Clinical Relevance of Sonographically Estimated Amniotic Fluid Volume

Polyhydramnios

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Polyhydramnios is an excessive amount of amniotic fluid within the amniotic cavity. The etiology of polyhydramnios may be idiopathic, the consequence of fetal structural anomalies, or the consequence of various fetal and maternal conditions. The clinical importance of polyhydramnios is found in its association with adverse pregnancy outcomes and the risk of perinatal mortality. The antenatal management of polyhydramnios can be challenging as there are no formalized guidelines on the topic. The purpose of this review is to provide a literature-based overview on the subject of polyhydramnios in singleton pregnancies, demonstrate its clinical implications, and describe a practical approach to its management.

Key Words—amniotic fluid; antenatal management; perinatal mortality; polyhydramnios

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Abbreviations

AFI, amniotic fluid index; AFV, amniotic fluid volume; IUGR, intrauterine growth restriction; RR, relative risk; SDP, single deepest pocket

Pregnancies complicated by polyhydramnios are at an increased risk of a wide variety of adverse outcomes. Given there are no guidelines or practice bulletins from the American College of Obstetricians and Gynecologists, Society of Obstetricians and Gynaecologists of Canada, Royal College of Obstetricians and Gynaecologists, or Royal Australian and New Zealand College of Obstetricians and Gynaecologists on the topic of polyhydramnios, its evaluation and management can be a challenging task for practitioners. The aim of this review is to provide a literature-based overview on the subject of polyhydramnios in singleton pregnancies, demonstrate its clinical implications, and describe a practical approach to its management.

Definition and Sonographic Assessment of Polyhydramnios

Polyhydramnios, also known as hydramnios, refers to an excessive amount of amniotic fluid. Within this review, we will use the terms *polyhydramnios* and *hydramnios* interchangeably. The overall incidence of polyhydramnios, irrespective of etiology, ranges in various studies from 0.2% to 2.0%.[1–8] Polyhydramnios is generally detected either by physical examination, if the uterus appears larger or measures larger than expected by the pregnancy dating, by sonography

at the time of the fetal anatomic survey, or when the development of other conditions warrants assessment of the amniotic fluid or fetal growth during a pregnancy. Polyhydramnios is defined in the literature in a number of different ways (Table 1).[1,9–15] Clinically, polyhydramnios is identified using either the clinician's subjective impression of an increased amount of amniotic fluid during a sonographic assessment or using a sonographic measurement to estimate the amniotic fluid volume (AFV). Two commonly used sonographic measurements that suggest a high volume of amniotic fluid include an amniotic fluid index (AFI) of 24 cm or greater[12] or a single deepest pocket (SDP) of 8 cm or greater.[1,14] The terms mild, moderate, and severe have been used to describe degrees of polyhydramnios. Mild hydramnios has been defined as an AFI of 25 to 30 cm[16,17] or an SDP of 8 cm or greater,[1] moderate hydramnios as an AFI of 30.1 to 35 cm[16,17] or an SDP of 12 cm or greater,[1] and severe hydramnios as an AFI of 35.1 cm or greater[16,17] or SDP of 16 cm or greater.[1]

Increasing severity of polyhydramnios appears to correlate with an increased risk of perinatal mortality and congenital abnormalities.[18,19] Up to 31% of pregnancies with severe polyhydramnios (AFI ≥35 cm) have a major congenital anomaly such as a central nervous system, cardiac, or gastrointestinal anomaly.[20] Unfortunately, sonographic assessment of amniotic fluid has not been shown to be very accurate in reflecting the actual AFV in the setting of either oligohydramnios or polyhydramnios.[21] Magann et al[22] found that the predictive ability of the AFI and SDP to identify hydramnios above the 95th or 97th percentile ranged between 33% and 46%. Furthermore, the addition of color flow Doppler imaging in the assessment of amniotic fluid does not increase one's ability to detect polyhydramnios via sonography.[23] Despite clear limitations, sonographic estimation of the AFV remains the clinical standard and is used to diagnose polyhydramnios and follow the values serially over time. In summary, whereas there are several definitions of polyhydramnios and the sonographic assessment may not always correlate with the actual AFV, the importance of the diagnosis lies in its association with potential peripartum complications.

Table 1. Definitions of Polyhydramnios

AFV >2000 mL[9]
AFV >95th percentile for gestational age[10]
AFV >97th percentile for gestational age[11]
AFI ≥24 cm[12]
AFI >25 cm[13]
SDP ≥8 cm[1,14]
Subjectively increased AFV[15]

Physiologic Characteristics of Amniotic Fluid and Polyhydramnios

Amniotic fluid provides an optimal environment for normal fetal growth and development. The AFV is the result of a series of complex and dynamic pathways influencing the movement of fluid into and out of the amniotic space. This balance is regulated by mechanisms that are not yet completely understood.[24] The main sources determining the AFV include fetal urine production, fetal swallowing, secretion of fetal lung fluid, movement of water and solutes between fetal blood and the placenta (intramembranous pathway), movement of water and solutes across the surface of the amnion and chorion (transmembranous pathway), secretions by the fetal oral and nasal cavities, and movement of fluid across fetal skin during early gestation.[25] A disturbance in any of these processes can result in an abnormally low or high AFV, referred to as oligohydramnios or polyhydramnios, respectively. The primary sources of amniotic fluid are fetal urine production, fetal lung fluid, and fetal oral and nasal secretions.[24] The main routes of amniotic fluid removal are fetal swallowing and absorption via the intramembranous pathway.[24] Polyhydramnios can result from an imbalance in any of these pathways. Decreased elimination of amniotic fluid, either from anomalies (eg, choanal atresia, esophageal atresia, tracheoesophageal fistula, and duodenal or intestinal atresia) or as a result of reduced swallowing ability or function, which can be due to neurologic impairment (eg, anencephaly) or neuromuscular disorders (eg, myotonic dystrophy), drug induced, or potentially a result of fetal hypoxia as evidenced in the ovine model, can all result in hydramnios.[26] Increased fetal urine production, polyuria, may occur as a result of abnormal fetal renal function (eg, Bartter syndrome[27]), a high fetal cardiac output state, a fetal brain abnormality, or maternal diabetes and can lead to the development of hydramnios.[28] In addition, movement of fluid across the exposed fetal cerebral and spinal tissues may contribute to excess fluid within the amniotic cavity and thus may explain the development of polyhydramnios in the setting of anencephaly and spina bifida.[29] Furthermore, conditions affecting the fetus such as isoimmunization, infections (eg, cytomegalovirus, toxoplasmosis, syphilis, and parvovirus), multiple gestations, fetal-maternal hemorrhage, and placental tumors have all been linked to hydramnios.[14,30,31]

Etiology of Polyhydramnios

Historically, idiopathic polyhydramnios accounts for approximately 50% to 60% of the total number of cases.[14,32] The remaining cases generally fall into one of the following categories: congenital anomalies and genetic disorders (8%–45%), maternal diabetes (5%–26%), multiple gestations (8%–10%), fetal anemia (1%–11%), and other (eg, hydrops fetalis, Bartter syndrome, and congenital viral infections).[1,4,6,20,32–38] Maternal substance abuse[39] and smoking[40] have also been linked to an increased risk of polyhydramnios, although the physiologic mechanisms of these potential causes are not completely understood. Alterations in the maternal metabolic status likely play an important role as a cause of polyhydramnios, as seen in the setting of gestational and pregestational diabetes.[31]

When there is no identifiable cause (eg, congenital fetal anomaly, genetic chromosomal abnormality, maternal diabetes, fetal infection, or multiple gestation) of hydramnios, it is categorized as idiopathic. There have been several studies focused on aquaporin channels, which may offer an insight into the physiologic changes that occur in the setting of idiopathic hydramnios. Aquaporins are membrane-bound water channel proteins that serve to regulate the movement of water across several different biological membranes.[41] In mice, Mann et al[41] showed that those mice without aquaporin 1 produced a greater amount of amniotic fluid and thus speculated that idiopathic hydramnios may be a result of aquaporin 1 channel deficiency in the human fetal membranes. However, Mann et al[42] subsequently demonstrated in further studies that, in fact, aquaporin 1 expression is increased in pregnancies complicated by idiopathic polyhydramnios and is likely a compensatory response to the increased fluid volume in humans, rather than a cause. Zhu et al[40] found an increase in the expression of aquaporin 8 in the amnion and aquaporin 9 within the amnion and chorion in the setting of idiopathic hydramnios, which may indicate an adaptive change in the fetal membranes and placenta to potentially regulate the AFV. The exact mechanism by which idiopathic hydramnios develops and is regulated appears to be complex and remains incompletely understood.

Fetal Anomalies and Aneuploidies Associated With Polyhydramnios

The second most common etiology for polyhydramnios is congenital anomalies and genetic disorders. The reported fetal anomaly risk ranges from 8% to 45% in the setting of polyhydramnios.[20] In 2002, Dashe et al[20] evaluated 672 pregnancies, of which 11% (77) were complicated by one or more major anomalies. The most common anomalies in this data set were central nervous system (28%), cardiac (22%), and gastrointestinal (14%) anomalies, followed by thoracic (11%), craniofacial (9%), skeletal (9%), renal (3%), and ventral wall (3%) anomalies. In another study, a group of 927 pregnancies complicated by polyhydramnios was evaluated, and common congenital defects included cardiovascular defects (16.6%), esophageal atresia (13%), renal defects (12%), neural tube defects (11.3%), microcephaly (5.3%), and duodenal atresia (4.9%).[43]

The incidence of fetal aneuploidy varies widely. In those with idiopathic hydramnios, the incidence of fetal aneuploidy ranges from 3.2% to 13.3%.[44,45] In 1999, Biggio et al[2] evaluated 370 patients with hydramnios including those with anomalies and maternal diabetes and found the incidence of fetal anomalies to be 8.4% and the incidence of fetal aneuploidy to be approximately 0.3% overall. Dashe et al[20] noted fetal aneuploidy in 10% of fetuses who were found to have anomalies by sonography and aneuploidy in only 1% in those without sonographic evidence of anomaly. Most commonly, fetal aneuploidy associated with polyhydramnios includes trisomy 21, trisomy 18, and trisomy 13, although other chromosomal alterations can also occur.[46,47]

The risk of a major fetal anomaly increases with increasing severity of hydramnios[17,20]; however, there is no significant difference in the risk of fetal aneuploidy.[20] In the setting of a normal sonographic evaluation, the likelihood of a major fetal anomaly has been shown to be approximately 1% with mild hydramnios (AFI >25 cm), 2% with moderate hydramnios (AFI >30 cm), and 11% with severe hydramnios (AFI >35 cm).[20] Importantly, the ability to detect the anomaly by sonography was not different according to the hydramnios severity.[20]

Polyhydramnios and Diabetes

Maternal pregestational and gestational diabetes may be associated with polyhydramnios. In an evaluation of 672 pregnancies with polyhydramnios by Dashe et al[20] in 2002, 5% were complicated by gestational diabetes (2% were being treated with insulin, and 3% were diet controlled), and 2% were complicated by pregestational diabetes. In a study by Idris et al[48] in 2010, among 314 pregnancies complicated by pregestational diabetes and with a gestational age later than 24 weeks, the incidence of polyhydramnios was 18.8%. The prevalence of hydramnios in gestational diabetes ranges from 8% to 20%[49] and can be found 30 times more frequently than in nondiabetic pregnancies.[50]

Generally, the hydramnios appears to be related to poor glycemic control.[48] Interestingly, even in the setting of strict glycemic control and gestational diabetes, neonates of women with hydramnios were significantly larger when compared to neonates of women with gestational diabetes and a normal AFV.[51] Poor diabetic control leading to maternal hyperglycemia results in fetal hyperglycemia and hyperinsulinemia. The exact mechanism of the polyhydramnios in the setting of maternal diabetes is not entirely understood. The proposed etiology is related to fetal polyuria as a result of increased osmotic diuresis due to the fetal hyperglycemia.[29] Higher amniotic fluid glucose concentrations have been shown to correlate with higher AFIs[52] and poorer glucose control.[53] There may also be an increase in fetal urinary output in macrosomic fetuses (often seen in diabetic pregnancies) due to an increase in cardiac output, an increase in blood volume, and thus an increase in the glomerular filtration rate.[28]

The presence of polyhydramnios in a pregnancy complicated by diabetes does not appear to convey an increased risk of perinatal mortality. Among 71 patients with hydramnios and pregnancies complicated by diabetes, Biggio et al[2] found no association with an increased risk of perinatal mortality. In 2001, Shoham et al[51] compared 184 women with gestational diabetes and hydramnios (AFI >25 cm) to 184 women with gestational diabetes and a normal AFI and found no association with an increased risk of perinatal morbidity or mortality. Similarly, Idris et al[48] found no significant increase in adverse pregnancy outcomes in pregnancies complicated by pregestational diabetes and polyhydramnios other than iatrogenic preterm delivery. This finding seems to indicate that it is not the polyhydramnios associated with maternal diabetes per se, but rather the poorly controlled diabetes and underlying disease process that is related to perinatal morbidity, mortality, and adverse pregnancy outcomes in diabetic pregnancies. Thus, if a pregnancy is complicated by diabetes (either pregestational or gestational) and hydramnios is present, we recommend that clinicians perform antepartum fetal surveillance as they would for a diabetic pregnancy without hydramnios. A targeted sonographic evaluation is recommended in the setting of hydramnios complicated by diabetes, although the incidence of major fetal anomalies in patients with diabetes and hydramnios (12%) is similar to the overall incidence of major fetal anomalies in those patients with hydramnios but without diabetes (11%).[20]

Perinatal Morbidity and Mortality Associated With Polyhydramnios

Pregnancies complicated by polyhydramnios are at an increased risk of adverse pregnancy outcomes, including perinatal mortality.[2,8,54] Golan et al[55] showed polyhydramnios to be related to an increased risk of the following maternal, fetal, and neonatal complications: pregnancy-induced hypertension (relative risk [RR] = 2.7), urinary tract infection (RR = 2.8), premature delivery (RR = 2.7), premature rupture of membranes (RR = 3.0), nuchal cord (RR = 3.3), abnormal fetal presentation (RR = 2.5), cesarean delivery (RR = 4.0), intrauterine fetal death (RR = 7.7), and neonatal death (RR = 7.7). In addition, there appears to be a relationship between polyhydramnios and delivery complications, such as an increased cesarean delivery rate,[2,54] fetal malpresentation at delivery,[56] delivery of a macrosomic fetus,[57] and fetal distress in labor.[54,58] Neonatal complications have also been linked to polyhydramnios, such as lower Apgar scores,[54,58] increased neonatal birth weight,[54] increased rate of neonatal intensive care unit admissions,[54,58] and neonatal death.[58] However, a pregnancy complicated by hydramnios (AFI >24 cm) at term identified during the labor process is not associated with an increased risk of delivering a compromised neonate.[57]

Biggio et al[2] evaluated 370 cases of polyhydramnios, including patients with fetal anomalies and maternal diabetes, and found there to be a significantly increased risk of perinatal mortality (49 of 1000) compared to 36,426 controls (14 of 1000). If one were to exclude the cases of anomalies (8.4% [31 patients]), the perinatal mortality risk would remain more than twice that of the control group (3.7% compared to 1.4%).[2] There were also 71 patients with diabetes, and no perinatal deaths occurred in this group.[2] Maymon et al[8] found hydramnios, diagnosed by either an AFI greater than 25 cm, an SDP greater than 8 cm, or subjective assessment, at term (>37 weeks) to be an independent risk factor for perinatal death after adjustment for potential confounding variables such as congenital anomalies and diabetes. Likewise, in the setting of preterm delivery, Mazor et al[56] found polyhydramnios to be an independent risk factor for perinatal mortality even after controlling for congenital anomalies and other factors that may influence perinatal morbidity and mortality.

Several studies have shown an increase in pregnancy complications and adverse pregnancy outcomes, including perinatal mortality, in the setting of idiopathic hydramnios. Panting-Kemp et al[59] compared 151 pregnancies with idiopathic hydramnios, defined as an AFI greater than 24 cm

with the absence of congenital anomalies, placental anomalies known to cause hydramnios, pregestational or gestational diabetes, and isoimmunization, to 302 pregnancies with a normal sonographically estimated AFV and found that those with idiopathic hydramnios were more likely to have a fetus with malpresentation (breech or transverse lie), have a higher likelihood of delivering a neonate weighing greater than 4000 g, and to undergo primary cesarean delivery. Contrary to other studies, they did not find an association of prematurity, low birth weight, or perinatal death with idiopathic hydramnios, and there were no perinatal deaths in either group.[59] Maymon et al[8] evaluated 1211 pregnancies with idiopathic hydramnios defined as an AFI greater 25 cm, an SDP of 8 cm or greater, or an increased volume by subjective assessment and found that after adjustment for congenital anomalies and diabetes, hydramnios was associated with a 5-fold increase in perinatal mortality. Idiopathic hydramnios has also been shown to be associated with an increase in morbidity and mortality after birth within the first year of life.[38] A review of all cases of idiopathic polyhydramnios in the literature by Magann et al[49] found an overall 2- to 5-fold increased risk of perinatal mortality.

Polyhydramnios, Cervical Length, and Preterm Labor

The frequency of preterm delivery in the setting of polyhydramnios ranges from 11.1% to 29.4%.[60] Preterm labor and subsequent preterm delivery are often thought to be directly related to polyhydramnios, as a result of the increasing volume of amniotic fluid. This correlation is reasonable to make considering that the increasing distention of the uterus can result in uterine contractions. Thus, one would expect there to be a higher rate of preterm labor and preterm delivery in those women with increasingly higher AFVs correlating with increasing severity of polyhydramnios. However, in a study by Many et al,[61] among 275 singleton pregnancies with polyhydramnios, the incidence of preterm delivery was 18.5%, but no significant difference was seen in the rate of preterm delivery with increasing severity of hydramnios. The rates of preterm delivery were 39% among those with congenital anomalies and 22% among those with maternal diabetes.[61] The rate of prematurity for those pregnancies with idiopathic hydramnios (12.6%) was shown to be similar to the control population in the study.[61] Therefore, it appears to be the underlying cause of hydramnios (eg, congenital anomaly or diabetes) as opposed to the excess amniotic fluid that determines when the preterm labor and subsequent preterm delivery will occur.[61]

Women with polyhydramnios do have a gradual shortening of their cervical length; however, it is not related to the severity of the hydramnios.[62] It remains unknown to what degree the cascade resulting in preterm labor and delivery is influenced by the underlying etiology of the hydramnios and how much is influenced by iatrogenic intervention during monitoring of these complicated pregnancies. The higher prevalence of preterm delivery in diabetic pregnancies is likely related to the higher rate of hypertension, fetal distress, and elective delivery commonly associated with these cases.[63]

Effect of Polyhydramnios on Uterine and Placental Hemodynamics

The exact mechanism responsible for fetal loss in the setting of polyhydramnios is unknown. There is evidence that amniotic pressure increases as a result of increasing AFV.[64] This increased pressure may lead to a lower umbilical artery pH on cord blood analysis.[65] In 17 patients with polyhydramnios, Fisk et al[64] demonstrated that the amniotic pressure was always above the normal mean for gestation; furthermore, the minimum depth of the SDP in the group with increased pressure (16 cm) exceeded the maximum SDP depth (14.5 cm) in the group with normal pressure. In those pregnancies with an SDP of 15 cm, amniotic pressure was always increased.[64] In 1994, Fisk et al[65] went on to show that with increasing amniotic pressure, both the fetal pH and Po_2 were significantly negatively correlated with the degree of elevation of the amniotic fluid pressure. In this study by Fisk et al,[65] some of the fetuses in the study were hydropic, had congenital fetal anomalies, or were from multiple pregnancies; yet the relationship between amniotic fluid pressure and fetal blood gases remained significantly associated after accounting for these potential confounding variables. In addition, in a study of 113 patients with idiopathic hydramnios (AFI >24 cm), the middle cerebral artery pulsatility index was significantly more likely to be abnormal compared to controls. As the AFI increased, the middle cerebral artery pulsatility index was shown to decrease, which may indicate shunting of blood flow by the fetus to vital organs such as the brain, due to fetal compromise.[66] Concisely, the underlying physiologic mechanism resulting in fetal death remains uncertain.

Intrauterine growth restriction (IUGR) is seen in approximately 3% to 6% of cases of polyhydramnios.[2,54,67] The finding of polyhydramnios with IUGR is of great concern for underlying major fetal anomalies, chromosomal abnormalities, or both.[47] Sickler et al[47] identified 39 fetuses

with both polyhydramnios (AFI ≥24 cm) and IUGR (defined as estimated fetal weight <10th percentile) and found these conditions to be an "ominous combination." In their group, Sickler et al[47] found major anomalies to be present postnatally in 36 of 39 fetuses (92%). In addition, chromosomal abnormalities were present in 15 of 39 fetuses (38%), including 10 fetuses with trisomy 18 and 1 fetus with trisomy 13. The overall mortality in this group with both polyhydramnios and IUGR was 59%.[47] The combination of hydramnios and small size for gestational age, defined as infant birth weight below the 5th percentile, has been shown to be an independent risk factor for perinatal mortality in several studies.[68,69] In a study of 152 small for gestational age (birth weight <5th percentile) neonates with polyhydramnios (AFI >25 cm or SDP ≥8 cm), there was an increased risk of peripartum complications, including labor dystocia, placental abruption, malpresentation, cord prolapse, and cesarean delivery.[69]

However, there does not appear to be a substantial effect of polyhydramnios on maternal uterine blood flow. In a study by Hershkovitz et al,[70] uterine artery Doppler velocimetric findings in patients with idiopathic hydramnios, defined in their study as patients with an AFI greater than 24 cm and without known fetal structural or chromosomal anomalies or diabetes, was not significantly different from those with a normal AFV, defined as an AFI between 6 and 24 cm. Doppler velocity studies such as umbilical artery Doppler are often used as a reflection of uteroplacental blood flow and resistance within the placenta as part of antepartum surveillance in the setting of IUGR. The use of umbilical artery Doppler studies in the setting of polyhydramnios without IUGR is not routinely indicated.

In some cases, polyhydramnios may resolve during the pregnancy. Hill et al[71] evaluated 41 pregnancies complicated by polyhydramnios that resolved before delivery. In 40 of these 41 cases, the hydramnios was either mild or moderate.[71] They found that those patients with resolving polyhydramnios were more likely to have glucose intolerance and fetal macrosomia.[71] Golan et al[55] observed 113 cases of hydramnios, 40% of which resolved. In these cases, the outcome was "favorable" and not at an increased risk of intrauterine fetal death or neonatal death compared to those patients with persistent or worsening hydramnios.[55] The risk of fetal aneuploidy appears to be extremely low in those pregnancies in which the hydramnios resolves.[72] There does appear to be a distinction between "acute" versus "chronic" development of hydramnios. Queenan and Gadow[4] described acute hydramnios as "a rampant fulminating process terminating in spontaneous labor, usually before the end of the second trimester." In their study of 6 cases with acute hydramnios diagnosed before 24 weeks' gestation, all 6 cases resulted in perinatal death.[4]

Evaluation of Polyhydramnios

Once the diagnosis of polyhydramnios is made, it is important to understand the proper evaluation and management of that ongoing pregnancy. Given the high risk of fetal anomalies and chromosomal abnormalities, a pregnancy complicated by hydramnios should undergo a targeted sonographic anatomic evaluation by either a maternal-fetal medicine specialist or a radiologist with expertise in this type of evaluation. The degree of the hydramnios should raise one's suspicion for fetal anomalies as the risk of anomalies increases with increasing severity of hydramnios.

One must also always consider the possibility of multiple gestations, which may be complicated by twin-to-twin transfusion syndrome, reflecting one fetus with polyhydramnios and the other fetus with oligohydramnios. If fetal hydrops is identified, further workup should be undertaken to attempt to determine whether the cause is immune mediated or non–immune mediated. Positive maternal antibody screening results would indicate the cause to likely be immune mediated, and further invasive fetal testing, such as cordocentesis, may be indicated if fetal anemia is suggested by abnormal middle cerebral artery Doppler findings.[11] In the setting of negative maternal antibody screening results, further work up may include screening for fetomaternal hemorrhage, maternal titers for infectious causes such as rubella, cytomegalovirus, toxoplasmosis, and parvovirus, screening for hemoglobinopathies, and a detailed patient and family history to evaluate for possible genetic disease etiologies.[11] In the absence of fetal anomalies or hydrops on sonographic examination, maternal testing for diabetes should be performed with a maternal glucose challenge test. There is no evidence advocating for or against repeating a screening glucose challenge test once polyhydramnios is detected if the previous test result during the current pregnancy was normal; however, repeated screening should be considered if there is suspicion for maternal glucose intolerance (eg, acanthosis nigricans or glucosuria).

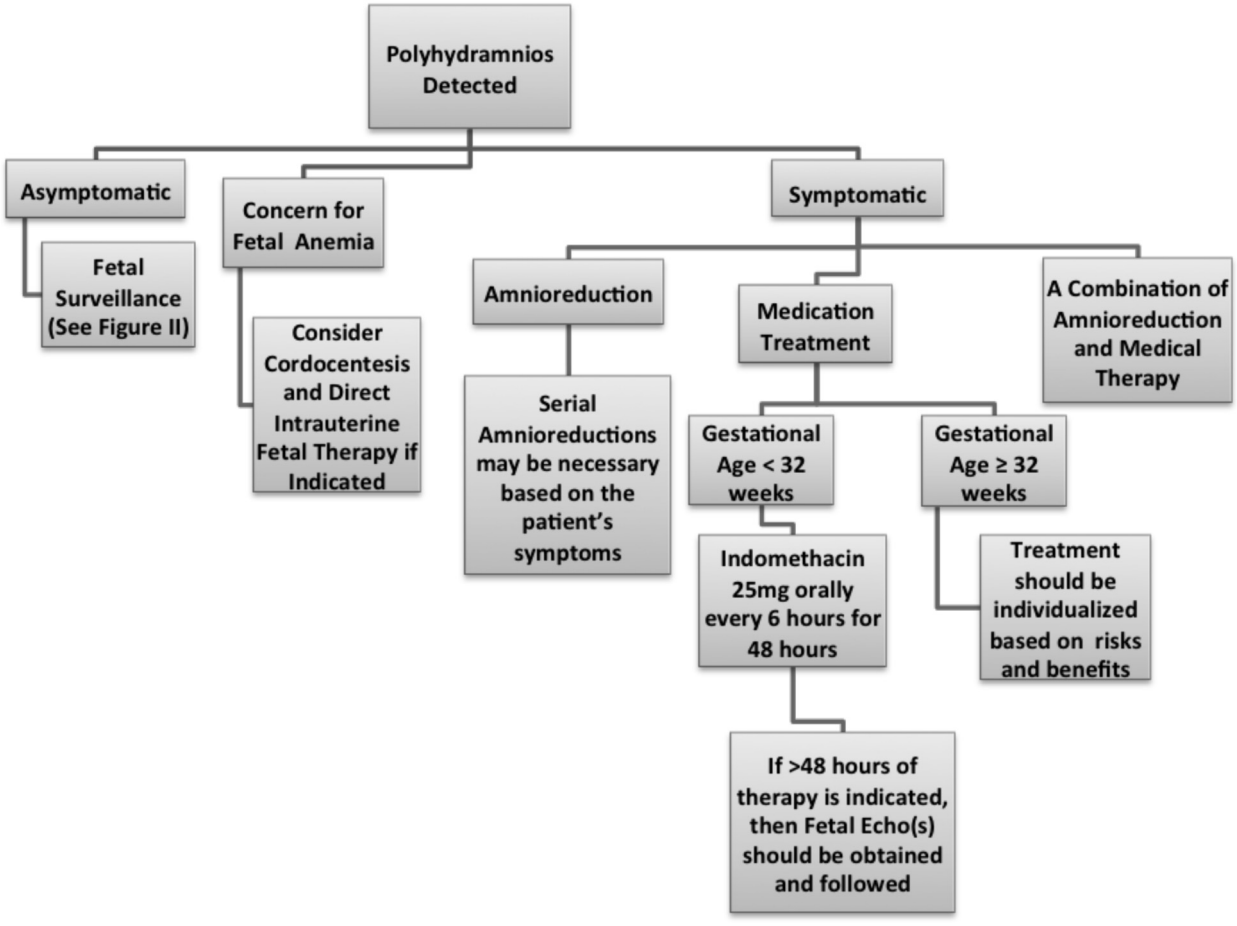
The next step in evaluation generally includes invasive testing. Amniocentesis for the fetal karyotype is controversial. Some investigators have suggested that all patients with idiopathic hydramnios have a fetal karyotype performed, given that the incidence of fetal aneuploidy has been found to be 3.2% to 13.3% in this setting.[44,45] Others suggest that in the setting of a sonographically normal fetus, the risk of fetal aneuploidy is low, likely 1% or less;

thus, fetal karyotyping may be offered but is not necessarily recommended.[20] However, if fetal anomalies are identified on sonographic examination, despite the degree of hydramnios, amniocentesis for fetal karyotype should be strongly considered, given the 10% risk of fetal aneuploidy.[20] Recall that in the setting of severe hydramnios, the risk of major fetal anomalies has been shown to be 11%[20]; thus, offering amniocentesis in this setting may also be warranted to complete the evaluation. In addition, noninvasive fetal DNA testing is available for the detection of the most common fetal aneuploidies (trisomy 13, 18, and 21) using circulating cell-free fetal DNA present within the maternal blood; however, amniocentesis remains the standard for full fetal karyotype assessment. It is currently recommended that amniocentesis be obtained for confirmation after cell-free fetal DNA testing. Other information may also be obtained with amniocentesis, such as titers for infection and evaluation for certain genetic diseases (eg, metabolic or neuromuscular disorders).[11] If fetal anemia is suspected or fetal hydrops is present, cordocentesis may be warranted to confirm the diagnosis of fetal anemia, which can be due to fetomaternal hemorrhage, infection (eg, parvovirus), hemolysis (eg, glucose-6-phosphatase deficiency), or immune-mediated causes (eg, Rh isoimmunization).

Treatment of Polyhydramnios

In a pregnancy complicated by polyhydramnios in which treatment appears to be indicated and is being considered, we recommend consultation with a maternal-fetal medicine specialist for assistance with the treatment plan and counseling the patient on the risks and benefits of these options. There are several potential avenues for treatment in pregnancies complicated by hydramnios (Figure 1). One option, if indicated, is via direct fetal therapy. This

Figure 1. Treatment of polyhydramnios.



therapy may consist of intrauterine fetal blood transfusion for fetal anemia, which can be the result of several causes, including immune hydrops fetalis, fetomaternal hemorrhage, and parvovirus B19 infection. Another fetal intervention may involve medication therapy to correct fetal arrhythmias in utero or fetoscopically guided laser ablation of anastomotic vessels in the shared placental circulation in twin-to-twin transfusion syndrome.[11] Ordinarily, a more conservative approach is indicated.

In asymptomatic patients with idiopathic hydramnios, Golan et al[55] reported that more than half resolved spontaneously. In these cases, serial sonographic examinations to assess the amniotic fluid status and fetal growth should be performed throughout the remainder of the pregnancy once hydramnios is diagnosed. If symptomatic polyhydramnios develops, which includes respiratory symptoms such as persistent shortness of breath and excessive uterine activity during the course of pregnancy, therapeutic options may include decompression amniocentesis or, after consultation with a maternal-fetal medicine specialist, treatment with prostaglandin inhibitors, such as indomethacin, for up to 48 hours.

The ability to prolong pregnancy using serial amniocenteses has also been demonstrated.[73] Serial amniocentesis for symptomatic polyhydramnios most commonly occurs in the setting of fetal anomalies or twin-to-twin transfusion syndrome. Elliott et al[73] reported that large-volume amniocentesis can be used to treat hydramnios in a series of 94 patients (including patients with idiopathic hydramnios, twins, twins with twin-to-twin transfusion syndrome, diabetes, and fetal anomalies/aneuploidy) who underwent a total of 200 therapeutic amniocenteses, with a complication rate of 1.5%. Typically, a range of 1 to 5 L is removed, or enough amniotic fluid is removed to leave a normal AFV (eg, SDP <8 cm).[73] The main risks of amnioreduction include preterm labor, placental abruption, preterm rupture of membranes, and intrauterine infection. Repeated procedures may be necessary and can be performed the following day or may be dictated by the patient's symptoms such as uterine contractions or respiratory compromise.[11]

Another option for the therapeutic treatment of symptomatic polyhydramnios is the use of prostaglandin inhibitors. The most common medication used is indomethacin, a prostaglandin synthesis inhibitor. The exact mechanism by which the AFV decreases after administration of indomethacin is not completely understood. Several mechanisms have been proposed for indomethacin's therapeutic effect: (1) decreased fetal urine production by impairing the normal prostaglandin-mediated response in the fetal renal vasculature, including decreased inhibition of vasopressin, resulting in increased free water absorption by the distal nephron of the fetal kidney; (2) enhanced fluid resorption by the fetal lungs with an increase in fetal breathing and also potentially a decrease in the production of fetal lung fluid; and (3) suspected increased fluid movement across fetal membranes.[11] Indomethacin has been used by investigators in the treatment of hydramnios in a variety of settings, such as idiopathic, multiples, maternal diabetes, and anomalies.[11] The dosing varies with each investigator, and there is not one universally recommended dosing regimen. One acceptable regimen is 25 mg orally every 6 hours for up to 48 hours.[11] The effectiveness of indomethacin treatment for polyhydramnios has been demonstrated in several studies.[11,74] As reported by Moise,[11] indomethacin treatment has been shown to be effective with respect to several etiologies of hydramnios during pregnancy, including idiopathic hydramnios, hydramnios related to maternal diabetes, as well as hydramnios in twins not related to twin-to-twin transfusion syndrome.

Maternal side effects related to indomethacin treatment are generally mild and limited to gastrointestinal side effects such as nausea and epigastric pain.[11] Severe side effects such as oliguria, decreased renal function, renal insufficiency with and without pulmonary edema, and cholestatic jaundice have been reported, but these are rare.[11] Fetal side effects can include oligohydramnios, and some advocate that twice-weekly sonographic evaluations of the AFV should take place to detect the development of oligohydramnios.[11] Other investigators propose that when using indomethacin for the treatment of hydramnios, one should discontinue the medication treatment when the pretreatment AFI value is reduced by more than two-thirds.[75] An important potential side effect of indomethacin treatment is fetal ductus arteriosus constriction. The risk of ductal constriction increases with advancing gestational age and is nearly a 50% risk at 32 weeks' gestation.[11] Constrictions of the ductus generally resolve within 24 hours after discontinuation of treatment.[11] Indomethacin treatment should generally not be used for longer than 48 hours without involvement by a multidisciplinary perinatal team including at least a maternal-fetal medicine specialist and a pediatric cardiologist. If long-term (>48 hours) indomethacin therapy is to be used in the treatment of hydramnios, a fetal echocardiogram 24 hours after initiation of treatment and then weekly can be used to monitor cardiac function and evaluate for ductal constriction, right ventricular size and contractility, and tricuspid regurgitation.[11] The finding of severe ductal constriction along

with tricuspid regurgitation may be associated with fetal hydrops and persistent neonatal-fetal circulation; thus, for these reasons, it is recommended that indomethacin be stopped in fetuses with these findings.[11] The use of indomethacin at 32 weeks' gestation or later is typically not recommended because of the increased risk of fetal circulatory effects[11] and should be individualized on a case-by-case basis in conjunction with a multidisciplinary perinatal team.[11] A final potential complication of fetal exposure to indomethacin during pregnancy is neonatal bowel (eg, ileum) perforation and necrotizing enterocolitis.[11] One study showed an incidence of necrotizing enterocolitis of 17% in premature neonates born within 1 week of indomethacin exposure compared to 6% in matched controls.[11] However, other studies have reported no adverse neonatal effects after indomethacin exposure.

Kirshon et al[75] demonstrated success using both therapies: serial amnioreductions followed by indomethacin therapy for the management of symptomatic hydramnios. Sulindac, a nonsteroidal anti-inflammatory medication, has also been used by some investigators in the treatment of hydramnios. This medication results in a decrease in the AFI after treatment while appearing to have less of a constrictive effect on the ductus arteriosus and less of an effect on fetal urine production.[11] There have yet to be any clinical trials evaluating this agent for the treatment of polyhydramnios; therefore, future investigations using sulindac are warranted.

Antenatal Management of Polyhydramnios

The role of antenatal testing in pregnancies complicated by polyhydramnios remains unclear. The American College of Obstetricians and Gynecologists recommends antenatal testing be performed in the setting of hydramnios.[76] However, there have been no randomized clinical trials to evaluate whether pregnancies complicated by polyhydramnios benefit from any form of such testing. Nevertheless, given the increased risk of adverse pregnancy outcomes and perinatal mortality, it seems prudent to implement antenatal fetal testing (Figure 2).

Depending on the gestational age and other comorbidities, antenatal testing is commonly performed in pregnancies complicated by polyhydramnios; however, the type of testing (nonstress test, biophysical profile, or contraction stress test) and the frequency of testing have not yet been validated by large studies and tend to vary among providers.[49] On the basis of the increased risk of perinatal mortality, we suggest at least weekly antenatal surveillance with a nonstress test starting at 32 to 34 weeks' gestation. In addition, serial sonographic examinations every 3 to 4 weeks should be performed to monitor fetal growth and to evaluate the AFV status. Delivery should occur at 39 weeks' gestation or later unless dictated by abnormal fetal test results or other pregnancy complications (eg, IUGR or preeclampsia), which may necessitate delivery earlier (ie, <39 weeks). Delivery at 37 weeks or later with documented fetal lung maturity is also an option.[49] Interestingly, Piazze et al[77] found all fetal lung maturity indices to be significantly lower in pregnancies with polyhydramnios when matched with controls. With close antepartum fetal surveillance and reassuring fetal testing, we believe delivery at 39 weeks' gestation or later to be a reasonable approach, especially in the setting of maternal discomfort due to severe hydramnios. There are no randomized trials that compare the outcome of expectant management of idiopathic hydramnios to intervention.

Delivery Considerations

There is no absolute contraindication to induction of labor or the use of oxytocin in the setting of polyhydramnios. However, it is important to use caution during the labor process because of the risk of placental abruption and cord prolapse after sudden rupture of membranes. Techniques such as transabdominal decompression amniocentesis in early labor and "needle" amniotomy should be considered to allow for slow release of amniotic fluid and thus avoid cord prolapse or placental abruption, which can occur with rapid release of amniotic fluid and subsequent uterine decompression.[11] The fetal presentation should be checked frequently during labor as the excess amniotic fluid allows for more fetal mobility, providing an increased risk of fetal malpresentation. It is also important to remember the potential risk of postpartum hemorrhage due to uterine atony as a result of an overly distended uterus. Cesarean delivery should be reserved for obstetric indications.

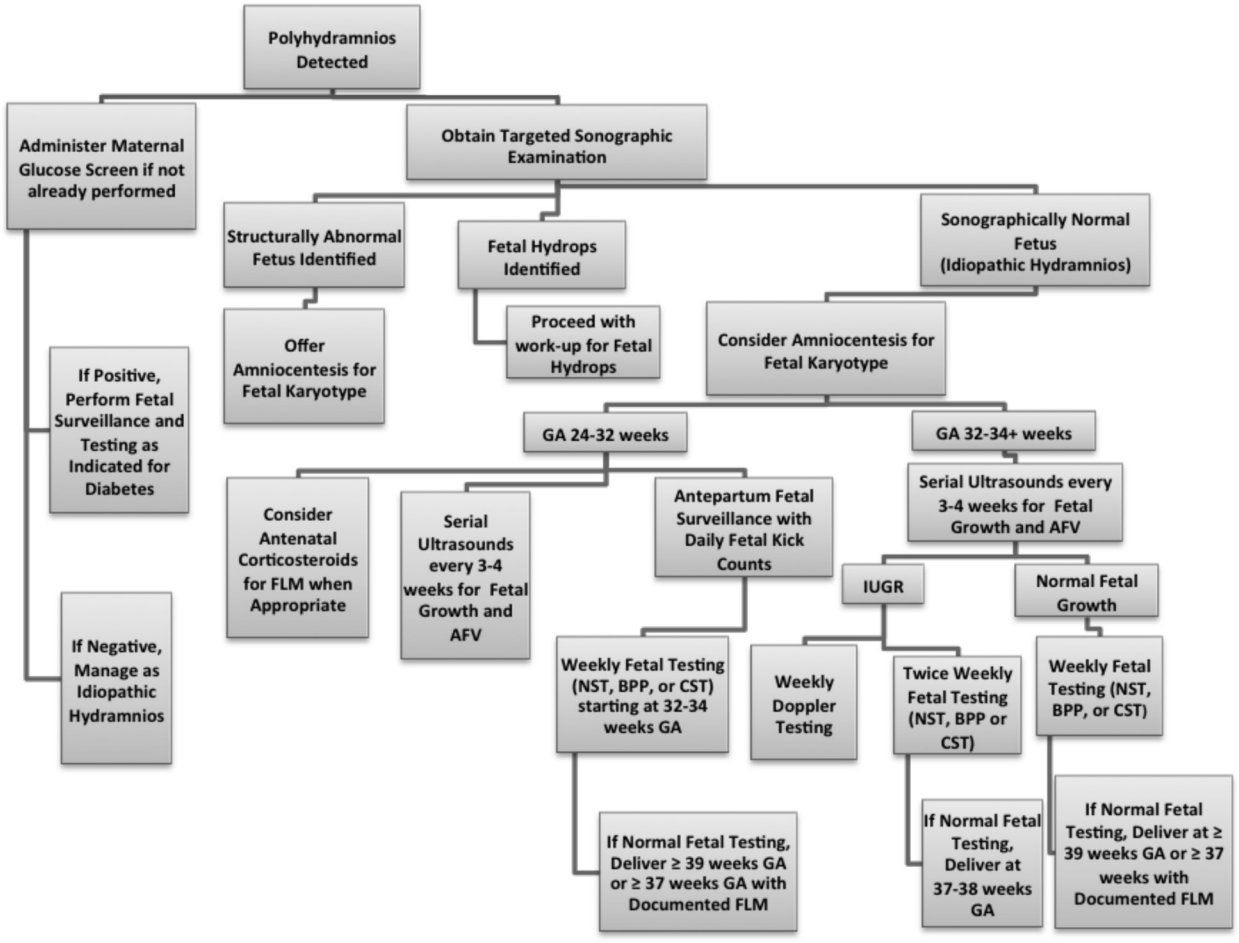
Conclusions

The clinical relevance of polyhydramnios is considerable given the link to congenital fetal anomalies, adverse pregnancy outcomes, and perinatal mortality. Despite controlling for fetal anomalies and maternal diabetes, the increased risk of perinatal mortality persists.[2] The combination of IUGR and polyhydramnios is especially worrisome and carries a high rate of perinatal mortality.[47] There are multiple accepted definitions of polyhydramnios, but most commonly, the AFV is estimated sonographically, using an AFI of 24 cm or greater or an SDP of 8 cm or greater to indicate polyhydramnios.

Abnormalities in any of the pathways responsible for maintenance of the AFV can result in polyhydramnios. Likewise, fetal structural anomalies (eg, esophageal atresia) and various fetal (eg, infection or neurologic impairment) or maternal (eg, diabetes) conditions can lead to the development of polyhydramnios. However, most cases are idiopathic. There is an increased risk of fetal anomalies in the setting of polyhydramnios, and this risk is higher with increasing severity of polyhydramnios. Polyhydramnios is also associated with a risk of fetal aneuploidy.

When polyhydramnios is identified, appropriate steps should be undertaken to ensure a complete maternal and fetal evaluation. Targeted sonography should be performed to evaluate for fetal anomalies or evidence of fetal hydrops, and genetic amniocentesis should be considered, especially if fetal anomalies are identified. Maternal screening for diabetes should also be performed. After consultation with a maternal-fetal medicine specialist, treatment of symptomatic polyhydramnios may be accomplished with either serial amnioreductions or medications, such as indomethacin. There are specific advantages, disadvantages, risks, and complications to each mode of therapy. Each case of polyhydramnios should be individualized according to gestational age, maternal comorbidities, and fetal testing to direct optimal intervention. We believe a practical approach to management of the pregnancy complicated by polyhydramnios includes serial sonographic examinations to monitor fetal growth and AFV, antepartum fetal surveillance (eg, weekly antenatal testing), and delivery at term with either documented fetal lung maturity or at 39 weeks' gestation or later.

Figure 2. Antenatal management of polyhydramnios. BPP indicates biophysical profile; CST, contraction stress test; FLM, fetal lung maturity; GA, gestational age; and NST, nonstress test.



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