, chorioamnionitis, placental abruption, non-reassuring fetal heart tracing, or induction of labor for patients who reached 34 weeks.

Maternal and obstetrical data were collected and maternal outcomes included gestational age at time of admission, latency period, chorioamnionitis, sepsis, placental abruption, admission to ICU, and death. The latency period was defined as the interval in days from the time of PPROM to delivery. Maternal chorioamnionitis was diagnosed in the presence of two or more of the following criteria: maternal fever greater than 38oC, maternal or fetal tachycardia (above 120 bpm and 160 bpm, respectively), leukocytosis (greater than 20,000/mm3), uterine tenderness or foul-smelling amniotic fluid.

Perinatal outcomes collected included gestational age at delivery, birth weight, Apgar scores at one minute, respiratory distress syndrome, neonatal sepsis, emergency intubation, phototherapy, length of stay in ICU and neonatal death. Neonatal sepsis was diagnosed by positive blood, urine or cerebrospinal fluid culture. Respiratory distress syndrome was based on clinical symptoms associated with radiographic findings (hyaline membrane disease) or respiratory insufficiency related to prematurity in an infant who needed ventilatory support for the first 4 hours of life.

Statistical analyses were performed using SAS JMP Pro (Windows version 12 Cary Inc., North Carolina). The results were expressed as mean standard deviation for continuous variables and number and percentages for categorical variables. Continuous variables were examined for their distributional characteristics and, when appropriate, were re-expressed to achieve normality. Student's t-test was used for continuous variables while percentages were compared using contingency tables and associated Chi-squares tests. All *p* values were expressed as exact values against the null hypothesis.

Results

A total of 78 patients with PPROM met the study criteria: 24 (31%) were included in group 1 (SDP <2cm) and 54 (69%) were included in group 2 (SDP 2cm). Both groups were similar with respect to maternal age, race and mean parity. Demographic characteristics are shown in Table 1. Patients with SDP <2cm were noted to have a significantly earlier gestational age at PPROM (p< 0.001). Latency periods were similar between groups (Table 1). Chorioamnionitis was diagnosed in 25 patients (32%) and maternal sepsis in 2 cases (2.6%). No patients were admitted to ICU and there were no cases of maternal death. There was no statistically significant difference between cases with SDP <2cm and those with SDP 2cm with regard to chorioamnionitis and sepsis (Table 1).

Table 1 Demographic variables and maternal outcomes between two groups with PPROM

Maternal age	SDP < 2cm (n = 24)	SDP 2cm (n = 54)	p
Race	29.5 5.06	28.7 7.60	0.577
African Americana	9 (37.5%)	31 (57.4%)	
Parity (number of births)	1.9 1.11	2.1 1.77	0.439
GA at PPROM (weeks)	27.1 2.52	29.4 3.12	0.001
Latency (days)	6.8 9.17	8.3 13.9	0.586
Chorioamnionitis (n)	7 (29%)	18 (33%)	0.715
Maternal sepsis (n)	1 (4%)	1 (1.8%)	0.55
Admission to ICU (n)	1 (4%)	0	0.327
Maternal death	0	0	--
Delivery indication			
Preterm labor	14 (58.33%)	31 (57.4%)	0.819
Chorioamnionitis	2 (8.3%)	11 (20.4%)	0.188
Abruption	5 (20.8%)	8 (14.8%)	0.51
Reached 34 weeks	1 (4%)	2 (3.7%)	0.239
NRFHT	2 (8.3%)	1 (1.9%)	0.169

a= African American versus non-African American

Indications for delivery were as follows: 50 patients due to preterm labor (64%), 13 patients due to chorioamnionitis (17%), 13 patients due to placental abruption (17%), 3 patients reached 34 weeks (3.8%) and 3 patients (3.8%) non-reassuring fetal heart tracing (NRFHT). There was no significant difference between groups when indications for delivery were compared (Table 1).

Neonatal outcomes are described in Table 2. Patients with SDP <2cm showed significantly earlier gestational age at delivery (p< 0.001), higher rate of RDS (p = 0.046), lower neonatal Apgar score at one minute (p = 0.012) and a lower birth weight (p< 0.001). Groups 1 and 2 were similar when evaluating neonatal sepsis (p=0.32), need for phototherapy (p=0.87), emergency intubation (p=0.225) and length of admission in ICU (p=0.081). There were 7 cases (9%) of neonatal death but no significant difference was noted between groups (p=0.113).

Table 2 Neonatal outcomes between two groups with PPROM

	SDP < 2cm (n=24)	SDP 2cm (n =54)	p value
GA at Delivery (weeks)	28.1 2.8	30.5 3.0	0.001
RDS (n)	19 (79.2%)	30 (55.6%)	0.046
Neonatal Sepsis (n)	9 (37.5%)	14 (26.4%)	0.324
Phototherapy (n)	16 (66.6%)	35 (64.8%)	0.873
Intubation (n)	10 (41.7%)	15 (27.7%)	0.225
ICU Length (days)	48.2 29.4	35.5 28.3	0.081
Apgar min 1	5.6 2.8	7.2 2.0	0.012
Birthweight (g)	1177 430	1676 568	<.0001
Neonatal death (n)	4 (16.7%)	3 (5.6%)	0.113

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Table 3 illustrates a correlation matrix, which demonstrates a positive correlation between gestational age and perinatal morbidities, such as gestational age at preterm premature rupture of membranes, gestational age at delivery, RDS, Apgar in the first minute, and birth weight. It indicates that the associations found between Group1-2 are confounded by gestational age.

Table 3 Correlation Matrix

	GAPP	GADel	RDS	BW	Apgar I'
GAPP	I	-	-	-	-
GADel	0.82	I	-	-	-
RDS	0.57	0.61	I	-	-
BW	0.72	0.9	0.53	I	-
Apgar I'	0.55	0.54	0.51	0.52	I

GAPP: Gestational Age at PPROM; GADel: Gestational Age at Delivery; RDS: Respiratory Distress Syndrome; BW: Birth Weight

Note: all correlations p <0.05

Discussion

The concept that oligohydramnios is associated with adverse outcomes is not new, however, results from previous studies have been conflicting and contradictory.[1-13] Our data indicated that oligohydramnios was associated with an earlier gestational age at PPROM. This finding is in disagreement with data published by most of the authors[1,8-10,12] and we believe that this association is the result of gestational age itself rather than a smaller single deepest vertical pocket.

In our study, the finding of a SDP <2cm was not associated with a shorter latency period when the results were controlled for gestational age. This finding is consistent with studies of Borna et al.,[9] Kurdoglu et al.[8] and Kacerovsky et al.[10] and in contrast to results published by Mercer et al.,[6] Vermillion et al.[3] and Piazze et al.[12] Interestingly, a study by Abbasalidadeh et al.[11] showed a longer latent phase with SDP <2cm when compared to cases with a normal SDP.

The theory behind the association between low residual amniotic fluid and short latency periods is speculative but essentially relies on the idea that PPROM can be caused by a preexisting intra-amniotic infectious process. This process is thought to induce an inflammatory response thereby triggering contractions and early labor. Although Vermillion et al found an association between oligohydramnios and a shorter latency period, he could not demonstrate a definitive association between chorioamnionitis and a shorter latency period. Kacerovsky et al.[10] measured the intra-amniotic inflammatory response by determining IL-6 concentration in the amniotic fluid but was unable to show an association between oligohydramnios and a higher intra-amniotic inflammatory response.[10]

Our study failed to demonstrate the association of SDP <2cm with the development of chorioamnionitis as described in most of the studies such as Ekin et al.,[1] Vintzileos et al.,[7] Vermillion et al.,[3] Borna et al.,[9] Kurdoglu et al.[8] and Park et al.[13] Evidence indicates that one of the functions of the amniotic fluid is to protect the amniotic cavity against microbial invasion due to its antimicrobial property. Once the membranes have ruptured, the cavity is vulnerable to ascending infection. Mercer et al.,[6] Piazze et al.[12] and Kacerovsky et al.[10] also failed to demonstrate this association. We agree that prophylactic antibiotic therapy may have reduced the impact of the association between oligohydramnios and chorioamnionitis as concluded by Mercer et al.[6]

Many studies have evaluated the relationship between oligohydramnios and rates of cesarean section due to a non-reassuring fetal heart tracing such as Vermillion et al.,[3] Borna et al.,[9] Piazze et al.,[12] Kurdoglu et al.,[8] Kacerovsky et al.[10] and Ekin et al.[1] They hypothesize that loss of amniotic fluid may cause cord compression, thereby leading to an abnormal fetal heart pattern. Their studies have been consistent in showing a statistically significant difference between groups with and without oligohydramnios. However, none of the studies compared the indications for delivery. Interestingly, our study had only three cases of emergent cesarean section due to NRFHT (3.8%). We found that 59% of patients were delivered secondary to preterm labor. When analyzing indications for delivery between groups, no statistically significant difference was noted.

In agreement with Park et al.[13] and Piazze et al.,[12] a SDP < 2cm was associated with an earlier gestational age at delivery between groups. This strong association has to be carefully evaluated since gestational age is a significant confounder for amniotic fluid volume, which may explain this finding. In Piazze et al.[12] study, there was no reference regarding adjusting for gestational age according to AFI. Also, in Park et al.[13] study, patients did not receive prophylactic antibiotics and some received tocolysis, which may have interfered with the association described in his study. Borna et al.[9] and Kurdoglu et al.[8] did not observe a difference in the gestational age of delivery between the groups.

We did demonstrate an association between oligohydramnios and specific perinatal outcomes such as RDS, lower Apgar score in the first minute of life, and lower birth weight. This is in agreement with findings by Park et al.,[13] Vintzileous et al.[7] and Kurdoglu et al.[8] It seems that Park et al.[8] and Kurdoglu et al.[8] did not control the results of these variables for gestational age, and Vintzileous et al.[7] study preceded the time where antibiotics and steroids were standard of care. For these reasons, we believe that these outcomes are the result of gestational age itself rather than the single deepest pocket. Other outcomes, such as need for phototherapy, intubation, and length of admission in ICU were similar between Groups 1 and 2.

A SDP < 2cm was not associated with the development of early sepsis in our study, which is consistent with studies performed by Ekin et al.,[1] Kurdoglu et al.,[8] Borna et al.[9] and Mercer et al.[6] We believe that the possible explanation is that this finding is a reflection of the lack of association between oligohydramnios and chorioamnionitis that was described previously. Another reason may be that all patients and newborns receive antibiotic prophylaxis as a standard of care. As described by Mercer et al.,[6] antibiotic treatment for PPROM in the setting of expectant management will decrease neonatal morbidity and sepsis. Vintzileous et al.[7] reported an association between oligohydramnios and neonatal infection however his study was performed in 1985 when antibiotics for PPROM were not standard of care.

We had 7 cases of neonatal death (9%), which is similar to results described by Kurdoglu et al.[8] (13%) however considerably higher than the rates described by Piazze et al.[12] (0.9%) and Kacerovsky et al.[10] (5.4%). No significant association was found between groups 1-2 in agreement with Kacerovsky et al.[10] This finding is discordant from the Kurdoglu et al.[8] study that found oligohydramnios was associated with increased rates of neonatal death, however this study was not controlled for gestational age.

Conclusion

The presence of oligohydramnios secondary to PPROM is not associated with adverse maternal and perinatal outcomes. Single

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deepest pocket has not been shown to be a good predictive marker of composite maternal and perinatal morbidity. The results also indicate that the gestational age is a strong confounder for amniotic fluid volume and previous research that has shown correlation of morbidity may have not considered these factor.

There are several limitations to our study. First, it was a retrospective observational study, which is only able to evaluate associations. Secondly, the analysis was based on a small sample size since we had to rely on archived information. The majority of cases identified during the study period were excluded due to insufficient information. Larger prospective studies would allow for a multivariate analysis, which may be beneficial in isolating the effect of single deepest pocket in maternal and perinatal morbidity.

Acknowledgments

None.

Conflicts of interest

None.

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