Chapter 5
Abnormal development of (intra)abdominal anatomy
Developmental, sonographic and clinical aspects

In this chapter the abnormal development and sonographic appearance of the fetal abdominal wall, gastrointestinal tract, and renal tract will be discussed. In the last subchapter the possible role of colour coded Doppler imaging in these anomalies will be addressed.

5.1 Fetal abdominal wall defects

Fetal anterior abdominal wall defects form a heterogeneous group of congenital anomalies. The most common types are omphalocele and gastroschisis. Ventral wall defects are also encountered in other, less frequent syndromes as the pentalogy of Cantrell, the Beckwith-Wiedemann syndrome, the body stalk anomaly, and cloacal extrophy.

Omphalocele results from failure of the two lateral ectomesodermal folds to meet in the midline between the 3rd and 4th week of gestation\textsuperscript{47, 146}. In contrast, gastroschisis is a defect resulting from vascular compromise of either the right umbilical vein or the omphalomesenteric artery. Initially, two umbilical veins are present. Physiologic involution of the right umbilical vein occurs between the 28th and 32nd day after conception. Premature involution may lead to ischemia and to resultant mesodermal and ectodermal defects\textsuperscript{47, 205}. Alternatively, at first both omphalomesenteric arteries branch from the dorsal aorta and extend to the right along the omphalomesenteric duct towards the yolk sac. The left one involutes, whereas the right one is transformed into the right mesenteric artery. The terminal end extends through the body stalk (umbilical cord) into the extraembryonic coelom. Disruption of this segment could result in right-sided periumbilical ischemia and a paramedian defect characteristic of gastroschisis\textsuperscript{103}. Associated intestinal atresia\textsuperscript{9} is found to be secondary to intestinal ischemia\textsuperscript{316} which may result from either compression of the mesenteric vessels by the relatively small abdominal wall defect or from torsion of the eviscerated bowel around its mesenteric axis\textsuperscript{131}.

The pentalogy of Cantrell is a very rare syndrome and consists of an omphalocele, a cardiac anomaly, and a defect of the lower sternum, diaphragmatic pericardium and anterior diaphragm. This association is thought to result from failure of the cephalic ectomesodermal fold to fuse with the caudal and two lateral folds during the embryonic period. Prognosis depends on the severity of the anomalies\textsuperscript{29}. 

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The Beckwith-Wiedemann syndrome is characterized by a coexisting omphalocele, macroglossia and visceromegaly. Most cases are sporadic although an autosomal pattern of inheritance with variable transmission has been reported. Neonates are at risk of hypoglycemia because of relative hyperinsulinemia associated with pancreatic islet hyperplasia and suffocation because of the macroglossia, and to develop malignant tumours. When they survive childhood, they have a relatively normal intelligence. It was recently suggested that congenital pancreatic cysts should be included in the Beckwith-Wiedemann phenotype.

The body stalk anomaly, also limb-body wall complex, is a sporadic complex of abnormalities having in common an anterior body wall defect with absence of umbilicus and umbilical cord through which the fetus is directly attached to the placenta. Severe maldevelopment of the cephalic, caudal, and lateral embryonic body folds, possibly of vascular etiology is believed to account for this complex anomaly. Failure of complete extraembryonic coelom obliteration accounts for the absence of the umbilical cord formation and the wide-based insertion of the amnioperitoneal membrane onto the placental chorionic plate. Fusion of the amnion and chorion takes place only at the margin of the placenta, instead of more centrally. As a result the abdominal organs herniate into a sac outside the abdomen; the sac is covered by amnion and peritoneum and is directly attached to the placenta. The disorder is further characterized by disruption of the lateral body wall, spine, limbs, face and cranium, isolated or in combination. The condition is uniformly fatal.

Cloacal extrophy is also a rare association of an omphalocele, extrophy of the bladder, imperforate anus and spinal defects, and results from defective fusion of the caudal ectomesodermal fold in the embryonic period. A prenatal sonographic diagnosis of this sequence has only been reported exceptionally. The defect may be fatal, but in milder forms corrective surgery can be offered.

In chapter 5.1.1 attention will focus on our experience with the two most frequent types of fetal abdominal wall defects, omphalocele and gastroschisis. Most recent reviews confirm the higher rate of associated anomalies and chromosomal defects in infants with omphalocele compared to infants with gastroschisis. In case of gastroschisis, fetal bowel damage is thought to result from compression of bowel loops and mesentery in the abdominal wall defect, or from lengthy exposure of the bowel to amniotic fluid. It has very recently been suggested that bowel exposure to amniotic fluid could result in an inflammatory response which could induce both perivisceritis and premature birth by the cytokine pathway.
As stated in chapter 5.1.1, in case of gastroschisis, small bowel thickening and dilatation have been associated with intestinal damage, and short- and long-term infant morbidity. The reliability of these prenatal sonographic predictors of intestinal compromise and poor clinical outcome is, however, still subject to debate. Although several authors advocate the clinical use of these markers, others consider their values unreliable and not clinically meaningful.

Also lately, no convincing evidence has been published to support routine Caesarean delivery in fetuses with an abdominal wall defect. Elective Caesarean section does not improve outcome in fetuses with gastroschisis. Querck et al. (1996) even reported that Caesarian deliveries were associated with worse outcomes in their retrospective analysis of 56 newborns with gastroschisis.

5.1.1 Prenatal diagnosis of fetal abdominal wall defects: a retrospective analysis of 44 cases

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Published in Prenatal Diagnosis 1996, 16, 411-417

Summary

Forty four fetal abdominal wall defects, consisting of 31 omphalocoeles, 11 cases of gastroschisis, and two body stalk anomalies (which are excluded from further analysis), were diagnosed at 12-39 weeks (median 26 weeks) of gestation. In 10/31 (32 per cent) cases of omphalocoele and in 4/11 (36 per cent) cases of gastroschisis, multiple congenital anomalies were diagnosed. A normal amount of amniotic fluid was present in 39 cases; in three cases of omphalocoele an abnormal amount of amniotic fluid (polyhydramnios, n=2; oligohydramnios, n=1) was seen. Prenatally, intrauterine growth retardation (IUGR) was diagnosed in each type of anomaly only once, although the birth weight was below the tenth centile in 23 per cent of omphalocoeles and in 36 per cent of cases of gastroschisis. An abnormal prenatal karyotype was established in 5/25 (20 per cent) cases of omphalocoele versus none in the gastroschisis group. In 36 cases an expectant obstetrical management was followed, and in six cases of omphalocoele the pregnancies were terminated because of severe multiple anomalies (n=3) or an abnormal prenatal karyotype (n=3). The preterm delivery rate (excluding terminations) was 12/25 (48 per cent) in the omphalocoele subgroup versus 8/11 (73 per cent) in the gastroschisis subgroup. The Caesarean section rate was almost identical (19 versus 18 per cent) in
both subgroups; the majority (n=5) were performed to protect the abdominal wall defect. The overall survival rate was 39 per cent in the omphalocele group; in all surviving infants this was the sole congenital anomaly and in each instance there was a normal karyotype. In the gastroschisis group, 8/11 (72 per cent) infants survived, of which two children also displayed unilateral hydronephrosis.

**Introduction**

Fetal abdominal wall defects represent a common group of congenital anomalies which are nowadays easily detected on ultrasonographic examination. An accurate differential diagnosis between the two most frequent types, omphalocele and gastroschisis, is of great importance since they differ in associated structural malformations and chromosomal anomalies, and hence in fetal outcome.

The prognosis of both isolated anomalies is generally excellent\(^{55,71,131}\). However, it depends on associated structural malformations and chromosomal anomalies in cases of omphalocele and on prematurity and long-term treatment results of short bowel syndrome associated with intestinal atresia in case of gastroschisis\(^{35,114,216}\). In this study we report 44 cases of ultrasonically diagnosed fetal abdominal wall defects with emphasis on the accuracy of the prenatal diagnosis, associated fetal malformations, chromosomal anomalies, perinatal management, and fetal outcome.

**Materials and methods**

During the period 1981-1993, a fetal abdominal wall defect was diagnosed on ultrasound in 44 patients who were referred to our level III centre at 12-39 weeks (median 26 weeks) of gestation for further evaluation because of suspected structural pathology at the referring hospital. The majority of cases (34/44; 77 per cent) were referred during the second half of the time span of our study (1987-1993). Maternal age ranged between 19 and 47 years (median 28 years); maternal parity varied between 0 and 6 (median 1). The diagnosis of a fetal abdominal wall defect was suspected on the demonstration of a mass adjacent to the anterior ventral wall. An omphalocele was suspected in cases of a midline defect covered by a membrane with insertion of the umbilical cord at the top of the herniated sac, whereas a gastroschisis was diagnosed when free bowel was seen in the amniotic fluid without a surrounding membrane and a normal umbilical cord insertion site. Polyhydramnios was defined as a largest fluid pocket of 10 cm or more; oligohydramnios as a largest vertical fluid pocket of 1 cm or less. Intrauterine growth retardation (IUGR) was diagnosed when the upper fetal abdominal circumference was situated below the tenth
centile of the reference curve\textsuperscript{33}. Postnatally, IUGR was defined as a fetal birth weight below the tenth centile according to the Kloosterman tables corrected for maternal parity and fetal sex\textsuperscript{116}.

At our Division of Prenatal Diagnosis, all fetal scans were performed using a Diasonics CV 100 (1981-1989; carrier frequency 3.5 and 5.0 MHz) or a Toshiba SSA 270 (1990-1993; carrier frequency 3.75 MHz).

Fetal karyotyping was performed in 34 cases by means of amniocentesis (n=21), transabdominal chorionic villus sampling (TA-CVS) (n=7), or cordocentesis (n=6). In the remaining ten cases, no fetal karyotyping was carried out because of premature labour (n=4), parental refusal (n=3), advanced gestational age \( \geq 36 \) weeks at the time of referral (n=2), or intrauterine death (n=1).

After birth all live neonates were immediately transferred to the pediatric surgical intensive care unit. The abdominal wall defect was wrapped in sterile gauzes and a stomach tube was placed in situ. Small omphaloceles and all cases of gastrochisis were closed primarily. Large omphaloceles (diameter > 5 cm) were treated conservatively followed by secondary surgical closure after complete covering by skin.

Details on pregnancy outcome were obtained from clinical records or from autopsy at our own centre or the referring hospital.

Results

Indications for referral to our centre were omphalocele (n=31), abdominal wall defect (not further specified) (n=7), gastrochisis (n=4), severe IUGR (n=1), and a combination of fetal ascites and polyhydramnios (n=1). Since maternal serum screening is not routinely used in The Netherlands, no information is available on maternal serum alpha-fetoprotein levels. Details on the prenatal and postnatal findings are presented in Tables I-III.

Of the 44 cases of fetal abdominal wall defects diagnosed in our centre, an omphalocele was established in 31 cases (Tables I and III), a body stalk anomaly in two cases (Table III), and a gastrochisis in 11 cases (Tables II and III). Omphalocele and gastrochisis are the two most common types of abdominal wall defects. Since body stalk anomalies differ embryologically from omphaloceles and are uniformly lethal, these two cases were omitted from further analysis. Both pregnancies were terminated and in both body stalk anomalies, a normal prenatal karyotype was established.
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Table 1 Prenatal data and fetal outcome in 21 fetuses with omphalocele as the only sonographic anomaly

<table>
<thead>
<tr>
<th>Case No.</th>
<th>US (weeks)</th>
<th>Prenatal karyotype</th>
<th>Delivery (weeks)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>13</td>
<td>n</td>
<td>38</td>
<td>ID</td>
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<tr>
<td>4</td>
<td>15</td>
<td>n</td>
<td>16</td>
<td>IUD</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>n</td>
<td>35</td>
<td>Alive</td>
</tr>
<tr>
<td>6</td>
<td>17</td>
<td>n</td>
<td>39</td>
<td>Alive</td>
</tr>
<tr>
<td>7</td>
<td>17</td>
<td>n</td>
<td>39</td>
<td>Alive</td>
</tr>
<tr>
<td>9</td>
<td>20</td>
<td>tri 18</td>
<td>34</td>
<td>IUD</td>
</tr>
<tr>
<td>10</td>
<td>20</td>
<td>n</td>
<td>21</td>
<td>IUD</td>
</tr>
<tr>
<td>11</td>
<td>20</td>
<td>n</td>
<td>28</td>
<td>IUD</td>
</tr>
<tr>
<td>13</td>
<td>22</td>
<td>n</td>
<td>38</td>
<td>Alive</td>
</tr>
<tr>
<td>14</td>
<td>22</td>
<td>n</td>
<td>39</td>
<td>ID</td>
</tr>
<tr>
<td>16</td>
<td>24</td>
<td>-</td>
<td>24</td>
<td>IUD</td>
</tr>
<tr>
<td>17</td>
<td>24</td>
<td>n</td>
<td>38</td>
<td>Alive</td>
</tr>
<tr>
<td>21</td>
<td>26</td>
<td>n</td>
<td>31</td>
<td>Alive</td>
</tr>
<tr>
<td>22</td>
<td>27</td>
<td>n</td>
<td>38</td>
<td>Alive</td>
</tr>
<tr>
<td>23</td>
<td>27</td>
<td>-</td>
<td>35</td>
<td>Alive</td>
</tr>
<tr>
<td>24</td>
<td>27</td>
<td>-</td>
<td>40</td>
<td>Alive</td>
</tr>
<tr>
<td>28</td>
<td>30</td>
<td>n</td>
<td>37</td>
<td>Alive</td>
</tr>
<tr>
<td>29</td>
<td>30</td>
<td>n</td>
<td>39</td>
<td>IUD</td>
</tr>
<tr>
<td>30</td>
<td>34</td>
<td>45X</td>
<td>34</td>
<td>ID</td>
</tr>
<tr>
<td>32</td>
<td>34</td>
<td>-</td>
<td>37</td>
<td>Alive</td>
</tr>
<tr>
<td>33</td>
<td>39</td>
<td>-</td>
<td>39</td>
<td>Alive</td>
</tr>
</tbody>
</table>

ID = infant death (i.e. beyond neonatal period); IUD = intrauterine death; n = normal; tri 18 = trisomy 18

Gestational age at the time of referral to our centre was 12-39 weeks (median 24 weeks) in cases of omphalocele and 19-38 weeks (median 27 weeks) when gastroschisis was diagnosed. A normal amount of amniotic fluid was present in 39 cases. Polyhydramnios was present in two cases and oligohydramnios in only one case, each of which was associated with an omphalocele. IUGR was established in each type of anomaly only once. Associated anomalies were seen prenatally in ten of the
Table II  Prenatal data and fetal outcome in seven fetuses with gastoschisis as the only sonographic anomaly.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>US (weeks)</th>
<th>Prenatal karyotype</th>
<th>Delivery (weeks)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>24</td>
<td>n</td>
<td>36</td>
<td>Alive</td>
</tr>
<tr>
<td>37</td>
<td>27</td>
<td>n</td>
<td>34</td>
<td>Alive</td>
</tr>
<tr>
<td>38</td>
<td>27</td>
<td>-</td>
<td>32</td>
<td>NND</td>
</tr>
<tr>
<td>39</td>
<td>27</td>
<td>n</td>
<td>37</td>
<td>Alive</td>
</tr>
<tr>
<td>41</td>
<td>34</td>
<td>-</td>
<td>35</td>
<td>Alive</td>
</tr>
<tr>
<td>42</td>
<td>34</td>
<td>-</td>
<td>37</td>
<td>Alive</td>
</tr>
<tr>
<td>43</td>
<td>35</td>
<td>n</td>
<td>36</td>
<td>Alive</td>
</tr>
</tbody>
</table>

NND = neonatal death; n = normal

omphaloceles, i.e., congenital heart disease (n=6), fetal hydrops (n=4), skeletal abnormalities (n=3), hypotelorism (n=2), and a single umbilical artery (n=2). Within the gastoschisis group, associated anomalies were found in four cases, i.e., renal tract anomaly (n=2), congenital heart disease (n=1), and a skeletal anomaly (n=1) (Table III).

Out of the 32 cases karyotyped prenatally, 25 were performed for an omphalocele and seven for a gastoschisis. Prenatally, an abnormal karyotype existed in five out of 25 cases (20 per cent) of omphalocele (trisomy 18, n=4; 45X, n=1) and in none of the cases of gastoschisis. In the ten cases not karyotyped prenatally, no abnormal karyotype was established postnatally.

A policy of expectant obstetric management was adopted in 25/31 (81 per cent) cases of omphalocele and in all 11 cases of gastoschisis. Termination of pregnancy (TOP) took place in six cases of omphalocele because of severe multiple congenital anomalies (n=3) and trisomy 18 (n=3). None of the pregnancies with gastoschisis were terminated.

For all 42 pregnancies together delivery took place between 12 and 39 weeks of gestation with preterm delivery (< 37 weeks) in 26/42 cases (62 per cent). When differentiating between the omphalocele subgroup and the gastoschisis subgroup, the percentages are 58 per cent (18/31) and 73 per cent (8/11), respectively. However, as all terminations of pregnancy took place below 30 weeks, the corrected preterm delivery rate (i.e., excluding cases of TOP) in the omphalocele subgroup is as high as 48 per cent (12/25).
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The Caesarean section rate was almost identical in the two subgroups: 6/31 cases (19 per cent) and 2/11 cases (18 per cent), respectively. Indications for Caesarean delivery were the size and presumed severity of the abdominal wall defect, predominantly in the earlier years of prenatal diagnosis (n=5); fetal distress (n=2); and a footling breech position in a bicornuate uterus (n=1).

The survival rate within the omphalocele group was only 39 per cent (12/31), as six pregnancies were terminated, seven infants died in utero, and six postnatally. Excluding the eight terminations of pregnancy, the corrected survival rate is 48 per cent.

Table III  Prenatal data and fetal outcome in ten fetuses with omphalocele, two fetuses with a body stalk anomaly, and four fetuses with gastroschisis, showing additional sonographic and postnatal findings.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>US (weeks)</th>
<th>Additional US anomalies</th>
<th>Prenatal karyotype</th>
<th>Delivery (weeks)</th>
<th>Outcome</th>
<th>Postnatal findings</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>Ectopia cordis</td>
<td>n</td>
<td>12</td>
<td>TOP</td>
<td>Inadequate information (Suction curettage)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fetal hydrops</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Scoliosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td>2 VC</td>
<td>n</td>
<td>21</td>
<td>IUD</td>
<td>2 VC</td>
</tr>
<tr>
<td>8</td>
<td>19</td>
<td>Complex cardiac anomaly</td>
<td>tri 18</td>
<td>20</td>
<td>TOP</td>
<td>Complex cardiac anomaly</td>
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<td></td>
<td>Fetal hydrops</td>
<td></td>
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<td>Abnormal hands and feet</td>
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<td></td>
<td></td>
<td></td>
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<td>12</td>
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<td>38</td>
<td>ID</td>
<td>Facial anomalies</td>
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<tr>
<td></td>
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<td>Fetal hydrops</td>
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<td></td>
<td></td>
<td>Prune belly</td>
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<tr>
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<td>22</td>
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<td>33</td>
<td>NND</td>
<td>Cloacal extrophy</td>
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<tr>
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</tr>
<tr>
<td>18</td>
<td>24</td>
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<td>n</td>
<td>24</td>
<td>TOP</td>
<td>Secundary thoracal deformation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 VC</td>
<td></td>
<td></td>
<td></td>
<td>2 VC</td>
</tr>
<tr>
<td>19</td>
<td>26</td>
<td>Fetal hydrops</td>
<td>n</td>
<td>27</td>
<td>TOP</td>
<td>Inadequate information</td>
</tr>
<tr>
<td>25</td>
<td>28</td>
<td>IUUGR</td>
<td>tri 18</td>
<td>30</td>
<td>TOP</td>
<td>IUUGR, VSD</td>
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<td></td>
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<td></td>
<td></td>
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<td>26</td>
<td>28</td>
<td>AVSD</td>
<td>tri 18</td>
<td>29</td>
<td>TOP</td>
<td>VSD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Scoliosis + abnormal hands and feet</td>
<td></td>
<td></td>
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Table III  Continued

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<thead>
<tr>
<th>Case No.</th>
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<th>Prenatal karyotype</th>
<th>Delivery (weeks)</th>
<th>Outcome</th>
<th>Postnatal findings</th>
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<tr>
<td>31</td>
<td>34</td>
<td>Complex cardiac anomaly</td>
<td>n</td>
<td>38</td>
<td>ID</td>
<td>Complex cardiac anomaly</td>
</tr>
<tr>
<td>20</td>
<td>26</td>
<td>Body stalk anomaly</td>
<td>n</td>
<td>26</td>
<td>TOP</td>
<td>Body stalk anomaly</td>
</tr>
<tr>
<td>27</td>
<td>29</td>
<td>Body stalk anomaly</td>
<td>n</td>
<td>29</td>
<td>TOP</td>
<td>Body stalk anomaly Spina bifida Unilateral renal agenesis Cloacal atresia</td>
</tr>
<tr>
<td>34</td>
<td>19</td>
<td>Ectopia cordis + AVSD</td>
<td>n</td>
<td>35</td>
<td>NND</td>
<td>Severe scoliosis</td>
</tr>
<tr>
<td>36</td>
<td>24</td>
<td>Unilateral hydronephrosis</td>
<td>n</td>
<td>35</td>
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<td>Unilateral hydronephrosis</td>
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<td>40</td>
<td>30</td>
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<td>34</td>
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<td>Kyphoscoliosis IUGR</td>
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<td>44</td>
<td>38</td>
<td>Unilateral hydronephrosis</td>
<td>-</td>
<td>38</td>
<td>Alive</td>
<td>Unilateral hydronephrosis</td>
</tr>
</tbody>
</table>

ID=infant death (i.e. beyond neonatal period); IUGR=intrauterine growth retardation; VSD=ventricular septum defect; tri 18=trisomy 18; TOP=termination of pregnancy; n=normal; NND=neonatal death; AVSD=atrioventricular septum defect; 2 VC=2 vessel cord; IUD=intrauterine death

The survival rate in the gastrochisis subgroup was 72 per cent (8/11), as perinatal death (intrauterine and neonatal mortality) occurred in three cases.

Of the 28 infants born alive, 25 underwent a surgical correction of their abdominal wall defect in the newborn period: 16/18 infants with an omphalocele and 9/10 neonates with a gastrochisis. Of the 20 children who ultimately survived their neonatal surgical correction, in all 12 cases of omphalocele and in four out of eight cases of gastrochisis the abdominal wall defect was the sole congenital anomaly. In two cases of gastrochisis, there was an associated bowel atresia, while in another two infants gastrochisis was associated with unilateral hydronephrosis. Our prenatal diagnosis of the abdominal wall defect was confirmed postnatailly in 30/31 cases of omphalocele and in 10/11 cases of gastrochisis. In one infant with prenatally diagnosed omphalocele, postnatal examination revealed no abdominal wall defect but multiple other congenital anomalies. One case of prenatally diagnosed gastrochisis turned out to be a ruptured omphalocele.
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Discussion

Abdominal wall defects can nowadays easily be detected by ultrasonography, as demonstrated by the large number \( \frac{33}{44} = 75 \text{ per cent} \) of correct referral diagnoses in this study.

The ratio of omphalocele to gastroschisis of 3:1 can be considered a reflection of the differences in incidence between both conditions, as reported by Baird and Macdonald (1981)\textsuperscript{44} and Lindham (1981)\textsuperscript{124}. Omphalocele has a reported incidence of approximately 1 in 5000, while the incidence of gastroschisis varies between 1 to 10,000 and 1 to 15,000 live births. In a more recent study, however, higher and equal incidences of omphalocele and gastroschisis were published\textsuperscript{150}.

Similar to Redford et al. (1985)\textsuperscript{188}, in nearly all instances an accurate prenatal differential diagnosis between omphalocele (30/31) and gastroschisis (10/11) could be made, as omphalocele is characterized by its central location at the base of the umbilical cord insertion site and the presence of a covering membrane consisting of peritoneum and amnion, whereas gastroschisis is usually located at the right paraumbilical area, devoid of a surrounding membrane and separated from a normal umbilical cord insertion. The distinction between these two entities is of great importance since they differ markedly in their typical pathological findings, frequency of associated malformations, chromosomal anomalies, and prognosis.

In our study the earliest correct diagnosis of an omphalocele was made at 12 weeks' gestation. This is supported by Cyr et al. (1986), who reported that a reliable diagnosis of an abdominal wall defect may not be possible before 12 weeks' gestation because of the "physiological" umbilical hernia between 6 to 12 weeks, caused by rapid elongation of the midgut which normally herniates into the base of the body stalk (umbilical cord) as a part of normal gut development\textsuperscript{44}.

The difference in median gestational age at time of referral (i.e., time of diagnosis at our level III centre) of 24 versus 27 weeks of gestation between an omphalocele and a gastroschisis may be determined by the easier detection of the covering membrane of an omphalocele with therefore easier recognition of this anomaly during scanning.

In 32 per cent (10/31) of our omphalocoeles associated structural anomalies were detected on ultrasonographic examination, the majority representing cardiac and skeletal anomalies and fetal hydrops. This is in agreement with De Veciana et al. (1994)\textsuperscript{48} but at variance with some other authors who reported percentages of up to 70-80 per cent\textsuperscript{71,221}. In our gastroschisis group, approximately the same rate (36 per cent) of non-intestinal
associated malformations was found on ultrasound examination, consisting of renal anomalies \( (n=2) \), a case of congenital heart disease \( (n=1) \), and a skeletal malformation \( (n=1) \), which is a slightly higher rate than reported previously\(^{38,204}\). However, the most frequently reported associated anomaly determining prognosis is secondary intestinal atresia\(^{23,52,216}\), which was substantiated in two of our liveborn neonates with gastoschisis.

Polyhydramnios has been noted in approximately one-third of fetuses with omphalocele and only in a minority of cases of gastoschisis\(^{104,221}\). The etiology of polyhydramnios in the presence of an abdominal wall defect is not always clear. It has been considered a marker for gastrointestinal obstruction\(^{153}\) and could be based on malrotation of the gut, which is always present in gastoschisis, or on the above-mentioned secondary intestinal atresia. We observed polyhydramnios in only two cases of omphalocele. Gastoschisis was always associated with a normal amount of amniotic fluid.

IUGR was only diagnosed once in each group, while birth weight was below the tenth centile\(^{116}\) in 11 cases (26 per cent), i.e., in 7/31 (23 per cent) cases of omphalocele and in 4/11 (36 per cent) cases of gastoschisis. The discrepancy in prenatal and postnatal diagnosis of IUGR can be explained by (i) the time elapsed between the initial scan at our level III centre and delivery and (ii) the limited value of the upper abdominal circumference measurement as a growth parameter, due to a reduced abdominal size associated with the abdominal wall defect and the amount of eviscerated abdominal content.

In the presence of an omphalocele, the rate of chromosomal abnormalities was 20 per cent \( (5/25) \). This is comparable to the rate of 22 per cent reported by De Veciana et al.\(^{1994}\)\(^{48}\), whilst others have reported up to 54 per cent\(^{71}\). In our study, trisomy 18 constituted the majority of chromosomal anomalies. In two of the abnormal karyotypes (trisomy 18, 45X) an omphalocele was the only ultrasonically detected fetal anomaly, whereas in the three other cases in which trisomy 18 was established, multiple congenital anomalies were present. This is in agreement with other authors who have reported an increased risk for an abnormal fetal karyotype in cases of omphalocele associated with other malformations and in the presence of an intracorporeal liver and/or small herniation size\(^{48,70,104,167}\). Because of the retrospective character of our study, unfortunately insufficient data were available on these two items. Information on the content of the omphalocele sac could only be gathered in 10/31 cases. In all ten cases, the sac contained bowel and liver; two cases of trisomy 18 were diagnosed while the other eight karyotypes were normal.
In accordance with the literature\textsuperscript{55,221}, no abnormal karyotypes were found in the presence of gastrochisis.

Although some authors advocate elective Caesarean section to reduce the risk of contamination and birth injury to the herniated visceral organs\textsuperscript{52,121}, the optimal mode of delivery in cases of a fetal abdominal wall defect has always been controversial\textsuperscript{55,114}. Unfortunately, no information is available from prospective randomized studies. Recent large retrospective series, however, have demonstrated no beneficial effect on fetal outcome of a Caesarean versus a vaginal delivery\textsuperscript{123,147}. In our centre we share this opinion; consequently, the majority of infants were delivered via the vaginal route. More than half of our eight Caesarian sections were performed for non-obstetrical reasons, i.e., to protect the abdominal wall defect because of fear of rupture of the membrane in omphalocele or mesenterial vascular injury in gastrochisis. This policy was abandoned in 1984. Caesarean section should therefore be reserved for obstetrical indications.

Fetal outcome in omphalocoeles is predominantly determined by the additional malformations and chromosomal anomalies\textsuperscript{35,104,114}. In isolated omphalocele the survival rate after postnatal surgical correction can be as high as almost 100 per cent\textsuperscript{55,71}. In our study there were no surviving infants out of the 10/31 omphalocoeles with multiple congenital anomalies, while of the 16 neonates who underwent surgical correction ultimately 12 infants survived. In all of these 12 infants the omphalocele was the only structural anomaly; all 12 karyotypes were normal. In giant omphalocoeles surgical correction is only performed after weeks to months following covering of the abdominal wall defect by ingrowing skin.

With respect to gastrochisis, the prognosis is generally excellent and the survival rate is mainly determined by the prematurity, sepsis, and sequelae related to correction of atresias such as intestinal adaptation problems\textsuperscript{35,114,216} which is currently less than 10 per cent\textsuperscript{131}. The presence of small bowel thickening and dilatation is reported to have a high correlation with intestinal damage and poor clinical outcome\textsuperscript{23}. Bowel dilatation of more than 17 mm on prenatal ultrasound appears to be associated with increased short- and long-term infant morbidity\textsuperscript{183}. Because of the retrospective analysis of our data, information on the size or thickening of the eviscerated intestines could only be gathered in a minority (2/11) of our cases of gastrochisis.
Nine out of ten liveborn infants with gastroschisis underwent surgical correction of their abdominal wall defect and ultimately eight of them survived. Although the prematurity rate was as high as 73 per cent, most of the surviving infants were born towards the end of the preterm period, i.e., between 34 and 37 weeks (n=5), while the other survivors were born beyond 37 weeks' gestation.

5.2 Obstructive bowel disease

Fetal gastrointestinal tract anomalies are often detected by ultrasound because of intra-abdominal echolucent cystic abnormalities associated with polyhydramnios. Complementary to our study (chapter 5.2.1), an anechoic area in the middle of the fetal neck has recently been suggested as a new marker for congenital oesophageal atresia in fetuses with both a small stomach size and polyhydramnios.\(^{108}\)

The limited value of an absent or small fetal stomach bubble as a predictor of oesophageal atresia has been confirmed by Stringer and colleagues (1995). Oesophageal atresia was present in only 15 fetuses with a small (n=53) or absent (n=34) stomach bubble. In 13 of these pregnancies polyhydramnios was present.\(^{213}\)

Non-visualization of the fetal stomach can be a transient, normal finding related to scanning during a period of physiologic emptying.\(^{96}\) However, in accordance with Pretorius et al. (1988)\(^{181}\) and Millener et al. (1993)\(^{145}\), McKenna et al. (1995) once again emphasized that non-visualization of the fetal stomach or a small fetal stomach in the second or third trimester is associated with a guarded prognosis (increased risk of structural anomalies, an abnormal karyotype, intrauterine or postnatal death).\(^{210}\) In these cases non-visualization of the stomach might result from oligohydramnios or an impaired swallowing mechanism.\(^{96}\)

Occasionally, echogenic masses in the fetal stomach can be visualized. These gastric pseudomasses are usually a transient phenomenon and considered a normal variant, caused by conglomerations of swallowed cells and cell fragments.\(^{96}\) They may also result from swallowed intra-amniotic blood following placental abruption\(^{95,223}\) or genetic amniocentesis.\(^{45}\)

Recently, gastro-oesophageal reflux has been demonstrated in-utero with combined pulsed and colour Doppler in a case of congenital pyloric atresia.\(^{194}\)

Apart for the detection of gastrointestinal obstructions, sonographic evaluation of the fetal digestive tract may be of value for the detection of an echogenic small bowel, a
Chapter 5

marker which has gained in popularity in recent publications. In general, fetal small bowel is considered hyperechogenic when it is more echogenic than the liver or as echogenic as bony structures\(^{98,169}\). Although this phenomenon can be a normal variant\(^ {96,236}\) (also see chapter 5.2.1), and even though most data are collected from populations with an increased risk for abnormal fetal outcome, based on advanced maternal age, abnormal maternal serum screening, or additional fetal abnormalities\(^ {13}\), a second-trimester echogenic small bowel should be considered as an increased risk for in-utero cytomegalovirus infection, growth retardation and fetal death, as well as chromosomal abnormalities\(^ {1,26,36,98}\). Abnormal ultrasound findings, like an echogenic bowel, have been reported to increase the risk for Down syndrome in women with a positive maternal serum screen for this syndrome\(^ {170}\). Normal sonographic findings, however, are less predictive of normalcy\(^ {170}\). In case of an hyperechoic fetal bowel also cystic fibrosis should be taken in consideration\(^ {43,132,152,207}\). Cystic fibrosis may otherwise present itself through polyhydramnios, meconium peritonitis, and a meconium ileus, related to impaction of abnormally thickened viscous meconium in the distal ileum with proximal small bowel dilatation\(^ {95,96}\). Others have, however, suggested that fetal echogenic bowel is not associated with an increased prevalence of cystic fibrosis mutations in pregnancies at low risk for this disease\(^ {199,203}\). Also, fetal swallowing of amniotic fluid following intra-amniotic bleeding has been reported as a cause of hyperechoic bowel\(^ {102}\).

Chapter 5.2.1 deals with our series of suspected gastrointestinal tract anomalies. As stated, although a number of congenital anomalies of the large bowel occur, including colon atresia, Hirschsprung's disease, and anorectal malformations, large bowel obstructions are detected by prenatal ultrasound only occasionally\(^ {6}\). This is predominantly determined by the wide variation in prominence and diameter of normal fetal colon and the overlap between physiologically and pathologically distended colon\(^ {96,176}\). Recently, in a series of 89 suspected fetal bowel lesions, Corteville et al.(1996) confirmed the poor sensitivity of prenatal ultrasound to detect large bowel lesions, whereas the sensitivity of ultrasonography was 100 per cent in the detection of small bowel lesions\(^ {43}\).
5.2.1 Prenatal ultrasonic diagnosis of obstructive bowel disease: a retrospective analysis

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Published in Prenatal Diagnosis 1994, 14, 1035-1041

Summary

Fetal obstructive bowel disease was diagnosed in 29 patients at 22-37 weeks (median 32 weeks) of gestation, seven (24 per cent) of whom also displayed other anomalies. Polyhydramnios was present in 20/29 cases (69 per cent). An abnormal karyotype existed in 7/29 cases (24 per cent), of which six were diagnosed prenatally (trisomy 21, n=5; 69,XXX, n=1) and one postnatally (trisomy 21). There was always an association with the ultrasonic "double bubble" sign. Obstructive bowel disease was confirmed postnatally in 20/29 (69 per cent) cases, i.e., oesophageal atresia (n=1), duodenal obstruction (n=12), and small bowel obstruction (n=7). Other anomalies existed in 6/29 (21 per cent) cases, i.e., multicystic kidney (n=1) and multiple congenital anomalies (n=5). The perinatal mortality rate was 35 per cent (7/20).

Introduction

Fetal obstructive bowel disease represents a common group of congenital anomalies, with a reported incidence of 1 in 1500 live-births. Because of the obstructed passage of amniotic fluid through the fetal gastrointestinal tract, it is often associated with polyhydramnios and abnormal sonographic appearances inside the fetal abdomen. Previous reports on fetal obstructive bowel disease have established an association with chromosomal defects and poor fetal outcome. It is therefore essential to define ultrasound markers which will allow early identification of these anomalies.

The present study reports on the findings of 29 consecutive cases of prenatally suspected fetal obstructive bowel disease with emphasis on the accuracy of ultrasound markers, the incidence of chromosomal anomalies, and fetal outcome.

Materials and methods

During the period 1980 - 1992, fetal obstructive bowel disease was diagnosed in 29 patients who were referred to our level III centre at 22-37 weeks (median 32 weeks) of
gestation for further assessment because of suspected structural pathology at the referring hospital. Maternal age varied between 17 and 39 years (median 28 years); maternal parity ranged between 0 and 3 (median 1).

The diagnosis of fetal obstructive bowel disease was suspected on (i) repeated absence or (ii) marked dilatation of stomach filling, (iii) the characteristic "double bubble" sign, or (iv) dilated bowel loops. Polyhydramnios was defined as a largest fluid pocket of 10 cm or more, oligohydramnios as a largest fluid pocket of 1 cm or less. Intrauterine growth retardation (IUGR) was diagnosed when the upper fetal abdominal circumference was situated below the tenth centile of the reference curve\textsuperscript{33}.

All fetal scans were performed using a Diasonics CV 100 (carrier frequency 3.5 and 5.0 MHz) or a Toshiba SSA 270 (carrier frequency 3.75 MHz). Fetal karyotyping was performed in 16 cases by means of amniocentesis (n=14), transabdominal chorionic villus sampling (TA-CVS)(n=1), or culturing fetal ascites (n=1). In the remaining 13 cases, no fetal karyotyping was performed because of advanced gestational age (≥ 36 weeks) at the time of referral (n=5), premature labour (n=5), or parental refusal (n=3). Postnatal karyotyping because of multiple structural anomalies was carried out in five infants. Details on pregnancy outcome were obtained from clinical records or from autopsy at the referring hospital or our own centre.

Results

Referral indications from the referring hospitals to our centre were dilated bowel loops or intra-abdominal cystic structures (n=12), polyhydramnios (n=5), renal anomalies (n=3), dilated fetal stomach (n=2), absent fetal stomach filling (n=2), severe IUGR (n=2), multiple congenital anomalies (n=2), and suspected intracranial pathology (n=1).

In our centre the diagnosis of fetal obstructive bowel disease was based on repeated absence (n=4) or marked dilatation (n=4) of the fetal stomach, the presence of the typical "double bubble" sign (n=10), and dilated bowel loops (n=11). Data on prenatal and postnatal findings as well as fetal outcome are presented in Tables I-IV.

In 22 cases obstructive bowel disease was the only anomaly, twice accompanied by IUGR (Nos. 10 and 29). In the remaining seven cases associated anomalies were seen, i.e., cardiac defects (Nos. 12 and 18), neural tube defects (Nos. 15, 16 and 20), skeletal anomalies (No. 9), and ascites (No. 21). Polyhydramnios was present in 20 cases,
Table I  Prenatal data and fetal outcome in four fetuses with ultrasonically absent stomach filling

<table>
<thead>
<tr>
<th>No</th>
<th>Ultrasound examination (weeks)</th>
<th>AF</th>
<th>Prenatal karyotype</th>
<th>Delivery (weeks)</th>
<th>Outcome</th>
<th>Postnatal karyotype</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35</td>
<td>PH</td>
<td>-</td>
<td>36</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>PH</td>
<td>-</td>
<td>31</td>
<td>7 months</td>
<td>n</td>
<td>mis MCA</td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>PH</td>
<td>-</td>
<td>36</td>
<td>IUD</td>
<td>-</td>
<td>mis MCA</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>PH</td>
<td>-</td>
<td>36</td>
<td>13 days</td>
<td>-</td>
<td>mis MCA</td>
</tr>
</tbody>
</table>

AF = amniotic fluid; PH = polyhydramnios; n = normal; IUD = intrauterine death; TP = true positive; mis = misclassification; MCA = multiple congenital anomalies

Table II  Prenatal data and fetal outcome in four fetuses with ultrasonically dilated fetal stomach

<table>
<thead>
<tr>
<th>No</th>
<th>Ultrasound examination (weeks)</th>
<th>AF</th>
<th>Prenatal karyotype</th>
<th>Delivery (weeks)</th>
<th>Outcome</th>
<th>Postnatal karyotype</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>37</td>
<td>n</td>
<td>-</td>
<td>39</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>6</td>
<td>36</td>
<td>n</td>
<td>-</td>
<td>40</td>
<td>Alive</td>
<td>-</td>
<td>FP</td>
</tr>
<tr>
<td>7</td>
<td>31</td>
<td>PH</td>
<td>n</td>
<td>37</td>
<td>IUD</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>PH</td>
<td>n</td>
<td>34</td>
<td>IUD</td>
<td>-</td>
<td>FP</td>
</tr>
</tbody>
</table>

AF = amniotic fluid; n = normal; PH = polyhydramnios; IUD = intrauterine death; TP = true positive; FP = false positive

oligohydramnios in three cases, and in the remaining six cases the amniotic fluid volume was normal.

An abnormal karyotype existed in seven out of 29 (24 per cent) cases, of which six were diagnosed prenatally (trisomy 21, n=5; 69,XXX, n=1), and one postnatally (trisomy 21). All seven abnormal karyotypes were associated with the "double bubble" sign and polyhydramnios.

In 27 cases, an expectant obstetric management was followed. One pregnancy was terminated because of the abnormal ultrasonic findings early in pregnancy (No. 16) and another because of an abnormal karyotype revealed by amniocentesis (No. 9; triploidy).
Table III  Prenatal data and fetal outcome in ten fetuses with ultrasonically 'double bubble' sign

<table>
<thead>
<tr>
<th>No</th>
<th>Ultrasound examination (weeks)</th>
<th>AF</th>
<th>Prenatal karyotype</th>
<th>Delivery (weeks)</th>
<th>Outcome</th>
<th>Postnatal karyotype</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>32</td>
<td>PH</td>
<td>69,XXX</td>
<td>35</td>
<td>TOP</td>
<td>-</td>
<td>TP MCA</td>
</tr>
<tr>
<td>10</td>
<td>25</td>
<td>n</td>
<td>tri 21</td>
<td>33</td>
<td>IUD</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>11</td>
<td>36</td>
<td>PH</td>
<td>-</td>
<td>37</td>
<td>Alive</td>
<td>tri 21</td>
<td>TP</td>
</tr>
<tr>
<td>12</td>
<td>30</td>
<td>PH</td>
<td>tri 21</td>
<td>34</td>
<td>NND</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>13</td>
<td>29</td>
<td>PH</td>
<td>tri 21</td>
<td>31</td>
<td>NND</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>14</td>
<td>34</td>
<td>PH</td>
<td>tri 21</td>
<td>36</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>15</td>
<td>36</td>
<td>PH</td>
<td>n</td>
<td>37</td>
<td>NND</td>
<td>-</td>
<td>TP MCA</td>
</tr>
<tr>
<td>16</td>
<td>22</td>
<td>oligo</td>
<td>n</td>
<td>23</td>
<td>TOP</td>
<td>-</td>
<td>TP MCA</td>
</tr>
<tr>
<td>17</td>
<td>32</td>
<td>PH</td>
<td>-</td>
<td>34</td>
<td>Alive</td>
<td>n</td>
<td>TP</td>
</tr>
<tr>
<td>18</td>
<td>31</td>
<td>PH</td>
<td>tri 21</td>
<td>38</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
</tbody>
</table>

AF=amniotic fluid; PH=polyhydramnios; n=normal; oligo=oligohydramnios; tri 21=trisomy 21; TOP=termination of pregnancy; IUD=intrauterine death; TP=true positive; MCA=multiple congenital anomalies

Delivery took place between 23 and 40 weeks of gestation, with preterm delivery (< 37 weeks) in 19 cases (65 per cent). Caesarean section was performed in four cases: in two cases because of a grossly enlarged fetal abdominal circumference with possible dystocia during vaginal delivery (Nos. 19 and 27); in one because of fetal distress (No.17); and in another because of cervical dystocia during a trial of scar (No.18).

Obstructive bowel disease was confirmed postnatally in 20 out of 29 cases (69 per cent), consisting of one case of oesophageal atresia, 12 cases of duodenal obstruction (duodenal atresia, n=9; annular pancreas, n=2; and paraduodenal hernia, n=1), and seven cases of small bowel obstruction (jejunal atresia, n=3; ileal atresia, n=2; meconium ileus and meconium pseudocysts because of cystic fibrosis, n=1; small bowel duplication, n=1). Table V shows the association between additional sonographic and postnatal findings, abnormal karyotype, and fetal outcome in this group of 20 correctly diagnosed gastrointestinal anomalies. In six cases, other anomalies than obstructive bowel disease were diagnosed (misclassifications): multicystic kidney (n=1) and multiple congenital anomalies (n=5), one of which also represented a multicystic kidney. Three infants revealed no structural pathology (false positives).
Table IV  
Prenatal data and fetal outcome in 11 fetuses with ultrasonically dilated bowel loops

<table>
<thead>
<tr>
<th>No</th>
<th>Ultrasound examination (weeks)</th>
<th>AF</th>
<th>Prenatal karyotype</th>
<th>Delivery (weeks)</th>
<th>Outcome</th>
<th>Postnatal karyotype</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>34</td>
<td>PH</td>
<td>-</td>
<td>35</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>20</td>
<td>35</td>
<td>n</td>
<td>-</td>
<td>35</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>21</td>
<td>31</td>
<td>PH</td>
<td>-</td>
<td>34</td>
<td>Alive</td>
<td>-</td>
<td>TP CF</td>
</tr>
<tr>
<td>22</td>
<td>35</td>
<td>PH</td>
<td>-</td>
<td>37</td>
<td>Alive</td>
<td>-</td>
<td>FP</td>
</tr>
<tr>
<td>23</td>
<td>32</td>
<td>PH</td>
<td>n</td>
<td>38</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>24</td>
<td>33</td>
<td>PH</td>
<td>n</td>
<td>38</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>25</td>
<td>31</td>
<td>PH</td>
<td>n</td>
<td>35</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>26</td>
<td>22</td>
<td>oligo</td>
<td>-</td>
<td>25</td>
<td>IUD</td>
<td>n</td>
<td>mis MCA (R)</td>
</tr>
<tr>
<td>27</td>
<td>35</td>
<td>n</td>
<td>n</td>
<td>39</td>
<td>Alive</td>
<td>-</td>
<td>mis R</td>
</tr>
<tr>
<td>28</td>
<td>22</td>
<td>n</td>
<td>n</td>
<td>36</td>
<td>Alive</td>
<td>-</td>
<td>TP</td>
</tr>
<tr>
<td>29</td>
<td>30</td>
<td>oligo</td>
<td>-</td>
<td>36</td>
<td>Alive</td>
<td>n</td>
<td>mis MCA</td>
</tr>
</tbody>
</table>

AF = amniotic fluid; PH = polyhydramnios; n = normal; oligo = oligohydramnios; IUD = intrauterine death; TP = true positive; FP = false positive; CF = cystic fibrosis; mis = misclassification; MCA = multiple congenital anomalies; R = multicystic kidney

As two terminations of pregnancy were requested and carried out and as perinatal death (intrauterine and neonatal mortality) occurred in eight cases and two infants died after the neonatal period in a further two cases, the overall survival rate is 59 per cent (17/29). However, when only the correctly diagnosed cases of obstructive bowel disease are included, the survival rate is 65 per cent (13/20).

Discussion

Gastrointestinal tract anomalies represent 15-20 per cent of all congenital anomalies. Major parts of the digestive tract are nowadays easily accessible to ultrasound examination. The fetal oesophagus is normally not visualized at ultrasound examination due to its position behind the fetal trachea and heart and the absence of oesophageal content. Only in case of oesophageal atresia without tracheo-oesophageal fistula it is sometimes possible to detect a blind ending proximal oesophagus.
### Chapter 5

**Table V Additional sonographic and postnatal findings, karyotype, and outcome of the 20 correctly diagnosed gastrointestinal anomalies**

<table>
<thead>
<tr>
<th>Case No</th>
<th>Additional US anomalies</th>
<th>Karyotype</th>
<th>Outcome</th>
<th>Additional postnatal findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent stomach</td>
<td>-</td>
<td>-</td>
<td>Alive</td>
<td>-</td>
</tr>
<tr>
<td>Dilated stomach</td>
<td>-</td>
<td>-</td>
<td>Alive</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>n</td>
<td>IUD (abruption)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Double bubble</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>9</td>
<td>Hydrocephaly, abn. arms and legs</td>
<td>69,-XXX</td>
<td>TOP</td>
<td>Hydrocephaly, abn. arms and legs, hypoplastic adrenals</td>
</tr>
<tr>
<td>10</td>
<td>-</td>
<td>tri 21</td>
<td>IUD (IUGR)</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>-</td>
<td>tri 21</td>
<td>Alive</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>AVSD</td>
<td>tri 21</td>
<td>NND</td>
<td>AVSD</td>
</tr>
<tr>
<td>13</td>
<td>-</td>
<td>tri 21</td>
<td>NND</td>
<td>Cardiac anomaly</td>
</tr>
<tr>
<td>14</td>
<td>-</td>
<td>tri 21</td>
<td>Alive</td>
<td>-</td>
</tr>
<tr>
<td>15</td>
<td>Holoprosencephaly</td>
<td>n</td>
<td>NND</td>
<td>Holoprosencephaly</td>
</tr>
<tr>
<td>16</td>
<td>Hydrocephaly, ascites</td>
<td>n</td>
<td>TOP</td>
<td>Hydrocephaly, ascites, cardiac anomaly, dysplastic kidney</td>
</tr>
<tr>
<td>17</td>
<td>-</td>
<td>n</td>
<td>Alive</td>
<td>-</td>
</tr>
<tr>
<td>18</td>
<td>Fallot</td>
<td>tri 21</td>
<td>Alive</td>
<td>Fallot</td>
</tr>
<tr>
<td>Dilated bowel</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>19</td>
<td>-</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>20</td>
<td>-</td>
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<td>Alive</td>
<td>-</td>
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<tr>
<td>21</td>
<td>-</td>
<td>-</td>
<td>Alive</td>
<td>CF</td>
</tr>
<tr>
<td>23</td>
<td>-</td>
<td>n</td>
<td>Alive</td>
<td>-</td>
</tr>
<tr>
<td>24</td>
<td>-</td>
<td>n</td>
<td>Alive</td>
<td>-</td>
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<tr>
<td>25</td>
<td>-</td>
<td>n</td>
<td>Alive</td>
<td>-</td>
</tr>
<tr>
<td>28</td>
<td>-</td>
<td>n</td>
<td>Alive</td>
<td>-</td>
</tr>
</tbody>
</table>

n=normal; IUD=intrauterine death; IUGR=intrauterine growth retardation; TOP=termination of pregnancy; tri 21=trisomy 21; NND=neonatal death; AVSD=atrioventricular septum defect; Fallot=tetralogy of Fallot; CF=cystic fibrosis
Repetitive absence of fetal stomach filling, particularly in the presence of polyhydramnios, could suggest oesophageal atresia\textsuperscript{37,101}. However, the value of this ultrasonic marker appears to be limited, since gastric fluid secretion as such may cause distension of the stomach\textsuperscript{37}. Moreover, in oesophageal atresia stomach filling may be expected because of the high association with tracheo-oesophageal fistula, through which amniotic fluid can pass into the fetal stomach\textsuperscript{95}. Also in cases of intrauterine growth retardation with or without oligohydramnios, absent stomach filling over a longer period is not an uncommon finding. In 60 per cent of the oesophageal atresias other associated malformations have been reported\textsuperscript{90,95,100}. In our study, oesophageal atresia was only present in one out of four cases with repeated absence of stomach filling, and there were no associated anomalies. The remaining three infants displayed multiple anomalies unrelated to the gastrointestinal tract, which confirms a previous report in which a high incidence of non-gastrointestinal structural pathology was established in cases of non-visualization of the fetal stomach\textsuperscript{101}.

Stomach dilatation was observed in another four cases, twice accompanied by polyhydramnios. After delivery, one case of malrotation of the gut and one case of jejunal atresia with secondary distension of the stomach was diagnosed. However, in the remaining two infants no congenital anomalies were established. These two false-positive findings highlight the marked variety in fetal stomach size in physiological circumstances as demonstrated by nomograms for fetal stomach size\textsuperscript{78}.

On a transverse cross-section of the upper abdomen, the typical "double bubble" sign is composed of an overdistended stomach in the left upper-abdominal quadrant connected with an enlarged duodenum on the right\textsuperscript{128}. Particularly in the presence of polyhydramnios, this is suggestive of duodenal obstruction. Associated structural anomalies have been reported in 50 per cent of cases\textsuperscript{85,95,110,228}, whereas trisomy 21 has been diagnosed in 30 per cent of all duodenal atresias\textsuperscript{62,84,95}.

In the present study the "double bubble" sign was associated with polyhydramnios in 80 per cent, structural pathology in 50 per cent, and an abnormal karyotype in 70 per cent of cases. Trisomy 21 constituted 86 per cent of all chromosomal anomalies. All 10 cases of suspected duodenal obstruction were confirmed after delivery, i.e., eight infants with a duodenal atresia and two cases of an annular pancreas. Our present data confirm previous reports\textsuperscript{16,25,50,102,128} that unlike abnormal stomach size, the "double bubble" sign is highly predictive for obstructive bowel disease, i.e., duodenal obstruction, and necessitates a detailed ultrasonographic examination with subsequent fetal karyotyping.

The small bowel is normally seen as a more or less echodense area located
centrally in the fetal abdomen. Peristalsis may be visible as early as 18 weeks of
gestation, whereas after 28 weeks separate bowel loops can be visualized\(^{95}\). An internal
diameter of more than 7 mm, especially in combination with strong peristaltic
movements, is suggestive of obstruction\(^{106}\).

Sometimes an unusual fetal small bowel pattern can be identified between 16 and
22 weeks of gestation, consisting of a well defined homogeneously hyperechoic
"pseudomass" which later in pregnancy is replaced by normal-moving fluid-filled small
bowl. Manco et al.(1986)\(^{136}\) and Fakhry et al.(1986)\(^{58}\) have postulated that this
phenomenon is a common normal variant and may be related to the increasing volume of
amniotic fluid being swallowed during fetal development, thus exceeding the resorptive
ability of fetal stomach and duodenum with subsequent filling of the distal small bowel.
Others have described an association with cystic fibrosis\(^{37,141,151}\) and, more recently, with
chromosomal abnormalities\(^{24,167,199}\).

The fetal colon appears from as early as 22 weeks of gestation as a large
hyperechoic tubular structure in the periphery of the fetal abdomen\(^{95,106,231}\). Peristalsis is
less clearly demonstrated than in the small bowel\(^{231}\). The mean diameter of the normal
colon increases approximately linearly with gestational age until 18 mm or more\(^{79,168}\).
However, like the fetal stomach, variation in size is considerable with a substantial
overlap between physiologically and pathologically distended colon. DeLorimier et
al.(1969)\(^{146}\) and Nixon and Tawes (1971)\(^{105}\) observed associated anomalies in only 7 per
cent of all bowel atresias, which is consistent with the hypothesis that bowel atresia is an
acquired defect due to an in utero vascular accident\(^{46,165}\), whereas oesophageal and
duodenal atresia should result from an early embryonic insult\(^{35,127,217}\).

Dilated bowel loops were established in 11 cases, six of which associated with
polyhydramnios and two with oligohydramnios. Bowel obstruction was confirmed in
seven infants, i.e., duodenal atresia (n=1), jejunal atresia (n=2), ileal atresia (n=2),
cystic fibrosis with meconium ileus and meconium pseudocysts (n=1), and small bowel
duplication (n=1). None of them revealed associated structural anomalies. Small bowel
obstruction can be associated with cystic fibrosis. This could be brought up when
counselling couples. Estroff et al.(1992) reported a relatively high incidence of 36 per
cent (4/11) in their population of correctly diagnosed dilated bowel loops\(^{54}\), while in our
seven correctly diagnosed bowel obstructions cystic fibrosis was only diagnosed once. In
the remaining four cases there were two infants with multiple non-gastrointestinal
anomalies, one with a multicystic kidney, and one with no malformations. None of these
11 infants displayed an abnormal karyotype.
Although we did not intend to exclude colonic obstructions, no fetuses with colonic obstructions were seen in our study. This is supported by Hertzberg and Bowie (1990), who report that colonic obstructions only occasionally have been reported antenatally while most cases do not present until after birth\textsuperscript{25}.

The differential diagnosis of suspected bowel obstruction based on intra-abdominal echoluent cystic abnormalities consists of urinary tract anomalies (multicystic kidneys, hydronephrosis and/or hydroureter), hydrometrocolpos, and other cystic anomalies such as choledochal, mesenterial, omental and ovarian cysts\textsuperscript{25,231}. Sometimes it is possible to simulate a double bubble-like sign by scanning the fetal trunk in a coronal plane causing bissection of a normal fetal stomach\textsuperscript{14}. However, suspicion of a gastrointestinal obstruction should arise when two or more cystic lesions in the presence of normal kidneys are seen at ultrasound examination, especially when they are interconnected, display increased peristalsis, or are associated with polyhydramnios.

Although polyhydramnios is a non-specific and insensitive marker, it was present in 75 per cent of our correctly diagnosed gastrointestinal tract obstructions and it was equally divided between oesophageal and duodenal obstructions (10/13 = 77 per cent) and small bowel obstructions (5/7 = 71 per cent). In obstructive bowel disease, polyhydramnios develops as a result of proximal obstruction and when the amniotic fluid swallowed exceeds the resorptive capacity of the remaining available intestinal surface\textsuperscript{154}, i.e., through regurgitation or a decrease in fluid passage through the fetal gut\textsuperscript{17}. It usually develops during the late second or third trimester of pregnancy. The late appearance of polyhydramnios and dilated bowel is determined by fetal swallowing, which only starts at 16-17 weeks of gestational age\textsuperscript{182} and by the increased formation and turnover rate of amniotic fluid in the second and third trimesters\textsuperscript{110}. Of the 15 correctly diagnosed gastrointestinal obstructions which were associated with polyhydramnios, this was established in the third trimester in all 15 cases. This explains the often late referral to our tertiary centre.

Finally, within the group of correctly diagnosed gastrointestinal anomalies (n=20), all seven abnormal karyotypes and six out of seven perinatal deaths were associated with the "double bubble" sign, which points to the need for a careful search for associated anomalies and subsequent prenatal karyotyping in this particular sonographic abnormality.

Although the numbers are small, a low incidence of associated congenital and chromosomal anomalies resulting in a good fetal outcome was demonstrated in the other three categories of suspected gastrointestinal obstruction.
5.3 Renal tract anomalies

The incidence of congenital malformations of the urinary tract is approximately 2 in 1000 pregnancies. Fetal renal tract anomalies are amongst the most common sonographically detected congenital malformations. Usually they are detected through intra-abdominal structural anomalies and/or a decreased amount of amniotic fluid. Several classifications of fetal urinary tract anomalies have been suggested. From a practical and clinical point of view renal agenesis, renal cystic disease, obstructive uropathy and renal tumours will be discussed.

5.3.1 Renal agenesis

Renal agenesis, both bilateral and unilateral, is considered a ureteral bud malformation and can be isolated or associated with other malformations, or chromosomal disorders. Of most clinical importance is bilateral renal agenesis (BRA), which has a reported incidence of 1 in 4000 births; two-thirds of infants are male.

Prenatally, BRA is characterized by failure to identify fetal kidneys, persistent and repetitive absence of fetal bladder filling, and second or third trimester oligohydramnios (as stated in paragraph 4.3.2, the contribution of fetal urine to the amniotic fluid volume is considered to be minor in the first trimester). Non-visualization of the fetal bladder is more significant than apparent visualization of the kidneys, because in BRA bowel may mimic kidneys. Also, the adrenal glands may assume an oval or reniform shape. False-negative diagnoses of BRA have been reported and were attributed to the sonographic misidentification of apparently hypertrophied fetal adrenal glands as fetal kidneys. Adrenal hypertrophy, however, does not seem to be a common finding in BRA.

Hoffman et al. (1992) reported on the flattened "lying down" adrenal gland as an additional sonographic indicator of renal agenesis. Sonographic criteria that may be helpful in distinguishing between these organs are identification of the renal capsule, and imaging of the hypechoic renal pyelum or medullary pyramids. Finally, other causes of oligohydramnios such as premature rupture of the membranes, and fetal growth retardation must be excluded. This especially since a high association between BRA and growth retardation has been reported. Reuss and co-workers (1987) have demonstrated that Doppler evaluation of the umbilical and internal carotid artery may
provide useful information as to the cause of the growth retardation and oligohydramnios\textsuperscript{190}. Procedures that can be of value in the evaluation of fetal renal function include maternal intravenous administration of frusemide\textsuperscript{225} and creation of an artificial amniotic fluid compartment by instillation of 5\% glucose/0.9\% saline solution\textsuperscript{89}. Also, intraperitoneal instillation of saline has been suggested as an alternative to improve visualization of fetal intra-abdominal organs in the presence of severe oligohydramnios\textsuperscript{150}. Haeusler et al.\textsuperscript{(1993)} reported a significant improvement of visualization of intra-abdominal organs in selected cases of suspected BRA after the combination of amnioinfusion and intraperitoneal instillation of saline solution\textsuperscript{89}. In the same year, we demonstrated that colour Doppler flow mapping and pulsed Doppler evaluation may be helpful in confirming the diagnosis of renal agenesis\textsuperscript{226}. This was confirmed in a study by Sepulveda et al.\textsuperscript{(1995)}\textsuperscript{201}. One has to be aware that false-negative results may be obtained with colour coded Doppler in case of an ectopic kidney.

Postnatally, lethal pulmonary hypoplasia, a typical facies with low set ears, and aberrant hand and foot positioning are prominent features of BRA.

Fetuses with unilateral renal agenesis are expected to have a normal amount of amniotic fluid. Obstetric management and fetal outcome will be mainly determined by the condition of the contralateral system and the presence and severity of associated anomalies\textsuperscript{218}. Some cases of unilateral renal agenesis may result from in-utero regression of multicystic dysplastic kidneys\textsuperscript{143}. The contralateral kidney may show compensatory hypertrophy\textsuperscript{74,100}.

5.3.2 Renal cystic disease

Renal cystic disease is a morphological description for an etiological heterogeneous group of disorders ranging from solitary cysts to several forms of polycystic and multicystic kidneys.

5.3.2.1 Polycystic kidney disease

As stated by Reuss (1989) the term polycystic kidneys should not be confused with multicystic kidneys nor should it be used as a general term to describe kidneys with multiple cysts. The so-called infantile form is transmitted in an autosomal recessive trait and the so-called adult form as an autosomal dominant trait\textsuperscript{192}.
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Autosomal recessive (infantile) polycystic kidney disease (ARPKD)

ARPKD has a reported incidence of 1:40,000 infants\textsuperscript{230}. Recently, a single ARPKD gene located on chromosome 6 was suggested\textsuperscript{165}. A primary defect of the collecting tubules with cystic dilatation appears to be responsible for ARPKD\textsuperscript{172}. The time of clinical presentation varies from intrauterine life to the juvenile age. The percentage of affected tubules decreases with age of onset\textsuperscript{112}.

Prenatal ultrasound typically demonstrates bilateral enlarged fetal kidneys that maintain their reniform shape but exhibit increased echogenicity caused by the multiple interfaces produced by the numerous tiny cysts\textsuperscript{129,195}. Often absent fetal bladder filling and oligohydramnios are present\textsuperscript{119}. Fetal renal biopsy can be of assistance in establishing the diagnosis\textsuperscript{182}. With MRI similar anatomical features as with ultrasound can be obtained\textsuperscript{194}. The prognosis depends on the clinical variety of ARPKD and varies from lethal pulmonary hypoplasia to diminished renal function.

Autosomal dominant (adult) polycystic kidney disease (ADPKD)

ADPKD is characterized by replacement of renal parenchyma with multiple cysts from variable size due to dilatation of tubular segments of the nephrons. ADPKD has a reported incidence of 1:1000\textsuperscript{208}; the etiology is unknown. The genetic defect is located on the short arm of chromosome 16\textsuperscript{189}; expression, however, is variable in severity and age of onset\textsuperscript{144}. The disease usually only becomes clinically manifest during adult life, although prenatal cases have been reported\textsuperscript{135,180}.

Prenatal ultrasound may show enlarged kidneys with increased parenchymal echogenicity or multiple cysts of variable size. The amount of amniotic fluid may be normal or decreased. Overt ADPKD has been associated with cystic lesions in other organs\textsuperscript{230}.

5.3.2.2 Multicystic dysplastic kidney disease (MDKD)

MDKD is a sporadic disorder which can be bilateral, unilateral or segmental and which is characterized by cystic lesions that correspond to dilated primitive collecting tubules. Multicystic kidneys are associated with a nonpatent drainage system. Historically, a "classic" and a "hydronephrotic" form of MDKD have been described\textsuperscript{22,173}. In the
classic form, the ureter is atretic and renal pelvis absent. The hydronephrotic form is less common and presumably the result of urinary obstruction early in embryogenesis\textsuperscript{59}. Eventually, both forms result in cystic degeneration of the renal parenchyma. More recently it was suggested that an intrinsic abnormality in the branching morphogenesis of the ureteric duct might be responsible for the development of MDKD\textsuperscript{139}. The true incidence of MDKD is unknown, as most cases are unilateral and often remain asymptomatic\textsuperscript{51,76}.

The prenatal sonographic findings correlate well with the pathologic appearance. The size of the kidney as well as the cysts may vary from small to extremely large and usually no renal pelvis can be visualized\textsuperscript{133,214}. Cysts may change in number and size either in utero or postnatally\textsuperscript{92,193}. In unilateral MDKD, the contralateral unaffected kidney may show compensatory renal growth\textsuperscript{74,137}. Oligohydramnios will be present in case of lethal bilateral MDKD\textsuperscript{115}. Raised fetal renal artery pulsatility indices have been described in multicystic kidney disease\textsuperscript{111}. In our own study similar results were found\textsuperscript{226} (chapter 5.4.1.2). Absence of renal artery waveforms, however, correlates with renal nonfunction\textsuperscript{72}. There is an increased risk for contralateral or non-renal associated anomalies\textsuperscript{3,115}.

In general, a nonsurgical conservative approach is practiced postnatally\textsuperscript{3,212}. The main indication for surgery in the asymptomatic patient may be the potential risk of complications, e.g. hypertension, later in life\textsuperscript{5}.

5.3.3 Obstructive uropathy

Fetal obstructive uropathies involve a heterogeneous group of developmental abnormalities that result in partial or complete obstruction of urinary outflow at any level of the urinary tract. Sonographic dilatation of any part of the fetal urinary tract is therefore highly suggestive for an obstructive uropathy, although this will not always be true\textsuperscript{20,83}. Conversely, absence of dilatation does not exclude an obstructive uropathy in all cases\textsuperscript{72,134}.

From a clinical point of view, obstructive uropathies can be divided in high-level (ureter) and low-level (urethra) obstructions. Sonographic detection of high-level obstructions consists of the demonstration of a dilated fetal renal pelvis (hydronephrosis) and/or ureter. Low-level obstructions can be recognized through visualization of a dilated fetal bladder and proximal urinary tract. Occassionally, a dilated urethra can be demonstrated.
5.3.3.1 High-level obstructive uropathy

Hydronephrosis is characterized by a persistent excess fluid collection within the renal pelvis. Congenital hydronephrosis is most commonly caused by an uretero-pelvic junction obstruction (UPJ)\(^{109}\). In most instances a functional UPJ is suspected, i.e., the junction is patent to passage of a probe\(^3\). Anatomical causes for UPJ are only found in a minority of patients\(^9\). Other causes for congenital hydronephrosis include uretero-vesical junction obstruction (UVJ), and vesico-ureteral reflux.

Benacerraf and co-workers (1990) have reported on a possible association between fetal renal pyelectasis and Down syndrome\(^19\). They found that the incidence of fetal Down syndrome was 3.3 per cent when fetal pyelectasis was present\(^19\). Nicolaides et al. (1992) reported that isolated bilateral hydronephrosis was associated with a 3 to 6 per cent incidence of chromosomal abnormalities\(^157\). On the contrary, Corteville et al. (1992) found that isolated fetal pyelectasis as an initial abnormality had a predictive value of 1 in 340 for Down syndrome\(^42\). They concluded that, although renal pyelectasis is more common in Down syndrome, genetic amniocentesis should be reserved for those cases presenting with other risk factors such as advanced maternal age, low maternal serum alphafetoprotein, or other sonographic abnormalities\(^42\).

Mild transient hydronephrosis without evidence of renal tract anomalies after birth has been described\(^15,148\), possibly as a reflection of the normal physiological changes in the size of the pyelum as result of a higher HFUPR prenatally. The same has been reported in neonates\(^101\).

Several authors have reported on criteria regarding the severity and prognosis of hydronephrosis\(^7,41,83,174,200\). Serial sonography is recommended to detect progressive obstruction with deterioration of renal function and development of oligohydramnios\(^83,174\). The degree and presence of hydronephrosis may depend on fetal bladder filling\(^177\). Oligohydramnios can both be the result of inadequate passage of urine or severely impaired renal function. The degree of dilatation does not always correlate with the severity of the obstruction. This can be explained by secondary pressure-related renal dysplasia with decreased urinary production, or by rupture of any part of the urinary tract resulting in decompression of the renal pelvis. Also, an uretero-pelvic atresia may be present.

The prognosis of obstructive uropathy depends on the localisation, severity and duration of obstruction\(^161\). Dilatation above the level of obstruction with an increase of pressure inside the urinary system possibly results in structural and functional changes.
within the kidney\cite{91}. A reliable sonographic diagnosis of secondary renal dysplasia is not always possible\cite{134}. Postnatal management is predominantly directed towards preservation of renal function and the prevention of infection.

5.3.3.2 Low-level obstructive uropathy

Infravesical obstructions produce a broad spectrum of sonographic features antenatally. The most prominent sign is a persistent distended fetal bladder (megacystis); occasionally a dilated proximal urethra (keyhole sign) and a secondary compensatory hypertrophied bladder wall may be identified. As a result of vesico-ureteral reflux, also secondary bilateral dilatation of the fetal ureter and renal pelvis can be observed\cite{93,134}. Causes for urethral level obstructions include posterior urethral valves (PUV), urethral stenosis or agenesis, and a persistent cloaca. A functional infravesical obstruction can be encountered in case of a lumbosacral meningomyelocele. PUV occur only in males and are the single most common cause of fetal bladder obstruction\cite{113}. Also in urethral stenosis, males are more commonly affected. Secondary to the infravesical obstruction, bladder decompression through development of a paranephric pseudocyst may occur\cite{80,133}, with secondary urinary ascites formation through leakage of this urinoma, or through transmural leakage across the bladder wall\cite{84}. In the same publication spontaneous remission of ascites and fetal urinary tract obstruction, caused by posterior urethral valves, was reported\cite{84}.

Distension of the fetal bladder and proximal urinary tract is associated with the Prune Belly syndrome\cite{14}, which is characterized by abdominal wall muscle deficiency, dilatation of the urinary tract and cryptorchidism; the vast majority are males.

In females, lower urinary tract dilatation may be related to urethral agenesis, the megacystis-microcolon-intestinal hypoperistalsis (MMIH) syndrome, and a persistent cloaca. The MMIH syndrome is a usually lethal autosomal recessive trait, characterized by a dilated unobstructed lower urinary tract in the absence of oligohydramnios\cite{84,210}. Persistent cloaca is a rare malformation characterized by a common outflow structure of the urogenital and intestinal tract, and believed to result from failure of the urorectal septum to join the cloacal membrane\cite{18}.

Congenital low-level obstructive uropathy is associated with poor perinatal outcome\cite{191}. Affected fetuses are at risk for oligohydramnios-induced pulmonary hypoplasia\cite{134,215} or renal failure. As the association between ultrasound findings and fetal renal function is poor\cite{133}, analysis of fetal urine biochemistry was expected to improve the
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selection of cases amenable to antenatal treatment\textsuperscript{162}. Ideally, fetuses with irreversible renal damage, with other abnormalities, and with abnormal karyotypes should be excluded\textsuperscript{159}. Urinary constituents change with gestational age due to renal maturation. High fetal urinary concentrations of sodium and calcium were found to be the best predictors of renal failure\textsuperscript{158,162}. In 1993, elevated levels of beta 2 microglobulin were added\textsuperscript{125}. New markers for fetal renal damage include increased fetal urinary insulin-like growth factor 1 (IUGF-1) and binding protein 3 (UIGBP-3)\textsuperscript{28}. Single measurements of any of these variables, however, are unlikely to be reliable predictors of irreversible renal damage\textsuperscript{166,209}. Although controversial, prenatal surgery does have a role in selected pregnancies\textsuperscript{162} and selected fetuses may benefit from in-utero decompression, either by open fetal surgery or by percutaneous vesico-amniotic shunt placement\textsuperscript{53}. The results of antenatal shunting, however, have initially been disappointing with an overall survival rate of 30 per cent\textsuperscript{138}. Recent reports suggest higher success rates\textsuperscript{107,108}. Disadvantages of open fetal surgery include the risks of hysterotomy, whereas catheter drainage can be associated with anatomical damage and iatrogenic ventral abdominal wall defects\textsuperscript{56}, and catheter obstruction and migration\textsuperscript{52}. More recently, Evans and co-workers reported that serial fetal bladder drainage and last urine values together with trend analysis of the pattern of change in values should be used for determination of the underlying presence or absence of severe renal damage and for selection of potential candidates for invasive in-utero intervention via vesico-amniotic shunt placement\textsuperscript{108}. Sequential measurements, however, seem to be impractical due to the narrow window of opportunity for useful surgical intervention\textsuperscript{209}. In 1995, Quintero et al. reported on in-utero percutaneous cystoscopy as a new tool to improve the diagnostic, prognostic and therapeutic possibilities in lower obstructive uropathy\textsuperscript{184}. From the same center it has been suggested that fetal vesicoinfusion might be of value to distinguish primary vesico-ureteral reflux from lower obstructive uropathy in fetuses with a sonographic dilated lower urinary tract\textsuperscript{185}.

Most recently, others have once again stressed that greater standardization of patient selection, diagnosis, treatment and outcome measurement is of paramount importance to allow an accurate assessment of the efficacy and proper role of fetal therapy\textsuperscript{65}. This especially since in the past, poor patient selection has led to futile attempts to intervene in hopeless cases, while on the other hand fetuses who would have done well even without intervention may have been put at unnecessary risk by operative procedures\textsuperscript{56}. To our knowledge, no data are available from randomized controlled trials to compare survival and postnatal renal function with and without vesico-amniotic shunt
placement. Noninvasive ways to evaluate remaining renal function include two-dimensional real-time ultrasound and the use of pulsed or colour coded Doppler. Colour coded Doppler imaging allows visualization of the renal perfusion and as such could be considered as a noninvasive method to evaluate renal function. Details on the role of colour Doppler in the presence of renal tract anomalies will be discussed in chapter 5.4.1.2.

5.3.4 Renal tumours

Congenital renal neoplasms occur only rarely. The most common fetal renal tumour is a mesoblastic nephroma which is a hamartoma with a usually benign course. Sonographically, it is a large, solitary, predominantly solid mass arising from and not separable from an adjacent normal kidney. Frequently, an otherwise unexplained polyhydramnios is present. Its sonographic appearance resembles the malignant Wilms' tumour, a nephroblastoma, which however occurs most often between the second and third years of childhood and is rarely seen in the fetus and neonate. Postnatally, usual treatment consists of nephrectomy.

When a suprarenal mass is detected in utero, one should meticulously try to specifically exclude an adrenal neuroblastoma, since early postnatal surgical treatment of this malignant tumor can be curative. Neuroblastomas can have a solid, purely cystic or complex sonographic appearance. The differential diagnosis includes bronchopulmonary sequestration, enteric duplication cyst, and upper-pole, cystic, dysplastic changes in a multicystic, dysplastic kidney.

5.4 Colour coded Doppler ultrasound and (intra)abdominal structural anomalies

Data presented on colour Doppler imaging are part of a report on the clinical significance of colour coded Doppler ultrasound in normal and abnormal fetal development which was prepared for the "Ontwikkelingsgeneeskunde" Committee of the Dutch Sickness Benefit Council (Ziekenfondsraad) during the period 1990-1993 (OG 89-023).
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In chapter 4.4 the additional value of colour coded Doppler imaging regarding normal (intra)abdominal vessel distribution has been discussed. In the following chapter the additional value of colour coded Doppler with respect to structural and functional information in cases of (intra)abdominal structural pathology will be addressed. Emphasis will be put on renal tract anomalies, abdominal wall defects, gastrointestinal obstructions, and intra-abdominal cysts. Details on material and methods have been described in chapter 4.4.

5.4.1.1 Renal tract anomalies

The prenatal diagnosis of renal tract anomalies has up to now predominantly been based on conventional two-dimensional real-time ultrasound. We addressed the question as to whether with colour coded Doppler imaging additional structural information could be obtained, as well as additional information with respect to the remaining renal function.

Colour coded Doppler allows visualization of the renal arteries and as such provides information about downstream impedance at renal level. In the presence of severe oligohydramnios (largest amniotic fluid pool < 1 cm), differentiation between IUGR as a result of uteroplacental insufficiency and bilateral renal agenesis may be difficult. The latter would be characterized by a rudimentary or absent renal artery and therefore absent renal perfusion. Postnatally confirmed renal pathology consisted of bilateral hydronephrosis (n=21), unilateral multicystic kidney (n=4) and bilateral renal agenesis (n=8). Pregnancy duration varied between 16 and 37 weeks (median 29 weeks). The role of colour coded Doppler in the assessment of renal structure and function is presented in detail in the next subchapter.
5.4.1.2 Fetal renal artery flow velocity waveforms in the presence of congenital renal tract anomalies

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Published in Prenatal Diagnosis 1993, 13, 545-549

Summary

Colour Doppler flow mapping of the renal arteries and subsequent pulsed Doppler measurement of impedance to flow in these vessels were attempted in 33 fetuses with postnatally confirmed renal pathology. The majority presented with unilateral or bilateral hydronephrosis (n=21) and bilateral renal agenesis (n=8). Renal artery blood flow could be visualized in all, except for the eight cases of bilateral renal agenesis. Bilateral flow velocity recordings were collected in six out of 12 cases of bilateral hydronephrosis and in five out of nine cases of unilateral hydronephrosis. The pulsatility index (PI), as a measure of downstream impedance, was in the normal range in 16 out of 18 kidneys (88 per cent) in bilateral hydronephrosis and in 12 out of 14 kidneys (85 per cent) in unilateral hydronephrosis. The PI was significantly higher in severe hydronephrosis compared with mild hydronephrosis. In four cases of unilateral multicystic kidney, the PI was always higher on the affected side. Colour Doppler flow mapping and pulsed Doppler evaluation may be helpful in our understanding of renal vascularization in renal pathology and in confirming the diagnosis of renal agenesis.

Introduction

With the advent of high-resolution real-time ultrasound scanners, the ability to image various organ systems in utero has greatly improved. This is particularly so for the urinary tract. The overall incidence of urinary tract malformations, excluding hypospadias, is about 3 per 1000 births\textsuperscript{36}. Recently, in a prospective population study by Livera et al.(1989), the incidence of structural renal tract abnormalities detected prenatally by ultrasound has been documented to be 0.65 per cent.

Colour-coded Doppler techniques allow the visualization of renal blood flow and as such non-invasive information on impedance at the renal level\textsuperscript{87,111,222}. It has been suggested that the observed decrease in vascular impedance with advancing gestational age is a consequence of renal angiogenesis and an increase in the total arteriolar cross-sectional vessel area.

In the presence of extreme oligohydramnios, differentiation between intrauterine
growth retardation and bilateral renal agenesis may be difficult. In the latter instance, renal arteries will be rudimentary or even absent, resulting in the absence of renal blood flow.

The objective of this study was to assess the role of colour Doppler flow mapping and pulsed Doppler in (i) establishing bilateral renal agenesis, and (ii) determining changes in renal vascular impedance in renal cystic disease and obstructive uropathy.

Patients and Methods

Measurement of impedance to flow was attempted in renal arteries using colour Doppler flow mapping and pulsed wave Doppler (Toshiba SSA 270 A, carrier frequency 3.75 MHz, and high pass filter 100 Hz) in 33 fetuses with postnatally confirmed renal pathology. In hydrenephrosis, the maximum diameter of the renal pelvis was divided into two groups: 10-15 mm (grade I) and > 15 mm (grade II). Gestational age ranged between 16 and 37 weeks (median 29 weeks).

First, a real-time image of a longitudinal view of the fetal kidneys was obtained. Using colour coded Doppler flow mapping, the renal arteries can be visualized branching from the abdominal aorta above the origin of the common iliac arteries\(^2\). Flow velocity waveforms were recorded following placing the Doppler sample gate over the proximal part of each renal artery. The angle of insonation was always kept below 20°. The pulsatility index (PI)\(^3\), as a measure of downstream impedance, was calculated from three consecutive flow velocity waveforms.

The difference in PI between grade I and grade II hydrenephrosis was tested using the paired Student t-test.

Results

Renal pathology consisted of unilateral or bilateral hydrenephrosis (n=21), unilateral multicystic kidney (n=4), and bilateral renal agenesis (n=8)(Table 1).

Whereas bilateral renal blood flow could be visualized in the presence of hydrenephrosis and multicystic kidney, this was not so in bilateral renal agenesis.

Bilateral flow velocity recordings were collected in six out of 12 cases of bilateral hydrenephrosis and in five out of nine cases of unilateral hydrenephrosis. In the case of unilateral recordings (n=10), these were always performed on the affected side. Failure to obtain bilateral recordings was due to an unacceptable insonation angle (> 20°)
(Intra)abdominal abnormalities

because of fetal position or not adhering to the protocol.

In bilateral hydronephrosis, the PI values were in the normal range in 16 out of 18 kidneys (88 per cent) according to the reference chart by Vyas et al. (1989)(22)(Figure 1). In unilateral hydronephrosis, PI values were in the normal range in 12 out of 14 kidneys (85 per cent)(Figure 1). In the five cases of unilateral hydronephrosis with bilateral recordings, the PI on the affected side was higher in three (5, 7, and 25 per cent) and lower in two (3 and 6 per cent) than on the contralateral normal side. The mean PI in grade II hydronephrosis (2.71±0.5(SD); n=13) was significantly higher (p<0.01) than that in grade I hydronephrosis (2.25±0.4(SD); n=19).

In the four cases of unilateral multicystic kidney, the PI of one was above the upper limit of the normal range and in the other three it was higher (12-23 per cent) on the affected side compared with the contralateral normal side (Figure 1).

Discussion

In this paper renal artery flow velocity waveforms have been studied according to a wide spectrum of congenital renal pathology.

Unilateral hydronephrosis is usually associated with a good fetal outcome, although renal function in the affected kidney may deteriorate with advancing gestation. The prognosis in bilateral hydronephrosis will be determined by the amount of amniotic fluid and the remaining renal function11. However, exact methods of determining fetal renal function are not yet available. Ultrasound does allow non-invasive measurement of fetal urine production12,224. Hourly fetal urinary production rates, however, are only a crude reflection of fetal diuresis. Fetal urine can be obtained through ultrasound-guided

<table>
<thead>
<tr>
<th>Table 1 Nature of renal pathology (n=33) relative to bilateral, unilateral, or absent renal artery flow velocity waveform recording</th>
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<tr>
<td><strong>Bilateral (n=14)</strong></td>
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<tr>
<td>Bilateral hydronephrosis (n=12)</td>
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<td>Unilateral hydronephrosis (n=9)</td>
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<td>Unilateral multicystic kidney (n=4)</td>
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<td>Bilateral renal agenesis (n=8)</td>
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Figure 1. PI data on bilateral hydronephrosis (●, n=18), unilateral hydronephrosis (○, n=14) and multicystic kidneys (□, n=4) relative to the normal range according to Vyas et al, 1989 (10th, 50th and 90th percentile).

PI data from both kidneys are interconnected. In multicystic kidneys, the highest values always originated from the affected side. The reduced PI value at 30 weeks (open circle) originates from the contralateral normal kidney in a case of unilateral hydronephrosis.

bladder needling for urinary electrolyte determination\textsuperscript{10,77}. Separate sampling from each kidney rather than the bladder was suggested on the assumption that bilateral renal damage secondary to low-level obstructive uropathy is not necessarily symmetrical in severity\textsuperscript{159}.

In normal pregnancy, impedance to fetal renal artery flow decreases with advancing gestational age\textsuperscript{222}. Animal experimental research suggests that renal pathology could be associated with raised downstream impedance\textsuperscript{40}.

In this study, both in bilateral and in unilateral obstructive uropathy, the majority of the renal artery PI values were not different from normal. Similar observations were made by Gudmundsson et al.(1991), who suggested that the gradual pressure rise within the urinary tract apparently does not affect renal arterial pressure\textsuperscript{86}. However, we observed a positive relationship between the renal artery PI and the severity of hydronephrosis, suggesting a relative increase in downstream impedance as a result of the
pressure rise. In fetal sheep, ureteral obstruction is followed by progressive vasoconstriction. It was demonstrated that this vasoconstriction is mediated at least in part by intrarenal vasoactive compounds, including eicosanoids and angiotensin II. Compensatory reduction in downstream impedance in the normal contralateral kidney in the presence of unilateral hydronephrosis could not be established from the few cases in our study; the PI on the hydronephrotic side was three times higher and twice lower than on the contralateral normal side.

Multicystic kidney is the most common form of cystic disease in infants; it is associated with a non-patent drainage system in which there is either pelvi-infundibular atresia, or an absent or atretic ureter. Failure to maintain an adequate blood supply to the metanephros and ureteric bud has been suggested as an explanation for this type of cystic disease. The renal artery PI from the multicystic kidney was situated above the normal range in two out of four cases studied and was always higher than on the contralateral normal side. Although these data are still few, they support the findings published recently by Kaminopetros et al. (1991), in which raised renal artery PI values were observed in the presence of multicystic kidney disease. Finally, no renal flow could be observed in bilateral renal agenesis. This is in agreement with absent renal artery development and as such, colour flow mapping may serve as an additional tool in the diagnosis of this type of pathology.

In conclusion, our data suggest that combined colour flow mapping and Doppler evaluation may be helpful in our understanding of renal vascularization in renal pathology. However, renal Doppler flow studies in hydronephrosis do not seem to provide convincing information regarding renal function. Colour flow mapping may be helpful in confirming the diagnosis of renal agenesis.

5.4.2 Abdominal wall defects

Colour coded Doppler assessment took place in 12 cases of omphalocele and once in a case of gastroschisis. Pregnancy duration varied between 20 and 31 weeks (median 27 weeks). In 11 out of 12 cases colour coded Doppler visualization of the umbilical vein resulted in an easier diagnosis of omphalocele. However, colour coded Doppler did not play a decisive role in the diagnosis of this entity. In another three cases in which an omphalocele was suspected with conventional real-time ultrasound, colour coded Doppler demonstrated a normal umbilical cord insertion into the anterior abdominal wall ruling out omphalocele. There were no false negatives or false positives. Additional chromosomal
analysis took place in 11 out of 12 cases of omphalocele, twice a trisomy 18 was established. Term delivery took place in eight cases, premature delivery occurred in four cases. Perinatal mortality was 50% (6/12). Also in the one case of gastroschisis, colour coded Doppler facilitated the demonstration of absence of an anatomic relation between the umbilical cord insertion site and the herniated viscera.

It was concluded that although colour coded Doppler may lead to a swifter diagnosis of omphalocele or gastroschisis, it did not contribute to the accuracy of the diagnosis or obstetric management.

5.4.3 Gastrointestinal obstructions

Three cases of bowel obstructions were further investigated during the "Ontwikkelingsgeneeskunde" project. Only in one case of a low intestinal obstruction associated with ascites a correct prenatal diagnosis could be made, based on colour Doppler visualization of the topographic relation between rectum and urinary bladder. In the other two cases, a duodenal atresia and one small bowel obstruction with meconium peritonitis, no additional structural or functional information was obtained with colour Doppler imaging. These numbers, however, are too small for a reliable analysis.

5.4.4 Intra-abdominal cysts

A total of nine cases of an abnormal intra-abdominal cystic structure was diagnosed, not related to stomach, gall bladder or urinary bladder. Pregnancy duration ranged between 16 and 38 weeks (median 28 weeks). Colour coded Doppler examination suggested the presence of an unilateral ovarian cyst in six cases based on the topographical relationship with the descending aorta, internal and external iliac artery. All six cases of ovarian cyst were confirmed postnatally. Colour coded Doppler did not contribute to the prenatal diagnosis in the remaining three cases. Postnatally, twice a mesenteric cyst was diagnosed and once the cyst could not be traced anymore. Additional chromosomal analysis took place in the three cases with an intra-abdominal cyst of unknown origin. All karyotypes were normal. Spontaneous delivery took place in seven cases, premature delivery in two cases.

It was concluded that colour coded Doppler contributed to the identification of ovarian cysts, but did not affect obstetric management.
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