Mechanisms and disorders associated with polyhydramnios

Deborah Krakow, MD
Center for Fetal Medicine
David Geffen School of Medicine at UCLA

Nemec U et al., Insights Imaging (2011)
Amniotic fluid balance

- Consequence of balance between the fetal and maternal systems which determines the ultimate volume of amniotic fluid
- Fetal urine production, swallowing, and membranous absorption contribute to overall fluid balance especially during late gestation
- Amniotic fluid volume rises to 25 ml at 10 weeks, to 400 ml at 20 weeks, plateaus to 800 ml at 28 weeks and then decreases around term to 400 ml
Alterations in Amniotic Fluid Volumes

- Quantitative alterations in amniotic fluid volumes accompany 7% of all pregnancies
- Polyhydramnios occurs in 1-3% of all pregnancies and oligohydramnios occurs in 3-5% of pregnancies
- Both conditions affect neonatal outcomes including effects on the maturity of organ systems
Clinical Relevance

• Relation to adverse pregnancy outcomes, including perinatal mortality
• Association with pregnancy complications
  – Fetal anomalies, Diabetes
• Delivery complications
  – Increased c-section rate, malpresentation, macrosomia, fetal distress in labor
• Neonatal complications
  – Lower APGAR scores, increased rate of NICU admission
Amniotic Fluid Volume

• Regulation of AFV is complex and incompletely understood
  • Fetal urine production
  • Secretion of fetal lung fluid
    • Fetal swallowing
• Movement between fetal blood and the placenta (Intramembranous Pathway)
• Movement across the surface of the amnion and chorion (Transmembranous Pathway)
Polyhydramnios

- Hydramnios is diagnosed when the AFI is $> \text{ or } = 24$ or $> \text{ or } = 25$ ($> \text{ or } = 95$ or $> \text{ or } = 97.5\%$), the single deepest pocket is $> \text{ or } = 8$, or the examiner's subjective assessment of having an increased amount of amniotic fluid volume.
Categorization of Polydramnios

- Mild - 25–30 cm
- Moderate - 30.1–35 cm
- Severe - 35.1 cm or more

Increasing AFV, increasing risk of adverse outcome/congenital anomalies

Polydramnios

• Associated with congenital anomalies of the GI tract, central nervous system, cardiac, respiratory, genitourinary, skeletal, and metabolic systems, maternal diabetes, isoimmunization, fetal infection (CMV, toxoplasmosis, syphilis, varicella, parvovirus, rubella, HSV), placenta tumors and multiple gestations

• Idiopathic polyhydramnios is defined as hydramnios that is not associated with the above...
Mechanisms associated with polyhydramnios

• Anomalies associated with physical inability to swallow (oro-facial, neurologic, musculoskeletal)

• Decreased fluid absorption in the GI tract (obstruction)

• Diabetes - increased fetal urine production from hyperglycemia

• Anencephaly - increased transudation of fluid from exposed meninges and lack of antidiuretic effect due to impaired arginine vasopressin secretion
Mechanisms of Polyhydramnios

- **Reduced Elimination**
  - Esophageal atresia, tracheal-esophageal fistula, duodenal atresia

- **Reduced Swallowing**
  - Neurological impairment (e.g. anencephaly, fetal swallowing)
    - Neuromuscular disorders (e.g. Myotonic Dystrophy)
      - Fetal hypoxia (ovine model)

- **Increased Production** (Barrter syndrome)
  - Abnormal renal function, fetal brain injury, diabetes
Genetic Implications

- Congenital fetal anomaly risk in the setting of polyhydramnios ranges 8-45%
- Common congenital anomalies include:
  - CNS anomalies
  - Cardiac anomalies
  - GI anomalies
  - Thoracic anomalies
  - Craniofacial anomalies
  - Skeletal anomalies
  - Renal anomalies
Examples of abnormalities seen with polydramnios

- congenital heart defects
- ventricular septal defect
- pulmonary valve stenosis
- atrial septal defect
- pulmonary atresia with ventricular septal defect
- transposition of the great vessels
- tetralogy of Fallot
- patent foramen ovale
- genitourinary system
- hydronephrosis
- hypospadias
- multicystic dysplastic kidney
- unilateral renal agenesis
- hydrocele
- ovarian cyst, suspected ovarian torsion
- urethral stricture
- musculoskeletal system
- poly-, syndactyly
- cleft lip and palate
- malposition of limbs
- complex malformations
- ileum atresia, dysmorphic face, skeletal malformation, vessel anomalies
- vessel anomalies, dislocation of stomach, dysmorphic, hydronephrosis
- ventricular septal defect, cerebral anomalies
- osteogenesis imperfecta, malformations of cardiovascular, gastrointestinal and respiratory systems
- hygroma colli syndromes
- Noonan syndrome
- charge syndrome
- jeune syndrome
- Poland syndrome
- osteogenesis imperfecta type
- gastrointestinal tract
- esophageal atresia
- gastroschisis
- anal atresia
- central nervous system
- holoprosencephaly
- porencephaly
- ventriculomegaly
- multiple cerebral anomalies
- respiratory tract
- congenital diaphragmatic hernia
- congenital cystic adenomatoid malformation
- congenital laryngomalacia and tracheomalacia
- chromosomal abnormality
- trisomy 21
- monosomy X
- 46,XY/47,XY

N=70
Outcomes in 807 cases with polyhydramnios

<table>
<thead>
<tr>
<th>perinatal outcome (n = 807)</th>
<th>TORCH (n = 24)</th>
<th>MALF (n = 70)</th>
<th>DIAB (n = 156)</th>
<th>IDIOP (n = 557)</th>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean</td>
<td>range</td>
<td>n</td>
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<tr>
<td><strong>maternal characteristics</strong></td>
<td></td>
<td></td>
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<tr>
<td>age (years)</td>
<td>28.9</td>
<td>17 – 39</td>
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<td>30.3</td>
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<tr>
<td><strong>pregnancy characteristics</strong></td>
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<tr>
<td>gestational age at delivery (weeks)</td>
<td>40</td>
<td>35 – 41</td>
<td></td>
<td>38</td>
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<tr>
<td>birth weight (grams)</td>
<td>3563</td>
<td>2370 – 4530</td>
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<td>3177</td>
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<tr>
<td>SGA (&lt; 10&lt;sup&gt;th&lt;/sup&gt; percentile)</td>
<td>1</td>
<td>4.2</td>
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<td>12</td>
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<tr>
<td>LGA (&gt; 90&lt;sup&gt;th&lt;/sup&gt; percentile)</td>
<td>5</td>
<td>20.8</td>
<td></td>
<td>11</td>
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<tr>
<td><strong>perinatal complications</strong></td>
<td></td>
<td></td>
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<tr>
<td>cesarean section</td>
<td>5</td>
<td>20.8</td>
<td></td>
<td>30</td>
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<tr>
<td>elective cesarean section</td>
<td>2</td>
<td>8.3</td>
<td></td>
<td>16</td>
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<tr>
<td>preterm delivery (&lt; 37 weeks)</td>
<td>1</td>
<td>4.2</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>moderately acidosis (pHart 7.0 – 7.19)</td>
<td>2</td>
<td>8.3</td>
<td></td>
<td>12</td>
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<tr>
<td>severe acidosis (pHart &lt; 7.0)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>1</td>
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<tr>
<td>5-min Apgar score ≤ 3</td>
<td>0</td>
<td>0</td>
<td></td>
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</table>

Outcomes in 524 cases with polyhydramnios

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Maximal amniotic fluid index:</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>&lt; 25 cm (n = 69)</td>
<td>25–29.9 cm (n = 291)</td>
<td>30–34.9 cm (n = 97)</td>
<td>≥ 35 cm (n = 67)</td>
<td></td>
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<tr>
<td>Normal anatomy scan†</td>
<td>58 (84.1)</td>
<td>217 (74.6)</td>
<td>51 (52.6)</td>
<td>14 (20.9)</td>
<td>&lt; 0.005</td>
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<tr>
<td>Aneuploidy‡</td>
<td>0/15 (0.0)</td>
<td>3/79 (3.8)</td>
<td>5/43 (11.6)</td>
<td>6/46 (13)</td>
<td>0.124</td>
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<tr>
<td>Mean gestational age at delivery (weeks)</td>
<td>39</td>
<td>38 + 3</td>
<td>37 + 5</td>
<td>36 + 1</td>
<td>0.027</td>
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<tr>
<td>Preterm delivery &lt; 37 weeks</td>
<td>5 (7.2)</td>
<td>46 (15.8)</td>
<td>19 (19.6)</td>
<td>31 (46.3)</td>
<td>&lt; 0.005</td>
<td></td>
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<tr>
<td>Early preterm delivery (&lt; 34 weeks)</td>
<td>0 (0.0)</td>
<td>17 (5.8)</td>
<td>7 (7.2)</td>
<td>13 (19.4)</td>
<td>&lt; 0.005</td>
<td></td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>44 (63.8)</td>
<td>153 (52.6)</td>
<td>54 (55.7)</td>
<td>42 (62.7)</td>
<td>0.431</td>
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<tr>
<td>Mean birth weight (g)</td>
<td>3577</td>
<td>3449</td>
<td>3385</td>
<td>2910</td>
<td>0.155</td>
<td></td>
</tr>
<tr>
<td>Small-for-gestational age§</td>
<td>2/57 (3.5)</td>
<td>14/250 (5.6)</td>
<td>7/81 (8.6)</td>
<td>9/56 (16.1)</td>
<td>0.030</td>
<td></td>
</tr>
<tr>
<td>Macrosomia (&gt; 4500 g)</td>
<td>4/57 (7.0)</td>
<td>15/250 (6.0)</td>
<td>3/81 (3.7)</td>
<td>2/56 (3.6)</td>
<td>0.732</td>
<td></td>
</tr>
<tr>
<td>5-min Apgar score &lt; 7</td>
<td>2/57 (3.5)</td>
<td>9/236 (3.8)</td>
<td>7/84 (8.3)</td>
<td>12/52 (23.1)</td>
<td>&lt; 0.005</td>
<td></td>
</tr>
<tr>
<td>Intrauterine fetal death</td>
<td>0 (0.0)</td>
<td>7 (2.4)</td>
<td>3 (3.1)</td>
<td>9 (13.4)</td>
<td>&lt; 0.005</td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>0 (0.0)</td>
<td>16 (5.5)</td>
<td>9 (9.3)</td>
<td>18 (26.9)</td>
<td>&lt; 0.005</td>
<td></td>
</tr>
</tbody>
</table>

| Anomaly                              | Maximal amniotic fluid index: |       |       |       |       |       |
|                                      | < 25 cm (n = 69)              | 25–29.9 cm (n = 291) | 30–34.9 cm (n = 97) | ≥ 35 cm (n = 67) | Total (n = 524) |
| Cardiac                              | 1 (1.4)                       | 20 (6.9) | 17 (17.5) | 18 (26.9) | 56 (10.7) |
| Thorax and lungs                     | 6 (8.7)                       | 19 (6.5) | 12 (12.4) | 18 (26.9) | 55 (10.5) |
| Gastrointestinal                     | 0 (0.0)                       | 14 (4.8) | 10 (10.3) | 13 (19.4) | 37 (7.1)  |
| Genitourinary                        | 2 (2.9)                       | 10 (3.4) | 8 (8.2)   | 3 (4.5)   | 23 (4.4)  |
| Musculoskeletal                      | 2 (2.9)                       | 16 (5.5) | 5 (5.2)   | 14 (20.9) | 37 (7.1)  |
| Central nervous system               | 1 (1.4)                       | 18 (6.2) | 5 (5.2)   | 7 (10.4)  | 31 (5.9)  |
| Single umbilical artery              | 0 (0.0)                       | 2 (0.7)  | 4 (4.1)   | 5 (7.5)   | 11 (2.1)  |
| Hydrops                              | 0 (0.0)                       | 7 (2.4)  | 6 (6.2)   | 7 (10.4)  | 20 (3.8)  |
| Estimated fetal weight < 10th percentile | 0 (0.0)                | 4 (1.4) | 1 (1)     | 2 (3)     | 7 (1.3)   |
| Total anomalies                      | 12                            | 110     | 68        | 87        | 277      |
Evaluation of Polyhydramnios

- Targeted ultrasound evaluation
  - Structural anomalies
  - Fetal hydrops
- Screen for maternal diabetes
- Consider amniocentesis
  - Fetal karyotype/microarray analysis
  - Directed genetic testing
    - Viral titers
Polyhydramnios

- 50-60% of polyhydramnios is “idiopathic”
- Review of the literature of outcomes of idiopathic polyhydramnios (corrected for congenital anomalies, N=7)
  - linked to fetal macrosomia
  - an increase in the risk of adverse pregnancy outcomes
  - 2- to 5-fold increase in the risk of perinatal mortality

Magann EF 2007 Obstet Gynecol Surv Dec;62(12):795-802
Idiopathic Hydramnios

• Consideration for some helpful antepartum screening tests
  • Rule out congenital anomalies
  • Rule out gestational diabetes
  • Formal fetal echocardiogram
  • Rule out infection - TORCH, parvo, syphilis
  • Doppler flow velocimetry of the middle cerebral artery
  • nonstress test (biophysical profile) at 32 weeks
  • serial growth Q3weeks
  • delivery prior to 39 weeks not indicated
  • prospective studies
Treatment of Polyhydramnios

- May resolve spontaneously
  - 50% chance of resolution if idiopathic and asymptomatic
- Direct fetal therapy if indicated
  - Intrauterine fetal blood transfusion
  - Intrauterine treatment with medication to correct fetal arrhythmias
    - Laser ablation for TTTS
- Decompression amniocentesis
- Medication treatment (e.g. Indomethacin)
Case study 1

CMV infection
Central nervous system
Ventriculomegaly
Microcephaly
Punctuate calcifications
Periventricular calcifications
Increased periventricular echogenicity
Ventricular cysts
Ventricular adhesions
Periventricular leukomalacia
Microphthalmia
Porencephaly
Lissencephaly
Polymicrogyria
Cerebellar hemorrhage
Cerebellar/vermian hypoplasia
Cerebellar calcifications
Callosal dysgenesis
Linear lenticulostriated echogenicities
Echogenic bowel
Echogenic liver foci
Hepatomegaly
Splenomegaly
Echogenic nephromegaly
Non-immune hydrops
Ascites
Pleural effusions
Cardiomegaly
Intrauterine growth restriction
Abnormalities of amniotic fluid volume
Case 2

Polyhydramnios
fetal ascites

Giant chorioangioma (>4 cm)
Treated with fetoscopy and devascularization
Indications include expectation of high mortality and morbidity
Case 3 - 26 weeks, G1PO
Acrofacial dysostosis - Rodriguez type

SF3B4 - heterozygosity for a nonsense mutation
Example 5

Cystic Adenoid Malformation of the Lung (CAML)
Case 6
38 y.o. G2P1, 36 weeks, AFI 32

Trisomy 21
Case 7, 19 weeks, G1P0, AFI 23 cm

Amyoplasia > 10 types, mostly autosomal dominant, but there are AR forms
Case 8, 33 weeks

Thanatophoric dysplasia - FGFR3