Review

Early detection of fetal structural abnormalities

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Abstract

Most published data on the detection of fetal anomalies at 11–14 weeks are from specialized centres with considerable experience in fetal anomaly scanning. However, there is still limited information on the feasibility and limitations of the screening of these anomalies compared with the now classical mid-gestation screening. This review indicates that overall, the detection rate of fetal anomalies at 11–14 weeks is 44% compared with 74% by the mid-pregnancy scan. Major abnormalities of the fetal head, abdominal wall and urinary tract, and of the umbilical cord and placenta, can be reliably detected at 10–11 weeks of gestation. Detection of other anomalies such as spina bifida, diaphragmatic hernia or heart defects is limited before 13 weeks of gestation. So far it cannot be stated that routine first trimester screening can be used on a large scale to evaluate the fetal spine and heart in the general population. In particular, in screening for congenital heart defects, the ability to perform a full cardiac examination increases from 20% at 11 weeks to 92% at 13 weeks. The early prenatal diagnosis of these anomalies may be improved by screening at 13–14 weeks rather than during the first trimester.

Keywords: anomalies, detection rate, fetal, ultrasound

Introduction

During the last decade, two significant processes have contributed to the increasing rate in early evaluation and diagnosis of fetal abnormalities. First, advances in ultrasound technology with the improvement of the high-resolution transvaginal equipment have enabled detailed anatomical investigation of the fetus earlier than the classical mid-pregnancy scan. For example, this advantage gained in the past 10 years is partly responsible for the increase in first trimester echocardiography and early diagnosis of cardiac abnormalities (Carvalho, 2004). Second, the introduction of nuchal translucency (NT) measurement (within the last decade) for the early screening for aneuploidies has resulted in large populations first in Europe, and subsequently in the USA (Nicolaides et al., 1997; Wapner et al., 2003), to be scanned by specialists in prenatal diagnosis at 11–14 weeks of gestation. The early detection of fetal anomalies may be beneficial for both high and low risk groups. A negative sonogram may be reassuring, especially for couples at increased risk. On the other hand, positive findings enable decisions in early gestation when surgical termination of pregnancy might be preferable. Early diagnosis of fetal abnormalities, usually performed at 14–16 weeks of gestation generally by a transvaginal scan, has been the subject of intensive investigation in recent years. Most studies show that the detection rate of such scans is approximately 60–87% (Yagel et al., 1995) compared with the routine second trimester scan. The data regarding first trimester scanning are limited and obtained from specific scans performed in high risk populations and from scans performed in low risk groups as part of early screening for aneuploidy programmes. The detection rate of these scans varies widely (23–33%), and is approximately half of the detection rate by the second trimester scan performed by these studies (Ghi et al., 2003; Fong et al., 2004).

The detection of fetal abnormalities in the first trimester differs from mid- and third-trimester scanning in several aspects. The resolution of the ultrasound equipment is around 1 mm and thus the small size of the fetal anatomical features is still a pivotal limiting factor before 12 weeks. Furthermore, many
fetal anomalies develop at the end of organogenesis over a variable period of time and many anomalies may not be apparent before the end of the first trimester, such as agenesis of the corpus callosum. Some anomalies have sonographic features that are different from those usually seen during the routine mid-trimester anomalies scan (i.e., anencephalus). By contrast, normal fetal developmental features, such as midgut herniation, have the same features as the pathological exomphalos and thus confirmation of the exact gestational age is crucial for such early diagnosis. Finally, dynamic changes in severity and sonographic appearance of abnormalities with advancing gestation cannot be evaluated by a single scan at 11–14 weeks.

This review analyses the potential of the so-called ‘first-trimester ultrasound examination’ in detecting common fetal anomalies, traditionally screened for by the mid-pregnancy scan. These anomalies have been reviewed according to the common organ systems, i.e. cranium and brain, abdomen, spine, urinary tract, heart, extremities, umbilical cord and placenta. The ‘first trimester’ of pregnancy theoretically ends at 12 weeks and 6 days of gestation, but most of the available literature includes ‘first trimester’ data up to 14 weeks of gestation; thus the detection rate of fetal anomalies has been evaluated before 14 weeks of gestation.

**Overall diagnosis of structural abnormalities**

The overall detection rate of structural abnormalities was evaluated using the data from eight screening studies (D’Ottavio et al., 1997, 1998; Hernadi and Toro csik, 1997; Economides and Braithwaite, 1998; Whitlow et al., 1999; Carvalho et al., 2002; Drysdale et al., 2002; Taipale et al., 2003; Chen et al., 2004). The criteria to be used for these studies were: upper gestational age limit at diagnosis of 13 weeks + 6 days and complete postnatal data of the outcome including analysis of the rate of anomalies discovered after birth. For the evaluation of the detection rate in early pregnancy, studies that focused on specific organs or anomalies have been excluded. These studies include 42,239 fetuses (average 5280 patients, study range 984–20,456), including 468 structural anomalies (1.1%) (Table 1). The overall detection rate of fetal abnormality by the early scan was 44% (range 18–65%) in these studies. About two-thirds of these were detected prior to 13 weeks of gestation. The evaluation by the mid-trimester scan was presented in seven of these studies with a combined, i.e. early and late scan, detection rate of 74% (range 59–89%). The combined detection rates for specific anatomical regions and anomalies are detailed in Table 2.

**Cranium and brain (Table 3)**

Anencephaly was the first abnormality of the central nervous system diagnosed in early pregnancy. Since the initial report, the sonographic features of many other CNS abnormalities have been described at the end of the first trimester. These anomalies include encephalocele, Dandy–Walker malformation, hydrocephalus and holoprosencephaly. Other CNS anomalies were described either in case reports or in small case series and their detection rate based on large cohorts is unknown. Overall, the early detection of these anomalies appears to be reliable, specifically in high-risk cases where recurrence is suspected. However, the detection rate of these anomalies in routine 11–14 week scans is unknown.

First trimester diagnosis of anencephaly is based on the demonstration of acrania (Souka and Nicolaides, 1997). Anencephaly develops through the failure of the anterior neuropore to close at around day 26 of embryonic development (Dias and Partington, 2004). Although controversial, animal models and sonographic findings suggest that the brain pathology progresses naturally from exencephaly to anencephaly due to the degeneration of the exposed cerebral tissue in the absence of the cranial vault (Bronshtein and Ornoy, 1991). The term exencephaly–anencephaly sequence has been proposed to define this phenomenon (Becker et al., 2000).

Anencephaly has been diagnosed in utero before 12 weeks; however, the ultrasonographic features of anencephaly in the first trimester are different from those found in the second trimester. Several case reports where diagnosis of anencephaly was confirmed by transvaginal sonography before 10 weeks gestation have been published (Sepulveda et al., 1997a; Chatzipapas et al., 1999; Becker et al., 2000). The sonographic features at an early stage include hypoplastic cranial pole with irregular echopatterns and a smaller crown–rump length (Figure 1a). After 10 weeks gestation, the absent echogenicity of the cranium and the deformed shape of the head, often described as the ‘Mickey Mouse face’ (Chatzipapas et al., 1999), raise suspicion of anencephaly (Figure 1b). Other authors have also highlighted that the presence of echogenic amniotic fluid is also an ultrasound marker of anencephaly (Cañici and Sepulveda, 2003).

The diagnosis of anencephaly can be reliably made at the 10–14 week scan. However, operators who perform routine dating or NT scan should be aware of the specific sonographic features of this severe anomaly and instructed to specifically search for these features. A multicentre study of a population with a prevalence of anencephaly of 87/100,000 found an initial detection rate of anencephaly at 11–14 weeks of 74% (Johnson et al., 1997). However, after the operators were trained for the specific sonographic features of acrania and anencephalus, the detection rate increased to 100%. A recent study (Cheng et al., 2003) assessing the detection rate of fetal acrania during first trimester screening for Down’s syndrome found that all cases (n = 7) of acrania (prevalence of 118/100,000) were diagnosed during the NT scan.

Encephalocele is a cranial defect with protrusion of the brain outside the cranium (Figure 2). When only the meninges protrude, it is called cranial meningocele. It is often associated with other anomalies such as microcephaly, spina bifida and hydrocephalus or part of Meckel–Gruber syndrome (Braithwaite and Economides, 1995; Sepulveda et al., 1997b; Tanriverdi et al., 2002).

Dandy–Walker malformation results from abnormal development of the rhombencephalon with complete or partial agenesis of the cerebellar vermis and cystic dilatation of the fourth ventricle and posterior cranial fossa. The classic type of Dandy–Walker malformation, with an enlarged posterior fossa and a large cerebellar defect and hydrocephalus, can be
Table 1. Overall detection rate of structural abnormalities by early (11–14 weeks) and mid-trimester ultrasound (US). DR = detection rate is calculated by the anomalies diagnosed in utero relative to anomalies identified prenatally and postnatally. Values in parentheses are percentages.

<table>
<thead>
<tr>
<th>Study</th>
<th>Early US</th>
<th>13 weeks</th>
<th>Early US</th>
<th>first and second trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Chen et al., 2004)</td>
<td>12–14 weeks (1609 age 35+) TA and TV</td>
<td>8/26 (31)</td>
<td>14/26 (54)</td>
<td>20/26 (77)</td>
</tr>
<tr>
<td>(Taipale et al., 2003)</td>
<td>13–14 weeks (20,465 low risk) TA and TV</td>
<td>NA</td>
<td>35/67 (52), cardiac anomalies excluded</td>
<td>NA</td>
</tr>
<tr>
<td>(Drysdale et al., 2002)</td>
<td>12–14 weeks (984 low risk) TA</td>
<td>3/28 (11)</td>
<td>5/28 (18)</td>
<td>24/28 (86)</td>
</tr>
<tr>
<td>(Carvalho et al., 2002)</td>
<td>11–14 weeks (2853 low risk) TA and TV</td>
<td>NA</td>
<td>29/130 (20.7); major anomalies 37.8%, minor anomalies 4.7%</td>
<td>82/130 (63); major anomalies 75.7%, minor anomalies 50.0%</td>
</tr>
<tr>
<td>(Guariglia and Rosati, 2000)</td>
<td>11–14 weeks (6634 low risk) mostly TA</td>
<td>22/63 (35)</td>
<td>37/63 (59)</td>
<td>51/63 (81)</td>
</tr>
<tr>
<td>(Whitlow et al., 1999)</td>
<td>11–14 weeks (10–16 weeks and 84.4%) combined</td>
<td>55/183 (30)</td>
<td>205/468 (44)</td>
<td>298/401 (74)</td>
</tr>
<tr>
<td>(D’Ottavio et al., 1998)</td>
<td>14 weeks (4080 low risk) TA and TV</td>
<td>NA</td>
<td>54/88 (61)</td>
<td>78/88 (89)</td>
</tr>
<tr>
<td>(Economides and Braithwaite, 1998)</td>
<td>12–14 (1632 low risk) TV</td>
<td>8/17 (47)</td>
<td>11/17 (65)</td>
<td>14/17 (82)</td>
</tr>
<tr>
<td>(Hernadi and Torocsik, 1997)</td>
<td>12 weeks (3991 low risk) TV only</td>
<td>14/49 (29)</td>
<td>20/49 (41)</td>
<td>29/49 (59)</td>
</tr>
<tr>
<td><strong>ALL</strong></td>
<td>55/183 (30)</td>
<td>205/468 (44)</td>
<td>298/401 (74)</td>
<td></td>
</tr>
</tbody>
</table>

Other studies that have reported early scanning up to 16 weeks were not included in this table:

- Guariglia and Rosati (2000) found a detection rate of 51.6% by transvaginal ultrasound performed at 10–16 weeks and 84.4% when combined with the second trimester scan. Taipale et al. (2003) found that the detection rate increased with experience (5 years) from 22% to 79%.
- Detection rate limited to cases diagnosed by 13 weeks gestation (definition of 1st trimester). NA = not applicable when the exact gestational age at diagnosis of each case was not provided.
- Detection rate at early gestation as defined by the study.

Table 2. Detection rate of specific anomalies by the early pregnancy scan. Review of publications represented in Table 1.

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Cases</th>
<th>Diagnosed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system</td>
<td>52/82</td>
<td>63</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>10/46</td>
<td>22</td>
</tr>
<tr>
<td>Urinary</td>
<td>33/76</td>
<td>43</td>
</tr>
<tr>
<td>Skeletal</td>
<td>20/78</td>
<td>26</td>
</tr>
<tr>
<td>Respiratory tract</td>
<td>0/3</td>
<td>0</td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td>23/37</td>
<td>62</td>
</tr>
<tr>
<td>Other</td>
<td>9/12</td>
<td>75</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>147/334</td>
<td>44</td>
</tr>
</tbody>
</table>

Table 3. Detection rate of central nervous system anomalies by the early pregnancy scan. Review of publications represented in Table 1.

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Cases</th>
<th>Diagnosed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system (total)</td>
<td>52/82</td>
<td>63</td>
</tr>
<tr>
<td>Anencephaly</td>
<td>23/25</td>
<td>92</td>
</tr>
<tr>
<td>Holoprosencephaly</td>
<td>12/14</td>
<td>86</td>
</tr>
<tr>
<td>Encephalocele</td>
<td>4/5</td>
<td>80</td>
</tr>
<tr>
<td>Spina bifida</td>
<td>12/27</td>
<td>44</td>
</tr>
<tr>
<td>Other</td>
<td>1/11</td>
<td>9</td>
</tr>
</tbody>
</table>
Figure 1. First trimester appearance of anencephaly. (a) Mid-sagittal view at 11 weeks. (b) ‘Mickey Mouse’ features at 12 weeks.

Figure 2. First trimester appearance of encephalocele in a case of Meckel–Gruber syndrome at 12 weeks. (a) Transverse view of the head, showing the brain protruding at the back of the cranium. (b) Mid-sagittal view. Note the absence of fetal nasal bones in profile.
recognized in early gestation (Achiron et al., 1993). Several cases of increased NT and generalized oedema associated with Dandy-Walker malformation have been described (Sherer et al., 2001; Chen et al., 2003). The identification of more minor variants is more complex.

Holoprosencephaly is a disorder caused by the failure of the prosencephalon or embryonic forebrain to divide sufficiently into the double lobes of the cerebral hemispheres. The result is a single-lobed brain structure and severe skull and facial defects. The most severe form, alobar holoprosencephaly (Figure 3), is incompatible with life. The two milder forms, semilobar and lobar, might result in a living child with varying degrees of neurodevelopmental disabilities. The diagnosis of holoprosencephaly has been reported as early as 10.5 weeks (Nelson and King, 1992). Several case studies have demonstrated the diagnosis of holoprosencephaly at the 10–14 week scan (Bronshtein and Wiener, 1991; Hamada et al., 1992; Zalens-Sprock et al., 1995; Tongsong et al., 1999; Turner et al., 1999; Wong et al., 1999; Blaas et al., 2000b; Sepulveda et al., 2004).

The diagnosis is usually based on two sonographic criteria: firstly, the intracranial finding of a single ventricle with a cerebral mantle and no visible midline structures, but fusion of the thalami and corpus striatum; and, secondly, facial abnormalities, including hypotelorism (Wong et al., 1999). Choroid plexus dysmorphology, characterized by failure to identify the ‘butterfly sign’, is also a warning sign of holoprosencephaly at the end of the first trimester (Sepulveda et al., 2004).

Spine
The diagnosis of spina bifida in the first trimester has been reported by several groups (Omtzigt et al., 1992; Sebire et al., 1997a; Blaas et al., 2000a; Buisson et al., 2002). The diagnosis of this anomaly has been made by direct visualization of the spinal anomaly and the protruding sac (myelomeningocele or meningocele) as early 10 weeks and 5 days of pregnancy (Bernard et al., 1997), or by indirect signs such as scalloping of the frontal bones (‘lemon shape’ head) (Sebire et al., 1997a). The detection rate of spina bifida in routine first trimester scans is unknown. While some have reported high detection rate by transvaginal sonography (Hernadi and Torocsik, 1997), others have shown that screening for spina bifida during routine NT scans is limited (Sebire et al., 1997a).

Figure 3. First trimester appearance of a case of alobar holoprosencephaly at 12 weeks (a) with altered appearance at 14 weeks (b).

Heart (Table 4)
Structural abnormalities of the heart and great vessels are the most common major birth defects, affecting about eight of 1000 live births (Hoffman, 1990). Early scanning and diagnosis of cardiac anomalies have recently gained much interest in high-risk populations. Fetuses with an increased NT and normal karyotype (Hyett et al., 1997; Hyett and Thilaganathan, 1999) at 11–14 weeks are at significantly greater risk of having congenital cardiac malformations. Therefore, it has been suggested that the NT measurement could be used as a screening method for congenital heart disease with a detection rate of 56 and 40% for NT above the 95th and 99th percentiles respectively (Hyett et al., 1999). However, others have reported a much lower sensitivity (15%) and negative predictive value (Mavrides et al., 2001). The additional use of pulsed wave Doppler velocimetry in the

Table 4. Detection rate of cardiovascular system anomalies by the early pregnancy scan. Review of the publications represented in Table 1. VSD = ventriculoseptal defect. AVSD = atrioventricular septal defect. Numbers in parentheses represent percentages.

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular (total)</td>
<td>10/46 (22)</td>
</tr>
<tr>
<td>Other</td>
<td>3/7 (43)</td>
</tr>
<tr>
<td>VSD or AVSD</td>
<td>6/21 (29)</td>
</tr>
<tr>
<td>Hypoplastic left heart</td>
<td>1/8 (13)</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>0/5 (0)</td>
</tr>
<tr>
<td>Transposition great arteries</td>
<td>0/3 (0)</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>0/2 (0)</td>
</tr>
</tbody>
</table>
ductus venosus at 11–14 weeks has also improved the detection of fetuses at risk of major cardiac abnormalities. In a survey of 142 fetuses with normal karyotype, absent or reversed A-wave in the ductus venosus had a detection rate of 100% of cardiac abnormalities (Matias et al., 1999). However, these data should be implemented with caution, due to the low specificity of the Doppler findings and the high overlap between Doppler abnormalities and the increased NT.

First trimester examination of the fetal heart can be performed by transvaginal (TV) or transabdominal sonography. In the early 1990s, several case reports and case series pioneered the use of TV echocardiography at early stages of gestation (Gembruch et al., 1990; D’Amelio et al., 1991; Achiron et al., 1994a,b; Allan et al., 1997). Subsequently, the visualization rate of the four-chamber view during early pregnancy by the TV route was investigated (Bronshtein and Wiener, 1991; Dolkart and Reimers, 1991; Johnson et al., 1992; Gembruch et al., 1993; Haak and van Vugt, 2003). Overall, 201 women were studied at 12 weeks to 12 weeks + 6 days, and 254 women at 13 weeks to 13 weeks + 6 days. The average visualization rate of the four-chamber view in these studies was 81 and 93% at 12 weeks to 12 weeks + 6 days and 13 weeks to 13 weeks + 6 days respectively. A more recent study has also evaluated the impact of TV sequential scanning at 11, 12 and 13 weeks gestation (Haak et al., 2002). These authors have demonstrated an increase in the ability to perform a full cardiac examination from 20% at 11 weeks to 92% at 13 weeks. This high success rate probably derives from better resolution TV probes and the operator’s increasing experience since the introduction of TV echocardiography. Gembruch et al. compared the visualization of the fetal heart via both TV and transabdominal routes, and showed that the four-chamber view can be visualized in 100% of cases when combining both approaches at 13 weeks gestation. In this study, the outflow tracts were better visualized by the transvaginal route up to 12 weeks (87 versus 33%). However, at 13–14 weeks the TV route was only marginally better in demonstrating the outflow tract (100 versus 90%), and there was no difference (100% of cases demonstrated) at 15 weeks (Gembruch et al., 2000).

Several studies have assessed the detection rate of fetal cardiac anomalies in high-risk patients during the NT measurement ‘period’ (10–14 weeks). In a study of 15 patients undergoing first trimester echocardiography, a satisfactory view of the four chambers and outflow tract was achieved in 11/15 (73%) patients (Carvalho et al., 1998). A reassuring scan correctly identified fetuses with a normal four-chamber heart and outflow tract views in 9/10 patients with a negative predictive value (NPV) of 90%. However, in two of the patients with normal scan a small ventriculoseptal defect (VSD), without haemodynamic implications, was found postnatally. A larger prospective study has evaluated the detection rate, negative and positive predictive value (PPV) of echocardiography (at 10–14 weeks) in a high-risk population (Huggon et al., 2002). In this study, 478 fetuses were evaluated and satisfactory views were obtained in 402 cases by transabdominal and in 13 by TV route (total 86%). Validation of the initial scan was available in only 241 fetuses. The NPV of normal 10–14 weeks echocardiography was 96% (189/196). A diagnosis of ‘definite’ cardiac abnormality had a PPV of 97% (33/34), with only one false positive case (ventricular disproportion). An abnormality was validated only in four out of six (67%) fetuses with a ‘suspected’ cardiac abnormality.

The data of these studies are not sufficient to state that routine first trimester echocardiography can be used on a large scale to evaluate the fetal heart in the general population. The NPV of early screening is probably sufficient to reassure high-risk patients, providing that echocardiography is repeated at 18–20 weeks (Huggon et al., 2002).

### Congenital diaphragmatic hernia

Congenital diaphragmatic hernia (CDH) can be diagnosed by the demonstration of intrathoracic viscera and mediastinal shift in the mid-trimester scan. About 50% of cases of CDH are associated with chromosomal abnormalities. The presence of CDH has been demonstrated in early scans (Aviram-Goldring et al., 2000). An increased NT is a risk factor for CDH, presumably representing the increased mediastinal pressure at early pregnancy and impedance to venous return (Figure 4). A study evaluating the NT in cases of CDH without chromosomal abnormalities has shown that the NT is increased (>95th percentile) in 37% of cases. However, the detection rate of CDH by the 11–14 weeks scan was only 1/19 (5%), while the detection rate by the second trimester scan was 75% (Sebire et al., 1997b).

### Abdominal wall (Table 5)

Abdominal wall defects have been commonly diagnosed at the end of the first trimester. Prenatal diagnosis of exomphalos is based on the demonstration of midline anterior abdominal wall defect with herniation of a peritoneal sac with its visceral contents and an umbilical cord insertion at the apex of the sac (Figure 5). Exomphalos is a true developmental anomaly, which explains the association with various other abnormalities, in particular cardiac, genitourinary, craniofacial, and diaphragmatic anomalies. In a screening study, omphalocele was diagnosed in 11/15,726 (0.07%) fetuses at 10–14 (Snijders et al., 1995) weeks and 38/43,896 (0.09%) fetuses at 10–16 (Blazer et al., 2004) weeks, and its finding was associated with trisomy 18 and 13 (Snijders et al., 1995). Exomphalos should be distinguished from the physiological herniation of the midgut, which can be seen up to 12 weeks gestation (Zalen-Sprock et al., 1997). This is particularly important for the NT and first trimester screening scan, since omphalocele can be reliably diagnosed only after 12 completed weeks of gestation, and final diagnosis should not rely on visualization of exomphalos between 11 weeks and 11 weeks + 6 days. There are also reports of delayed midgut reduction where an initial diagnosis of a small exomphalos (at 14–16 weeks) disappeared on a second trimester scan (Bromley and Benacerraf, 1993; Blazer et al., 2004). The visualization of exomphalos also assists in the early diagnosis of rare syndromes such as pentalogy of Cantrell (Hsieh et al., 1999), Beckwith–Wiederman (Winter et al., 1986) and other syndromes (Meizner et al., 1995).

Gastroscisis is a sporadic defect with evisceration of the intestine through a small abdominal wall defect located just lateral to an intact umbilical cord. Although the incidence is comparable to omphalocele, reports on first trimester diagnosis of gastroscisis are rare (Guzman, 1990; Kushnir et al., 1990; Whitlow et al., 1999). This is probably because...
Table 5. Detection rate of abdominal thoracic anomalies by the early pregnancy scan. Review of the publications represented in Table 1. GIT = gastrointestinal tract, TEF = tracheo-oesophageal fistula, CCAM = congenital cystic adenomatoid malformation. Numbers in parentheses represent percentages.

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal wall and GIT (total)</td>
<td>23/37 (62)</td>
</tr>
<tr>
<td>Omphalocele</td>
<td>15/18 (83)</td>
</tr>
<tr>
<td>Gastroschisis</td>
<td>7/9 (78)</td>
</tr>
<tr>
<td>Oesophageal atresia/TEF</td>
<td>1/5 (20)</td>
</tr>
<tr>
<td>Small bowel obstruction</td>
<td>0/1 (0)</td>
</tr>
<tr>
<td>Anal atresia/imperforate anus</td>
<td>0/4 (0)</td>
</tr>
<tr>
<td>CCAM</td>
<td>0/1 (0)</td>
</tr>
<tr>
<td>Diaphragmatic hernia</td>
<td>0/2 (0)</td>
</tr>
</tbody>
</table>

Figure 4. Thirteen week appearance of congenital diaphragmatic hernia (left sided) with the stomach and heart at the same anatomical level.

Figure 5. Appearance of a major exomphalos at 12 weeks. The fetal body anatomy is grossly distorted by the protrusion of the liver outside the abdomen (a). Doppler investigation demonstrates a direct connection with the fetal aorta (b).
gastrochisis is not directly linked with a specific chromosomal anomaly or abnormal NT thickness.

Bladder and cloacal extrophy are rare but devastating anomalies (Figure 6) that occur as a result of failed closure of the anterior abdominal wall at the ventral end of the cloacal membrane (Langer, 2003). Bladder extrophy is often associated with other genitourinary anomalies and cloacal extrophy is usually accompanied by an omphalocele, imperforate anus, diastasis of the pubis, and absent genitalia (Meizner et al., 1995). Although surgical reconstruction can be accomplished in most cases, long-term problems with urinary continence remain. Bladder extrophy may be recognized sonographically by absence of the bladder, as well as through recognition of associated genito-urinary anomalies. First trimester diagnosis of these anomalies is rare and the diagnosis of the exact type of malformation at such an early stage is limited (Taipale et al., 2004).

Urinary tract (Table 6)

The fetal kidneys can be visualized from 9 weeks of gestation and are seen in almost all fetuses at 12 weeks using transabdominal ultrasound (Green and Hobbins, 1988; Braithwaite et al., 1996). They initially appear in the transverse plane as hypechoic oval structures on both sides of the fetal spine. In the longitudinal axis, they appear along the paravertebral plane of the fetal spine. A detailed view of the fetal kidneys by TV sonography has enabled development of normograms for the kidney diameters at the first trimester (Rosati and Guariglia, 1996).

Bilateral renal agenesis is usually diagnosed at the beginning of the second trimester due to anhydramnios. Since most of the amniotic fluid before 11 weeks is not produced by the fetal kidneys, this absence of amniotic fluid cannot help to detect renal agenesis during the first trimester. However, prenatal diagnosis of bilateral renal agenesis has been reported after 12 weeks gestation (Bronstein et al., 1994), where hypechoic masses seen at the renal beds were proved to be the adrenals.

Polycystic kidney disease has rarely been diagnosed during the first trimester. Retrospective examinations obtained from early scans in patients diagnosed with autosomal recessive polycystic kidney disease have demonstrated that the kidneys can be hypechoic from 14 weeks of gestation (Bronstein et al., 1992). Another manifestation of polycystic kidneys, independent of polycystic kidney disease, is the association with Meckel–Gruber syndrome, i.e. encephalocele, polydactyly and polycystic kidney. First trimester diagnosis of Meckel–Gruber has been described in case reports (Tanniriverdi et al., 2002) and case series in low- and high-risk patients (Braithwaite and Economides, 1995; Sepulveda et al., 1997b). When a high index of suspicion is practised in high-risk cases, all three features of this syndrome, including polycystic kidneys, can be seen at 13 weeks of gestation (Sepulveda et al., 1997b).

Multicystic dysplastic kidneys have only recently been described by ultrasound in early pregnancy (Fong et al., 2004). The usual presentation of this anomaly is in the second trimester, probably after sufficient urine production and fluid accumulation in the dilated tubules.

Megacystis or pathological enlargement of the bladder, is characterized by a longitudinal diameter >6 mm at 11–14 weeks (Sebire et al., 1996). Megacystis (Figure 7) may be associated with chromosomal abnormalities (20%), obstructive uropathy (26%) and other extra-renal anomalies (30%) (Jouannic et al., 2003). About half of the cases resolve spontaneously by 20 weeks (Sebire et al., 1996). In fetuses with normal karyotype, a bladder diameter >15 mm is associated with progressive obstructive uropathy (Liao et al., 2003) and the outcome of these fetuses is poor, with or without in-utero therapy (Jouannic et al., 2003). However, when the bladder length is 7–15 mm, the resolution rate is about 90%.

Umbilical cord and placenta

The cord diameter has been measured in pregnancy (Ghezzi et al., 2001) and an increased diameter has been found to be associated with a higher rate of chromosomal abnormalities (Ghezzi et al., 2002). This could be due to the fact that the Warton’s jelly becomes edematous very rapidly in cases of fetal hydrops (see below).

A single umbilical artery (SUA) has been detected in early gestation by TV (Blazer et al., 1997) and transabdominal sonography (Sepulveda et al., 1996). The detection rate of SUA in the first trimester is still unknown. The optimal location for evaluation of the number of arteries has also not been evaluated in early pregnancy. In a cross-section of the umbilical cord, the umbilical artery:vein ratio in fetuses with SUA is usually bigger (>0.5) then in patients with two arteries (<0.5) (Sepulveda et al., 1996).

Other anomalies of the cord have also been presented such as umbilical cord cysts (single or multiple) (Ross et al., 1997; Sepulveda et al., 1999; Ghezzi et al., 2003), short cord suggesting body stalk anomalies (Smrcek et al., 2003) and malinsertion of the cord (Monteagudo et al., 2000). Diagnosis of umbilical cord cysts during the first trimester (Figure 8) has been described by several authors (Rempen, 1989; Ross et al., 1997; Sepulveda et al., 1999; Ghezzi et al., 2003). The prevalence of umbilical cord cysts at 7–13 weeks gestation is approximately 2–3% (Sepulveda et al., 1999; Ghezzi et al., 2003). The significance of these cysts is not established. While some report a high incidence of about 20% of fetal chromosomal or structural defects (Ross et al., 1997), others found that most of the cysts resolve and are not associated with fetal abnormalities (Sepulveda et al., 1999). Whenever a cyst is found, a thorough examination of the umbilical cord should be performed in order to define single or multiple cysts. It has been suggested that these two entities may have a different outcome, as a single umbilical cord cyst is more likely to be a benign finding, whereas multiple cysts are associated with increased risk of aneuploidy (16%) and miscarriage (66%).

Placenta praevia is not a structural abnormality. However, its significance cannot be over-emphasized and the diagnosis of placenta praevia in the first trimester is important for counselling of patients. It is specifically important in cases where previous uterine surgery was performed and there is an increased risk of placenta accreta. The incidence of placenta praevia at the first trimester is about 5% (Rosati and Guariglia, 1996).
Figure 6. Appearance of cloacal exstrophy in first trimester.

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary (total)</td>
<td>33/76 (43)</td>
</tr>
<tr>
<td>Obstructive uropathy</td>
<td>26/52 (50)</td>
</tr>
<tr>
<td>Renal dysplasia</td>
<td>6/13 (46)</td>
</tr>
<tr>
<td>Renal agenesis</td>
<td>1/7 (14)</td>
</tr>
<tr>
<td>Other</td>
<td>0/4 (0)</td>
</tr>
</tbody>
</table>

Figure 7. Megacystis at 12 weeks associated with bilateral hydronephrosis. Longitudinal bladder diameter is increased and there are signs of early onset renal pelvis dilatation.

Figure 8. Umbilical cord cyst at 11 weeks in a case of trisomy 18, shown in two views (a) and (b).
When the placenta covers the internal os during the 11–14 week TV scan and the distance between the os and the placental edge is greater than 14 mm, the incidence of placenta praevia at term is about 5–18%, compared with 0.16% in the general population (Taipale et al., 1997; Rosati and Guariglia, 2000).

Molar changes in the placenta have been described in early pregnancy (Jauniaux and Nicolaides, 1997). The prenatal diagnosis of placental moles is based on the ultrasonographic demonstration of sonolucent areas within the placenta (Figure 9). In a complete mole, there is a characteristic ‘snow storm’ appearance in the absence of a fetus. When the sonolucent areas are demonstrated in association with a fetus, the differential diagnosis includes triploid or diploid partial mole, twins with a normal fetus (with its own placenta) and a complete mole, or benign hydropic degeneration such as mesenchymal dysplasia (Jauniaux et al., 1997).

Chorioangiomata are usually diagnosed by ultrasound during the second trimester (Jauniaux and Ogle, 2000; Zalel et al., 2002), and so far there has been no description of a chorioangioma at 11–14 weeks.

### Cystic hygroma

Cystic hygroma develops due to malformation of the fetal neck lymphatic vessels. Accumulation of lymph results in nuchal or jugular cystic hygroma (Chervenak et al., 1983). Most of the recent publications regarding the prenatal diagnosis of cystic hygroma present data on early diagnosis between 10 and 15 weeks gestation. The hygromas can be single or multiloculated, and are mainly located lateral or posterior in the cervical region. About 40% are associated with chromosomal abnormalities and another 20% with structural anomalies (Zalen-Sprock et al., 1992b). Although early diagnosis is common, false positive cases have been described.

![Figure 9. Molar appearance of the placenta at 12 weeks in a pregnancy complicated by mesenchymal dysplasia.](image)

![Figure 10. (a) Sonographic appearance of a ‘space suit’ in fetus at 13 weeks of gestation. (b) Note the hydrothorax and ascites as part of fetal hydrops.](image)
These can be due to a translucent area between the amnion and chorion which is mistakenly as a hygroma, or when a cephalocele is diagnosed as a hygroma (Zalen-Sproc et al., 1992a).

Fetal hydrops

All cases of fetal hydrops diagnosed at the end of the first trimester are of non-immune origin (Jauniaux, 1997). The typical sonographic appearance of hydrops in early pregnancy is that of a fetal ‘space-suit’ (Figure 10) (Shulman et al., 2000). Generalized hydrops in early pregnancy is associated with chromosomal abnormalities such as Turner’s syndrome (Bronshtein et al., 2003), and structural abnormalities (Shulman et al., 2000). Several series and reviews have found that about 85% of the fetuses presenting with first trimester hydrops have structural abnormalities, and at least 50% present with an aneuploidy (Has and Recep, 2001). Rarer causes of hydrops in the first trimester include primary infection with parvovirus (Sohan et al., 2000), genetic diseases (Van Dorpe et al., 1996) and thoracic lesions (Jauniaux et al., 2002).

References


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