ULTRASOUND MARKERS OF ANEUPLOIDY

Nooshin Amjadi, MD
Fellowship of perinatalogy
Shahid Beheshti University
Of Medical Sciences
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SOFT MARKERS

- findings of uncertain significance.
- often associated with normal fetuses (normal variants)
- have no clinical sequelae.
- Transient carry an increased risk for fetal aneuploidy.
- correlation with the patient's biochemical risk status should be done.
- Increased nuchal translucency
- Absent nasal bone
- Echogenic bowel
- Pyelectasis
- Shortened long bones (humerus, femur)
- Echogenic intracardiac focus
- Choroid plexus cysts
• Isolated soft markers are identified in 11 to 17 percent of normal fetuses
• a detailed evaluation of fetal anatomy should be performed whenever one or more soft markers has been identified.
Increased nuchal translucency

- Evaluation of NT is the most reliable and widely used sonographic marker of trisomy 21.
- The translucent nuchal space at the posterior fetal neck
- An increase in the NT measurement is associated with an increased risk of fetal aneuploidy, structural anomalies (major cardiac abnormalities, diaphragmatic hernia, exomphalos, body stalk anomaly, skeletal abnormalities,...), genetic syndromes, and adverse outcome.
- The risk increases as NT increases
<table>
<thead>
<tr>
<th>Nuchal translucency</th>
<th>Chromosomal Defects</th>
<th>Normal karyotype</th>
<th>Major fetal abnormalities</th>
<th>Alive and well</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;95&lt;sup&gt;th&lt;/sup&gt; centile</td>
<td>0.2%</td>
<td>1.3%</td>
<td>1.6%</td>
<td>97%</td>
</tr>
<tr>
<td>95&lt;sup&gt;th&lt;/sup&gt;–99&lt;sup&gt;th&lt;/sup&gt; centiles</td>
<td>3.7%</td>
<td>1.3%</td>
<td>2.5%</td>
<td>93%</td>
</tr>
<tr>
<td>3.5–4.4 mm</td>
<td>21.1%</td>
<td>2.7%</td>
<td>10.0%</td>
<td>70%</td>
</tr>
<tr>
<td>4.5–5.4 mm</td>
<td>33.3%</td>
<td>3.4%</td>
<td>18.5%</td>
<td>50%</td>
</tr>
<tr>
<td>5.5–6.4 mm</td>
<td>50.5%</td>
<td>10.1%</td>
<td>24.2%</td>
<td>30%</td>
</tr>
<tr>
<td>≥6.5 mm</td>
<td>64.5%</td>
<td>19.0%</td>
<td>46.2%</td>
<td>15%</td>
</tr>
</tbody>
</table>
Echogenic bowel

• 1 to 3 percent of normal fetuses and 10 to 25 percent of fetuses with Down syndrome.

chromosomal defects
fetal growth restriction
cystic fibrosis
congenital infection
intraamniotic bleeding
gastrointestinal obstruction
Nuchal fold

• is measured in the second trimester
• measurement between the outer edge of the occipital bone to the outer margin of the skin and is taken in the axial plane.
• the most sensitive (40 to 50 percent) and specific (99 percent) single ultrasound marker for Down syndrome in the second trimester.
Absent nasal bone

echogenic line within the bridge of the nose. The nasal bone is:

**present** if this line is more echogenic than the overlying skin.  
**absent** if it is not visualized, or less echogenic, than the overlying skin.

- The optimum time for nasal bone assessment is at CRL of 65 to 74 mm (13 to 13.5 w).

The nasal bone is absent in:
- 60–70% of trisomy 21 fetuses,
- 50% of trisomy 18 fetuses
- 30% of trisomy 13 fetuses.
Maxillary Length
• Ear length
• Femur and humerus length
• Single umbilical artery found in about 1% of deliveries associated with malformations of all major organ systems chromosomal defects

  • At 11–13+6 weeks single umbilical artery is found in about 3% chromosomally normal fetuses and in 80% of fetuses with trisomy 18 (seven fold increase in risk of trisomy18).

  single umbilical artery per se should not be an indication for fetal karyotyping.
Megacystis

- fetal bladder can be visualized in about 80% of fetuses at 11 weeks and in all cases by 13 weeks. (bladder length is normally less than 6 mm)
- megacystis in the first-trimester longitudinal bladder diameter of ≥ 7 mm is found in about 1 / 1,500
• Longitudinal bladder diameter is 7–15 mm: incidence of trisomies 13 and 18, is about 20%, in the chromosomally normal group, spontaneous resolution of megacystis in about 90%.

Megacystis with bladder diameter ≥ 15 mm: incidence of chromosomal defects is 10% in the chromosomally normal group, the condition is associated with progressive obstructive uropathy.
Exomphalos

- incidence of chromosomal defects, mainly trisomy 18, is 60%, 30% at mid-gestation and 15% in neonates.
Fetal heart rate

- trisomy 13 and Turner syndrome → tachycardia
- trisomy 18 and triploidy → bradycardia
- trisomy 21 a mild increase in FHR.
- FHR is unlikely to improve first trimester screening for trisomy 21 but it is a useful measurement in identifying fetuses with trisomy 13.
Trisomy 21

- increased NT
- 60–70% absent nasal bone
- 25% short maxilla
- 80% abnormal Doppler waveforms in the ductus venosus.
Trisomy 18

- moderately severe early onset fetal growth restriction
- bradycardia
- %30 exomphalos
- %55 absent nasal bone
- %75 single umbilical artery
Trisomy 13

- %70 tachycardia
- mild early onset fetal growth restriction
- megacystis
- holoprosencpehaly
- %40 exomphalos
Turner syndrome

• %50 tachycardia
• mild early onset fetal growth restriction.
Triploidy

- moderately severe early onset asymmetrical fetal growth restriction
- %30 bradycardia
- holoprosencephaly
- exomphalos
- %40 posterior fossa cyst
- %30 molar changes in the placenta
SECOND TRIMESTER ULTRASONOGRAPHY

- Ventriculomegaly
- Holoprosencephaly
- Choroid plexus cysts
- Dandy Walker complex
- Facial cleft
- Micrognathia
- Nasal hypoplasia
- Nuchal edema
- Cystic hygromas
- Diaphragmatic hernia
- Cardiac defect
• Esophageal atresia
• Renal defects
• Short limbs
• Clinodactyly
• Overlapping fingers
• Polydactyly
• Syndactyly
• Talipes
• Fetal growth restriction
• Exomphalos
• Duodenal atresia
Ventriculomegaly

- birth prevalence 1/1000
- Chromosomal (%10) and genetic defects
- brain hemorrhage or infection
- The commonest chromosomal defect: T21, T18, T13, Triploidy
Axial ultrasound shows a second trimester fetus with a lateral ventricular measurement of 12 mm (calipers). The choroid plexus (arrow) is displaced from the medial wall of the ventricle. This finding was isolated.
Holoprosencephaly

- birth prevalence 1/10000
- chromosomal defect (%30), genetic disorder

The commonest chromosomal defect: trisomies 13 and 18
commonly associated with a wide variety of mid-facial abnormalities
Choroid plexus cysts

- Prevalence: 2% of fetuses at 16–24 weeks in more than 95% of cases they resolve by 28 weeks.
- There is an association between choroid plexus cysts and chromosomomal defects particularly trisomy 18.
Dandy-Walker complex

- abnormalities of the cerebellar vermis, cystic dilatation of the fourth ventricle and enlargement of the cisterna magna.
- birth prevalence: 1/30,000.
- Causes: Chromosomal defects (%40), more than 50 genetic syndromes, congenital infections, teratogens such as warfarin.
- trisomies 18 or 13 and triploidy.
Facial cleft

- Prevalence: 1/800 live births
- Genetic, environmental factors, chromosomal defects (postnatal < 1%, prenatal 20%)
- T13 and 18
FIGURE 11-11. Anterior coronal plane of the fetal face demonstrating unilateral cleft lip.
Micrognathia

- birth prevalence: is about 1/1,000.
- genetic syndromes, chromosomal defects (study, %60) mainly trisomy 18 and triploidy
Nasal hypoplasia

- 65% of trisomy 21 fetuses
- defined by a nasal bone non visible or with \( \leq 2.5 \text{ mm} \).
- nasal hypoplasia is likely to be the single most sensitive and specific second trimester marker of T21.
Diaphragmatic hernia

- prevalence: is about 1/4,000
- condition is sporadic
- The prevalence of chromosomal defects, mainly trisomy 18, is about 20%.
Cardiac abnormalities

• 4–7/1,000 live births
• multiple genetic and environmental factors
• %25 have chromosomal defect
• ≥90% fetuses with trisomy 18 or 13 and 40% of those with trisomy 21 or Turner syndrome
• In the second trimester, 15 to 30 percent of fetuses with Down syndrome have an echogenic intracardiac focus, while this is seen in 4 to 7 percent of normals.
Exomphalos

- birth prevalence: 1 per 4,000.
- is sporadic, genetic syndrome, Chromosomal defects, mainly T18 and 13, are found in about 30% of cases at midgestation and in 15% of neonates.
- The prevalence of chromosomal defects is four-times higher when the exomphalos sac contains only bowel than in cases where the liver is included.
FIGURE 4-11. Large liver containing omphalocele (arrows) in a second trimester patient. The omphalocele is larger than the native fetal abdomen.
Esophageal atresia

- Prevalence: of 1/3,000.
- Sporadic
- Prenatally, chromosomal defects mainly trisomy 18, are found in about 20% of cases.
Duodenal atresia

- prevalence: is about 1/5,000
- mostly sporadic
- autosomal recessive pattern of inheritance.
- Trisomy 21 is found in about 40% of cases.
FIGURE 4-4. Duodenal atresia in a Down syndrome fetus. A transverse axial scan of the abdomen in the third trimester shows the classic “double-bubble” sign; polyhydramnios was also present.
Urinary tract abnormalities

- are commonly found in many chromosomal defects.
- The risk is similar for fetuses with unilateral or bilateral involvement, different types of renal abnormalities, urethral or ureteric obstruction, and oligohydramnios or normal AFI.
- Prevalence of chromosomal abnormalities in females is double that in males.
- The pattern of chromosomal defect is related to the different types of renal abnormalities.
  - Mild hydronephrosis: trisomy 21
  - Moderate/severe hydronephrosis, multicystic kidneys, or renal agenesis: trisomies 18 and 13.
pyelectasis

- as renal pelvic diameter of $\geq 4$ mm at 15 to 19 weeks.
- pyelectasis in 10 to 25 percent of fetuses with Down syndrome and 1 to 3 percent of euploid fetuses.
Cystic hygroma

- a thin-walled, subcutaneous uni- or multilocular subcutaneous mass filled with lymphatic fluid. It results from a localized area of lymphatic dysplasia with dilatation and/or leakage of lymph from the lymphatic vessels.
- may be accompanied by generalized lymphedema.
- First trimester cystic hygromas are often associated with trisomies, whereas second trimester cystic hygromas are often associated with monosomy.
FIGURE 5–65. Monosomy X. Transverse axial view of the neck demonstrates large septated masses. (Courtesy of P. Jeanty, 1999, thefetus.net.)
Limb abnormalities

- relative shortening of the long bones: T 21, 18, triploidy, Turner syndrome
- Syndactyly :triploidy
- clinodactyly and sandal gap: T 21
- polydactyly : T 13
- overlapping fingers, rocker bottom feet and talipes : T 18.
FIGURE 4-49. Plantar view of the foot in a second trimester fetus.
Fetal growth restriction

• association between chromosomal defects and IUGR is underestimate, because of abortion or intrauterine death.

• Fetal growth restriction associated with aneuploidy can occur as early as the first trimester.

• The commonest chromosomal defects are triploidy and trisomy 18.

• Prevalence of chromosomal defects is ↑ structural abnormalities
  the AFI is normal or increased
  normal Doppler flow velocity
<table>
<thead>
<tr>
<th>Sonographic marker</th>
<th>Trisomy 21</th>
<th>Normal</th>
<th>Positive LR</th>
<th>Negative LR</th>
<th>LR for isolated marker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuchal fold</td>
<td>107/319 (33.5%)</td>
<td>59/9331 (0.6%)</td>
<td>53.05 (39.37-71.26)</td>
<td>0.67 (0.61-0.72)</td>
<td>9.8</td>
</tr>
<tr>
<td>Short humerus</td>
<td>102/305 (33.4%)</td>
<td>136/9254 (1.5%)</td>
<td>22.76 (18.04-28.56)</td>
<td>0.68 (0.62-0.73)</td>
<td>4.1</td>
</tr>
<tr>
<td>Short femur</td>
<td>132/319 (41.4%)</td>
<td>486/9331 (5.2%)</td>
<td>7.94 (6.77-9.25)</td>
<td>0.62 (0.56-0.67)</td>
<td>1.6</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>56/319 (17.6%)</td>
<td>242/9331 (2.6%)</td>
<td>6.77 (5.16-8.80)</td>
<td>0.85 (5.16-8.80)</td>
<td>1.0</td>
</tr>
<tr>
<td>Echogenic focus</td>
<td>75/266 (28.2%)</td>
<td>401/9119 (4.4%)</td>
<td>6.41 (5.15-7.90)</td>
<td>0.75 (0.69-0.80)</td>
<td>1.1</td>
</tr>
<tr>
<td>Echogenic bowel</td>
<td>39/293 (13.3%)</td>
<td>58/9227 (0.6%)</td>
<td>21.17 (14.34-31.06)</td>
<td>0.87 (0.83-0.91)</td>
<td>3.0</td>
</tr>
<tr>
<td>Major defect</td>
<td>75/350 (21.4%)</td>
<td>61/9384 (0.65%)</td>
<td>32.96 (23.90-43.28)</td>
<td>0.79 (0.74-0.83)</td>
<td>5.2</td>
</tr>
</tbody>
</table>
phenotypic expression Trisomy 21

- nasal hypoplasia
- increased NF
- Mild ventriculomegaly
- cardiac defects (VSD)
- intracardiac echogenic foci
- duodenal atresia and echogenic bowel
- hydrenephrosis
- shortening of the femur and more so of the humerus, sandal gap
- clinodactyly or mid-phalanx hypoplasia of the fifth finger.
phenotypic expression Trisomy 18

- strawberry-shaped head
- choroid plexus cysts,
- absent corpus callosum
- enlarged cisterna magna,
- facial cleft, low-set ears, microphthalmus, micrognathia
- nuchal edema
- heart defects
- diaphragmatic hernia
- esophageal atresia
- exomphalos, usually with bowel only in the sac
- single umbilical artery
- renal abnormalities
- echogenic bowel,
- Myelomeningocele (NTD)
- Growth restriction
- shortening of the limbs
- radial aplasia, overlapping fingers and talipes or rocker bottom feet.
phenotypic expression Trisomy 13

- Alobar holoprosencephaly
- microcephaly
- facial abnormalities (cyclopia, midline facial clefts, anophthalmia)
- cardiac abnormalities
- enlarged and echogenic kidneys
- exomphalos and post axial polydactyly
- NTD
- ventriculomegaly
Triploidy

- molar pregnancy
- severe asymmetrical growth restriction.
- mild ventriculomegaly
- Micrognathia
- cardiac abnormalities
- myelomeningocele
- syndactyly, and ‘hitch-hiker’ toe deformity
Turner syndrome

- large cystic hygromas, generalised edema, mild pleural effusions and ascites
- cardiac abnormalities (coarctation)
- horseshoe kidneys
• The use of the genetic sonogram, particularly for patients who have had prior first trimester serum screening, remains controversial.

• Using the genetic sonogram to modify the prior risk from maternal age or second trimester serum screen is currently accepted practice by most centers.
For detection of Down syndrome, the genetic sonogram alone:

- have sensitivity: 59 to 87% 
- positive likelihood ratios: 3 to 20% 
- negative likelihood ratios: 0.1 to 0.4%

When the genetic sonogram is used to modify standard serum screening results, sensitivity has been estimated to be at least 90 percent.