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REVIEW

Window to the Womb: Amniotic Fluid and Postnatal Outcomes

Julie R Whittington[1], Taylor Ghahremani[2], Andrew Friski[1], Andrew Hamilton[1], Everett F Magann[1]

[1]Women's Health Department, Naval Medical Readiness and Training Center Portsmouth, Portsmouth, VA, USA; [2]Department of OB/GYN, University of Arkansas for Medical Sciences, Little Rock, AR, USA

Correspondence: Julie R Whittington, Women's Health Department, Naval Readiness and Training Command Portsmouth, 620 John Paul Jones Circle, Portsmouth, VA, 23321, USA, Tel +1-979-848-9665, Email Julie.whittington09@gmail.com

Abstract: Amniotic fluid volumes are tightly regulated, and amniotic fluid derangement can indicate maternal complications or fetal abnormalities. Ultrasound estimate of amniotic fluid provides a tool to evaluate the maternal-fetal-placental interface in real-time. Oligohydramnios and polyhydramnios are associated with adverse maternal and neonatal outcomes. Oligohydramnios is associated with adverse maternal and neonatal outcomes including cesarean delivery, operative vaginal delivery, induction of labor, postpartum hemorrhage, small for gestational age neonate, intrauterine demise, neonatal death, NICU admission, and APGAR less than 7 at. 5 minutes of life Polyhydramnios is associated with adverse outcomes including cesarean delivery, induction of labor, placental abruption, shoulder dystocia, cord prolapse, postpartum hemorrhage, intrauterine fetal demise, NICU admission, neonatal death, APGAR less than 7 at 5 minutes of life, large for gestational age neonate, and respiratory distress syndrome. Therefore, Amniotic fluid should be evaluated when maternal or fetal well-being is in question.

Keywords: oligohydramnios, polyhydramnios, perinatal outcomes, single deepest pocket

Introduction

Amniotic fluid has many important functions and is regulated by multiple factors. It is integral to fetal development, including fetal pulmonary, gastrointestinal, and musculoskeletal maturation. It also acts to cushion the fetus from trauma. It is also believed to be sterile and possesses bacteriostatic properties.[1,2] Amniotic fluid is regulated by fetal swallowing, fetal urine production, lung secretions, and intramembranous absorption.[3] Amniotic fluid abnormalities (either increased or decreased fluid) are due to dysregulation of these processes from maternal or fetal disease. Normal amniotic fluid volume has been extensively studied using direct measurement, dye dilution methods, and ultrasound estimation.[4,5] Ultrasound estimation of amniotic fluid gives clinicians the ability to obtain a real time assessment of fetal status – a window to the intrauterine environment. Thus, measures of amniotic fluid have been considered a vital sign for fetal wellbeing.[6] Amniotic fluid abnormalities have been associated with many adverse maternal and neonatal outcomes.[7,8] In this review, adverse outcomes of polyhydramnios and oligohydramnios are explored.

Oligohydramnios

Diagnosis and Etiology of Oligohydramnios

Oligohydramnios has multiple definitions with differing thresholds depending on technique. The most accurate techniques for measuring amniotic fluid volume (AFV) are the direct measurement of amniotic fluid using the dye dilution or measurement of fluid at delivery.[9] However, the dye-dilution technique is invasive, and facilities may not be equipped to perform this technique and the direct measurement of AFV can only occur at delivery, precluding its utility in preventing possible adverse outcomes.[10] Amniotic fluid volumes of less than 200mL and 500mL measured by dye-dilution techniques have been used as thresholds for defining oligohydramnios.[11,12] Less invasive, sonographic estimates of amniotic fluid volume are performed using one of two common techniques, measurement of the single deepest pocket

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and the amniotic fluid index. The amniotic fluid index (AFI) is the summation of the single deepest pocket of amniotic fluid in each the 4 quadrants of the abdomen.[13] The four quadrants are identified by the linea nigra which divides the abdomen into right and left halves and by the umbilicus that divides the abdomen into upper and lower halves. The largest pocket in each quadrant that is at least 1 cm wide and with only transient fetal small parts or cord is measures and summed. Oligohydramnios has been defined as a single deepest vertical pocket (SDP) less than two centimeters, amniotic fluid index (AFI) of less than five centimeters, or less than 5% for gestational age.[14,15] Of the non-invasive sonographic techniques and definitions, a multitude of studies conclude that oligohydramnios as defined by an SDP of less than 2cm is the best current method for clinically diagnosing oligohydramnios because it has a lower rate of detection which in turn leads to a lower rate of intervention with no increase in poor perinatal outcomes when compared to AFI.[16–20]

The etiology of decreased amniotic fluid can be attributed to abnormalities of fetal urination, rupture of membranes, intramembranous and transmembranous pathways or idiopathic. Loss of fluid via rupture of membranes should always be considered. Abnormalities of fetal urination may be secondary to congenital anomalies such as bilateral renal agenesis, bilateral multicystic dysplastic kidneys, posterior urethral valves, and urethral atresia which all can lead to decreased or nearly absent amniotic fluid. Decreased renal blood flow secondary to medications that block the renin-angiotensin system could also lead to abnormalities in fetal urination and decreased amniotic fluid.[21] Common causes of uteroplacental insufficiency such as hypertensive disorders, anemia, coagulopathies, diabetes, smoking and other medications can also contribute to decreased amniotic fluid. It has also been shown that maternal hydration can affect AFV.[22] Abnormalities related to intramembranous and transmembranous pathways are less understood but variability in protein expression within the amnion could be the cause of a proportion of idiopathic cases.[23] As it is currently understood, oligohydramnios is complicated, and is often multifactorial in etiology.

Maternal and Neonatal Outcomes with Oligohydramnios

Several studies have analyzed the maternal and fetal outcomes associated with oligohydramnios. One systematic review and meta-analysis looking at retrospective and prospective studies over a period of 35 years showed that for pregnancies with idiopathic oligohydramnios without other comorbidities (n = 27,526), patients were more likely to undergo an emergency cesarean section for fetal intolerance of labor (RR, 2.16; 95% CI, 1.64–2.85), have an infant affected by meconium-aspiration syndrome (RR, 2.83; 95% CI, 1.38–5.77), and infant admission to the NICU (RR, 1.71; 95% CI, 1.20–2.42). However, the study showed no difference in the rates of having meconium-stained amniotic fluid.[24] The same systematic review and meta-analysis examined the outcomes of oligohydramnios in pregnancies with other comorbidities (n = 8067) including diabetes, both pre-gestational and gestational, hypertension in pregnancy, Rh alloimmunization, and fetal growth restriction. These patients were more likely to have an infant with low birth weight (RR, 2.35; 95% CI, 1.27–4.34), but interestingly no difference in the number of Newborn Intensive Care Unit (NICU) admissions, need for emergency cesarean section for fetal intolerance of labor, infant with meconium aspiration syndrome, and APGAR score <7.[24]

Furthermore, a separate systematic review and meta-analysis examined the perinatal outcomes of isolated oligohydramnios in term and post-term pregnancies compared to those with normal amniotic fluid volume. Patients with isolated oligohydramnios were more likely to undergo interventions including cesarean section and operative vaginal delivery (13% vs 5%; OR: 2.30; 95% CI: 1.00–5.29).[25] This study showed no differences in rates of meconium stained amniotic fluid, APGAR scores, umbilical cord pH, small for gestational age neonates, NICU admission, or perinatal death. Another systematic review and meta-analysis of 35,999 patients investigated the relationship between isolated oligohydramnios at term and adverse perinatal outcomes. Pregnancies affected by isolated oligohydramnios had high rates of induction of labor (OR 7.56, CI 4.58–12.48), cesarean delivery (OR 2.07, CI 1.77–2.41), APGAR score <7 at 1 and 5 minutes (OR 1.53, CI 1.03–2.26, and OR 2.01, CI 1.3–3.09, respectively), and NICU admissions (OR 1.47, CI 1.17–1.84).[26] There were no significant differences in umbilical cord pH of <7.1, or meconium stained amniotic fluid.

Outcomes may differ depending on gestational age at delivery. A retrospective study involving 1213 patients with isolated oligohydramnios observed differences in perinatal outcomes based on gestational age at time of delivery. The patients were stratified into early-term (37+0–38+6 weeks), full-term (39+0–40+6 weeks), and late-term (41+0–41+6 weeks). The rate of cesarean section was highest in the early-term group at 37.8% compared to 30.1% in the full-term

group, and 35.3% in the late term group (p = 0.03).[27] Newborn jaundice was also highest in the early-term group at 3.5% (p = 0.01), and meconium stained fluid was highest in the late-term group at 12.9% (p = 0.03).[27]

Another retrospective analysis of maternal and fetal outcomes examined the differences between patients induced due to idiopathic oligohydramnios, patients in spontaneous labor with normal amniotic fluid, and induction of labor for late term pregnancy with normal amniotic fluid (total n = 27,708). The number of neonates that were small for gestational age was significantly higher in the idiopathic oligohydramnios induction group (P < 0.001), incurring a 2.18-fold increased risk.[28] No differences were observed in the rates of NICU admission, however. Induction for the oligohydramnios group had a nearly 3-fold increased risk of cesarean section compared to spontaneous labor [ORa: 2.72 95% CI (2.28–3.24)].[28]

In low- and middle-income countries, the rate of oligohydramnios in a prospective study of over 12,000 patients was 0.7%. Regarding neonatal outcomes, this study showed an increased risk of stillbirth (OR 5.16, 95% CI 2.07, 12.85), neonatal death within the first 28 days of life (OR 3.18, 95% CI 1.18, 8.57), low birth weight (OR 2.10, 95% CI 1.44, 3.07), and preterm birth (OR 2.73, 95% CI 1.76, 4.23).[29] Maternal outcomes of pregnancies affected by oligohydramnios were more likely to have postpartum hemorrhage (5.7% vs 1.7%, OR 2.94, 95% CI 1.31, 6.61), fetal malposition (5.7% vs 1.9%, OR 2.44, 95% CI 1.07, 5.59), and cesarean delivery (28.7% vs 13.5%, OR 2.07, 95% CI 1.41, 3.03) compared to pregnancies without oligohydramnios.[29]

One study focused more specifically on whether oligohydramnios had an influence on fetal heart rate tracings during induction of labor at term (n = 3787). The rate of oligohydramnios was 3.9% in this population.[30] There was no statistically significant difference in the characteristics of the fetal heart rate tracings in the 2 hours preceding delivery, nor was there a difference in the composite neonatal morbidity between the two groups. However, in patients with oligohydramnios, fetal tachycardia sustained for 30 minutes or greater was associated with composite neonatal morbidity (31.3 vs 5.3% adjusted odds ratio 8.63, 95% confidence interval 2.18, 34.1), which included having 1 or more of the following: infant death prior to hospital discharge, respiratory distress, hypoxic ischemic encephalopathy (HIE), need for hypothermic therapy, meconium aspiration syndrome, sepsis or suspected sepsis, seizures, hypoglycemia.[30]

Oligohydramnios is associated with adverse maternal and neonatal outcomes including cesarean delivery, operative vaginal delivery, induction of labor, postpartum hemorrhage, small for gestational age neonate, intrauterine demise, neonatal death, NICU admission, and APGAR less than 7 at. 5 minutes of life in some, but not all, studies. It is likely that the etiology of oligohydramnios drives the difference in outcomes.

Polyhydramnios

Diagnosis and Etiology of Polyhydramnios

Polyhydramnios (also called hydramnios) is defined as an excessive accumulation of amniotic fluid in the uterus. The incidence varies from 0.2% to 2%.[7] Actual increased amniotic fluid volume can be identified antepartum or at the time of delivery as previously referenced in this manuscript. Polyhydramnios has been defined as actual amniotic fluid volumes of greater than 1500 cc, greater than 2000 cc, greater than the 95th percentile or greater than the 97.5th percentile for a given gestational age.[12,31–34]

In daily clinical practice, ultrasound is used to diagnose polyhydramnios. An AFI of greater than 24 centimeters (95%) or 25 centimeters (97%) categorizes a pregnancy as having polyhydramnios.[33,35] The second technique is the single deepest pocket, largest vertical pocket or maximum vertical pocket. All these terms can be used interchangeably. If the single largest pocket is ≥8 cm with a horizontal measurement of at least 1 cm, the pregnancy would be labeled as having hydramnios.[36] The third ultrasound technique is the subjective assessment of the amniotic fluid volume by an experienced examiner. This technique is the visualization of the amniotic fluid volume without measurements. This technique has been shown to have similar predictability as the AFI and SDP pocket techniques in determining if the amniotic fluid volume is high (polyhydramnios).[37]

The etiology of polyhydramnios can generally be divided into 3 categories. The largest of these is idiopathic, which compromises approximately 50–60% of the cases of polyhydramnios.[38] Pregnancies labeled as idiopathic polyhydramnios are those that, after a thorough assessment is undertaken, no reason for the polyhydramnios can be identified. This is followed by fetal anomalies, aneuploidy, genetic diseases, and placental abnormalities which affects 8% to 45% of

pregnancies complicated by hydramnios.[39] Most of the identified cases in this group are the result of open neural tube defects, central nervous system conditions that interfere with fetal swallowing, gastroesophageal conditions that obstruct the gastroesophageal tract or conditions that result in increased urine production from high output cardiac failure. Another cause of hydramnios is Bartter syndrome, which is characterized by impaired ion transportation resulting in salt wasting and polyuria.[40] The third category is women with pre-gestational or gestational diabetes, which complicates 20–25% of patients with hydramnios.[41,42] This is thought to be due to polyuria from fetal hyperglycemia, however other mechanisms have been suggested, such as osmotic shift of fluid into the amniotic cavity.[43]

Maternal and Neonatal Outcomes and Polyhydramnios

Many studies have been performed to evaluate the impact of polyhydramnios on obstetrical outcomes. Aviram et al performed a retrospective cohort study comparing pregnancy outcomes between women with isolated, elevated amniotic fluid index with women with normal amniotic fluid index at the time of admission. Exclusion criteria included women with gestational or pre-gestational diabetes, gestational age less than 34 weeks, and fetuses with chromosomal or structural anomalies. Of the 31,376 women in the study, 215 (0.7%) had isolated polyhydramnios. This study found that women with isolated polyhydramnios had elevated rates of labor induction (adjusted odds ratio 1.7, 95% confidence interval 1.01–2.8), cesarean delivery (adjusted OR 2.6, 95% CI 1.7–4.0), placental abruption (adjusted OR 8.4, 95% CI 2.00–35.4), abnormal fetal heart rate tracings (adjusted OR 2.6, 95% CI 1.6–4.5), prolonged first stage of labor (adjusted OR 3.6, 95% CI 1.97–6.7), higher rates of shoulder dystocia (adjusted OR 3.4, 95% CI 1.2–9.7) and respiratory distress syndrome (adjusted OR 38.9, 95% CI 4.6–332.6). Their findings suggest isolated polyhydramnios at time of admission for labor, when occurring at or beyond 34 weeks of gestation, is associated with several adverse outcomes.[44]

Adamczyk et al performed a study investigating the development of children with an antenatal diagnosis of idiopathic polyhydramnios. The study was conducted over 12 months after delivery and included 64 healthy pregnant patients with idiopathic polyhydramnios, defined as AFI > 20cm. A vast majority of parents, 96%, responded that they believed the development of their child was normal. Further testing of the children revealed abnormalities in 44% of the children. 30% had organic or functional neuromuscular disorders, defined as abnormal muscle tone, speech, swallowing or breathing difficulties including vomiting, excessive regurgitation or idiopathic apnea. 19% had an isolated small malformation. 3% were noted to also be small for gestational age and were diagnosed with genetic syndromes ($P < 0.001$). 14% of children were diagnosed with more than one abnormality described above. The findings of the study suggested functional disorders of the gastrointestinal tract, CNS and the neuromuscular disorders may be responsible for the development of idiopathic polyhydramnios and that co-existing SGA with polyhydramnios increases risk of genetic diseases. Of note, only the findings associated with birth weight obtained statistical significance.[45]

In a differing retrospective study by Abele et al, 272 pregnancies with idiopathic polyhydramnios, defined by single deepest vertical pocket >8 cm, were evaluated to determine the proportion and type of fetal anomalies associated with polyhydramnios. Eighty-nine (32.7%) of the pregnancies were found to have prenatal diagnosis of a fetal anomaly. An additional 65 (23.9%) of the pregnancies were found to have polyhydramnios in the setting of diabetes. Of the remaining 118 (43.4%) pregnancies, 11 (9.3%) had a postnatal diagnosis of an anatomic anomaly – gastrointestinal atresia being the most prevalent followed by renal abnormalities. The findings of the study suggest that an underlying cause of polyhydramnios will not be determined prior to delivery in 40% of pregnancies and that 10% will have anatomic anomalies found after delivery. Fluid volume, estimated fetal weight and maternal age did not appear to impact detection of these anomalies antenatally.[46]

Understanding that in many cases of polyhydramnios the etiology is only discovered after delivery, Fishel-Bartal evaluated whether addition of fetal MRI studies could aid with diagnosis. Forty-six fetuses with AFI greater than or equal to 25 cm were included in the retrospective study and all underwent ultrasound evaluation with a neurosonogram and a fetal MRI. In total, the neurosonogram detected CNS abnormalities in 12 (26%) cases and MRI detected 23 (50%) abnormalities. There was no significant difference in findings based solely on AFI, but the sample size was insufficient to determine a true association between severity of polyhydramnios and incidence of anomalies. MRI did appear to be

superior with detection of brain anomalies when comparing non-isolated vs isolated polyhydramnios (62.9% vs 31.6%, p = 0.019). The authors' conclusion was that fetal MRI may aid in evaluation of polyhydramnios, but the cost-effectiveness of this approach is yet to be proven.[47]

Maymon et al, citing conflicting data of polyhydramnios in regards pregnancy outcomes, attempted to better define its impact. A total of 60,702 patients were included in the study. One thousand two hundred and eleven were diagnosed with polyhydramnios, defined as AFI greater than 25 cm, vertical pocket greater than 8 cm or increased by subjective assessment. When comparing pregnancies with polyhydramnios and those with normal amniotic fluid volume, they found a higher rate of cesarean delivery (22.8% vs 8.5%, P < 0.01), antepartum death (0.6% vs 0.2%, P < 0.005), postpartum death (2.8% vs 0.4%, P < 0.01), placental abruption (0.9% vs 0.3%, P < 0.001), fetal distress (6.1% vs 3.65%, P < 0.0015), meconium-stained fluid (17.8% vs 15%, P < 0.001), low Apgar score at 5 minutes of life (2.95% vs 1%, P < 0.01), malpresentation (6.8% vs 2.9%, P < 0.01), clinical chorioamnionitis (0.3% vs 0.1%, P < 0.05), cord prolapse (2.2% vs 0.3%, P < 0.01), and large for gestational age (23.8% vs 8.1%, P < 0.01). The authors concluded that, within term pregnancies, idiopathic polyhydramnios itself is a risk factor for adverse obstetrical outcome and surveillance is warranted.[48]

In another retrospective cohort study, Harlev et al stratified five study groups based on severity of polyhydramnios and compared them to determine if a critical value exists for polyhydramnios and associated obstetrical risk. The five groups, AFI <20 (n = 9974), 20–23 (n = 2771), 24–27 (n = 1315), 28–31 (n = 494), and >32 (n = 260), were analyzed and a linear relationship between the severity of polyhydramnios existed with increased incidence of hypertensive disorders, diabetes mellitus, preterm labor, macrosomia, placental abruption and low birth weight. The authors concluded that, due to the increased rates of these adverse events beyond AFI of 20 cm, notably a normal value, the cut-off for polyhydramnios should be reconsidered.[49]

Crimmins et al conducted a study that evaluated polyhydramnios with and without accelerated growth, specifically in the setting of women with normal oral glucose challenge tests. A total of 282 singleton, nonanomalous pregnancies with 1hr glucose <130 were included in the study after development polyhydramnios (AFI >24cm or maximum vertical pocket >8cm) or accelerated fetal growth (abdominal circumference >95th percentile). They found that antenatal diagnosis of polyhydramnios resulted in higher incidence of birth weight >90th% and postpartum hemorrhage. Pregnancies with polyhydramnios and accelerated growth were at an even higher risk (OR 18.5, 95% CI 8.9–38.6 and OR 4.2, 95% CI 2.4–7.6, respectively).[50]

Recently, Pagan et al completed a systematic review and meta-analysis of outcomes with idiopathic polyhydramnios. They found there were higher odds of neonatal death (OR 8.68, 95% CI 2.91–25.87), intrauterine fetal demise (OR 1.94, 95% CI 2.5–23.38), NICU admission (OR 1.94 CI 1.45–2.59). They also found higher odds of 5-minute APGAR less than 7 (OR 2.21, CI 1.34–3.62), malpresentation (OR 2.73, 95% CI 2.06–3.61) and cesarean delivery (OR 2.31, 95% CI 1.79–2.99). The authors recommended consideration for antenatal testing due to the findings noted.[51]

Polyhydramnios is associated with adverse outcomes including cesarean delivery, induction of labor, placental abruption, shoulder dystocia, cord prolapse, postpartum hemorrhage, intrauterine fetal demise, NICU admission, neonatal death, APGAR less than 7 at 5 minutes of life, large for gestational age neonate, and respiratory distress syndrome. It is also associated with previously unrecognized anomalies.

Conclusion

Sonographic assessment of amniotic fluid is used in practice daily and gives clinicians the ability to evaluate an important facet of fetal well-being. Amniotic fluid abnormalities (oligohydramnios and polyhydramnios) are associated with significant risks to both the pregnant person and the neonate. (Table 1) The discovery of amniotic fluid abnormalities may lead to increased fetal surveillance, timely delivery, and improve maternal and neonatal outcomes. The value of the ability to easily assess amniotic fluid status non-invasively, at the bedside, cannot be overstated, as it provides a "window to the womb".

Table 1 Adverse Outcomes Associated with Amniotic Fluid Abnormalities

	Oligohydramnios	Polyhydramnios
Maternal Outcomes	Cesarean Delivery Operative Vaginal Delivery Induction of Labor Postpartum Hemorrhage	Cesarean Delivery Induction of Labor Placental Abruption Shoulder Dystocia Cord Prolapse Postpartum hemorrhage
Fetal/Neonatal Outcomes	Intrauterine demise NICU Admission Neonatal death APGAR < 7 at 5 minutes Small for gestational age	Intrauterine demise NICU Admission Neonatal death APGAR <7 at 5 minutes Large for gestational age Respiratory distress syndrome

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Disclosure

JRW, AF, and AH are military service members. EFM reports he is one of the co-authors on the chapter on the ultrasound assessment of amniotic fluid volume for UpToDate. The author reports no other conflicts of interest in this work.

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