Original Paper

Fetal Diagn Ther 1992;7:102–115

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Fetal Gastro-Intestinal and Abdominal Wall Defects: Associated Malformations and Chromosomal Abnormalities

Abstract

During an 8-year period (1983–1991), blood karyotyping was performed in 235 fetuses with abdominal wall or gastro-intestinal tract defects. The overall incidence of chromosomal abnormalities was 29% (trisomy 21, n = 12; trisomy 18, n = 44; trisomy 13, n = 7; deletion of the short arm of chromosome 5, n = 1; unbalanced translocation involving chromosomes 4 and 15, n = 1; triploidy, n = 1; Klinefelter's syndrome, n = 1; and Beckwith-Wiedemann syndrome with mosaic duplication 11p15, n = 1). The karyotype was abnormal in 42 (36%) of the 116 fetuses with exomphalos, in none of the 26 with gastroschisis, in 10 (43%) of the 23 with duodenal atresia, in 18 (75%) of the 24 with lack of visible stomach, in 1 (4%) of the 24 with dilated bowel and in 2 (7%) of the 27 with echogenic hepatic nodules or abdominal cysts. Abnormal karyotypes were more commonly encountered when there was ultrasonographic evidence of multiple malformations (43%) compared to isolated defects (2%). Survival in fetuses with exomphalos (33%), absent stomach (4%), and large bowel obstruction (13%) was poor, whereas in those with gastroschisis (73%) or abdominal cysts (88%) survival was high; in small bowel obstruction and in duodenal atresia, survival was 65 and 57%, respectively.

Key Words

Fetal karyotype
Cordocentesis
Ultrasonography
Exomphalos
Gastroschisis
Oesophageal atresia
Duodenal atresia
Intestinal obstruction
Abdominal cyst

Introduction

Congenital abnormalities of the abdominal wall and gastro-intestinal tract are amenable to surgical correction, and postnatal studies have established that their prognosis is primarily dependent on the presence or absence of other major organ system malformations and chromosomal abnormalities (table 1) [1–13]. Since these abnormalities can now be

Received:
December 8, 1991
Accepted:
February 11, 1992

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S. Karger AG, Basel
1015–3837/92/
0072–0102$2.75/0

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Table 1. Summary of reports on postnatally diagnosed exomphalos providing data on the frequency of other defects and survival depending on the absence (isolated) or presence (multiple) of additional defects

Author	Cases	Other defects %	Survival, %	
			isolated	multiple
Mayer et al. [1]	28	–	92	10
Grosfield et al. [2]	47	66	94	61
Kirk and Wah [3]	38	29	–	–
Wladimiroff et al. [4]	46	–	84	20
Carpenter et al. [5]	25	64	78	50
Mabogunje and Mahour [6]	57	46	96	69
Hasan and Hermansen [7]	17	65	100	21
Yazbeck et al. [8]	92	45	86	34
Calisti et al. [9]	12	83	50	20
Lafferty et al. [10]	21	43	92	67
Kohn and Shi [11]	17	88	100	53
Larsson and Kullendorff [12]	35	37	–	–
Tucci and Bard [13]	28	43	94	17

diagnosed antenatally, accurate prenatal evaluation of both the primary defect and associated abnormalities is essential for effective pregnancy management.

The reported incidence of associated abnormalities and prognosis are derived mainly from postnatal studies, and the extent to which the results are sufficiently accurate for counselling the parents of fetuses with antenatally diagnosed lesions is uncertain. Previous studies of antenatally diagnosed malformations, such as exomphalos, have demonstrated that the incidence of associated abnormalities is higher and the prognosis poorer than those reported in the pediatric literature (tables 1, 2) [1–26]. The most likely explanation for this discrepancy is that in the pediatric studies, the results are based largely on neonates who present to the pediatric surgeons and therefore do not include fetuses with multiple defects that die in utero or in the early neonatal period.

Using strict criteria for the differential diagnosis of fetal abdominal wall, gastrointestinal defects and abdominal cysts, this study reports the findings of malformations in other organ systems, the karyotype and outcome of 235 cases.

Patients and Methods

During an 8-year period (1983–1991), blood karyotyping was performed at 16–39 (median = 23) weeks gestation in 235 fetuses with abdominal wall or gastrointestinal defects who were referred to our centre for ultrasound examination and further assessment.

The diagnosis of exomphalos was based on the demonstration of the midline anterior abdominal wall defect, the herniated sac with its visceral contents, and the umbilical cord insertion at the apex of the sac. In gastroschisis, the abdominal wall defect was adjacent to the normally inserted umbilical cord, and the eviscerated bowel (plus liver in 2 cases) was freely floating in the amniotic fluid. Duodenal atresia was diagnosed by the presence of the characteristic double-bubble appearance of the dilated stomach and proximal duo-

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denum. If in the presence of polyhydramnios the stomach was not visible on repeated ultrasound examinations, oesophageal atresia was suspected; other possible diagnoses included lack of fetal swallowing due to arthrogryposis and intrathoracic compression due to cystic adenomatoid malformation or pleural effusion. In small bowel obstruction, there were distended, fluid-filled loops of bowel. Large bowel obstruction was suspected when a loop of dilated bowel was seen in the lower abdomen and there was no accompanying polyhydramnios. Other abnormalities of the gastrointestinal tract included mesenteric or omental cysts (which may be indistinguishable from ovarian cysts), liver nodules or cysts, suprarenal cysts, and hyperechogenic pancreas.

In all cases, a systematic search was made for the detection of any associated malformations (Aloka SSD-650 or Hitachi EUB 340, 3.5 MHz or 5 MHz curvilinear transducer). Subsequently, the parents gave informed consent for rapid fetal karyotyping, which was performed by cytogenetic analysis of fetal blood obtained by cordocentesis.

Details on the outcomes of pregnancies were obtained from the referring hospitals.

Results

In the 235 fetuses with anterior abdominal wall and gastro-intestinal defects, the karyotype was abnormal in 68 (29%) of the cases (table 3). The most frequently found chromosomal abnormalities were trisomy 21 (18%), trisomy 18 (65%) and trisomy 13 (9%). Trisomy 21 was mainly found in association with duodenal atresia and trisomies 13 and 18 in

Table 2. Summary of reports on antenatally diagnosed exomphalos providing data on the relation between abnormal karyotype and the presence of defects other than exomphalos, contents of the exomphalos and the sex of the fetuses

Author	Incidence of chromosomal abnormalities				
	total	other defects		exomphalos contents	
		absent	present	bowel	liver ± bowel
Nakayama et al. [14]	1/10	1/4	0/6	0/1	1/9
Nielson et al. [15]	2/8	0/3	2/5	–	–
Nicolaides et al. [16]	8/12	1/3	7/9	–	–
Gilbert et al. [17]	19/35	1/10	18/25	–	–
Sermer et al. [18]	4/10	0/2	4/8	–	–
Eydoux et al. [19]	12/46	7/27	5/19	–	–
Hughes et al. [20]	13/30	3/8	10/22	10/10	3/20
Nyberg et al. [21]	10/26	4/17	6/9	8/8	2/18
Benacerraf et al. [22]	4/22	0/7	4/15	4/6	0/16
Holzgreve et al. [23]	5/10	–	–	–	–
Rizzo et al. [24]	7/12	2/6	5/6	–	–
Shah et al. [25]	2/4	–	–	–	–
Van de Geijn et al. [26]	10/22	0/4	10/18	–	–
Present study	42/116	1/29	41/87	25/44	17/72

[1] 47,XXY; 45,XO; 46,XY,5p–; 46,XY,7q–; 46,XY,14q–; 46 XY,8p+; 46,XY,5p+; 46,XX,i,(18p); 46,XX,t(9,11); 46,XY/49,XY,+2,+7,+19; 46,XY,–14,+t,dic(13q14q); 69,XYY; 69,XXY (n = 2); 46,XX,17p–; 46,XY,+13; 46,XY,–18+i(18q); 46,XY–13+der(13)t(13q18p); 46,XX/46,XX,dup(11p15).

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oesophageal atresia and exomphalos. Abnormal karyotypes were more commonly encountered when there was ultrasonographic evidence of multiple malformations (43%; 66 of 154 cases) compared to isolated defects (2%; 2 of 81 cases).

The mean maternal age in the group with chromosomally abnormal fetuses (mean = 30, range 19–48 years) was significantly higher (mean difference = 4 years, SEM = 0.9, t = 4.5, $p < 0.0001$) than that of pregnancies with chromosomally normal fetuses (mean = 26, range 16–42 years). The maternal age distribution and the incidence of fetal chromosomal abnormalities are shown in figure 1. The maternal age-related risk in the literature for women undergoing second-trimester amniocentesis is 1% at 35–36 years, 1.3% at 37–

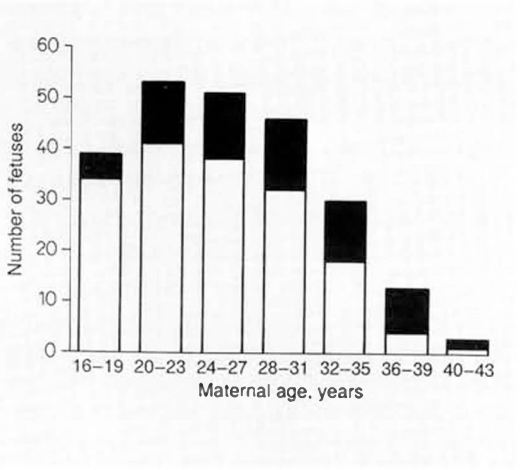

Fig. 1. Maternal age distribution and the incidence of fetal chromosomal abnormalities (dark shaded) in 235 fetuses with gastrointestinal and/or abdominal wall defects.

Incidence of chromosomal abnormalities					
fetal sex		chromosomal defects			
male	female	Tr 13	Tr 18	Tr 21	other[1]
0/4	1/6	–	1	–	–
0/3	2/5	2	–	–	–
7/9	1/3	–	7	–	1
17/26	2/9	–	17	–	2
–	–	1	2	–	1
–	–	2	6	–	3
–	–	5	4	2	2
6/11	4/15	4	4	1	1
–	–	2	1	–	1
–	–	1	3	–	1
–	–	2	5	–	–
–	–	–	1	–	1
–	–	1	6	–	3
36/73	6/43	6	32	–	4

Tr = Trisomy.

Table 3. Karyotype in 235 fetuses with abdominal wall or gastro-intestinal defects

Karyotype	n
46,XX	89
46,XX	78
47,XX,+13	2
47,XX,+13	4
46,XX,–14+t(13;14)	1
47,XX,+18	7
47,XX,+18	38
47,XX,+21	5
47,XX,+21	7
47,XXY	1
69,XXY	1
46,XY,5p–	1
46,XY,+t(4;15)	1
46,XX/46,XX,dup(11p15)	1

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38 years, 2% at 39–40 years and 3.9% at 41 years or more [27]. In our group of fetuses with isolated abdominal wall or gastro-intestinal defects, there were only 2 pregnancies with a chromosomally abnormal fetus; the mothers were 31 and 38 years old, respectively. In contrast, in the group where gastrointestinal defects were accompanied by other malformations, the incidence of chromosomal abnormalities increased from 30% in women of <26 years to 84% in women of >35 years.

Table 4. Findings in 24 fetuses with absent stomach bubble including maternal age (Age), gestation at referral (GA), additional malformation and/or growth retardation (IUGR) diagnosed by ultrasound, karyotype, outcome, gestation at delivery (Age) and postnatal or post-mortem diagnosis

Case No.	Age years	GA weeks	IUGR	Additional malformations					
				skull	face	brain	chest	abdomen	extremities
1	28	30	+						OF
2	23	32	+						rocker-bottom feet
3	22	27	+	S, BC		CPC	DH, CD	H1, Exom	OF, talipes
4	38	31	+	S	MG		CD	Exom	OF, talipes, SF
5	32	34	+				CD	H1	clinodactyly
6	29	23	+	S			CD		OF, rocker-bottom feet
7	30	25	+			CPC	CD		OF, talipes
8	27	24	+	S, BC		ACC	CD		OF, talipes
9	20	37	+	S, BC	MG	PFC	CD		OF
10	29	26	+	S	MG	CPC			OF
11	25	20		S, BC			CAM		OF, talipes
12	23	32	+	S	FC				OF
13	26	23		S			DH	Exom	OF, talipes, SF
14	31	30	+	S					OF
15	37	24	+	S	MG		CD		OF
16	19	24	+		MG	CPC	CD	H2, Exom	OF
17	29	33		S, BC			CD	H1, Exom	OF, talipes, SF
18	34	35							
19	25	21			MG				OF
20	28	29							
21	37	22			FC		pl + per		talipes
22	25	31	+				CAM		
23	27	27	+						talipes, FlW
24	23	32							talipes, FlW

In the first 20 cases, the presumptive diagnosis of oesophageal atresia was made, and in the last 4 cases, the stomach was not visible because of intrathoracic compression or lack of swallowing. Other fetal abnormalities included strawberry shaped skull (S), brachycephaly (BC), micrognathia (MG), facial cleft (FC), chloroid plexus cysts (CPC) or posterior fossa cyst (PFC), absent corpus callosum (ACC), diaphragmatic hernia (DH), pleural and pericardial effusions (pl+per), cystic adenomatoid malformation (CAM), cardiac defects (CD), mild (H1) or moderate (H2) hydronephrosis, exomphalos (Exom), overlapping fingers (OF), clinodactyly, flexed wrists (FlW), talipes and relatively short femur (SF).

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Exomphalos

The fetal karyotype was normal in 74 (64%) and abnormal in 42 (36%) of the cases (table 2; n = 116). Although the male to female ratio in the chromosomally normal fetuses was 37:37, in the abnormal group the ratio was 36:6. The karyotype was abnormal in 25 (57%) of the 44 fetuses with bowel only in the exomphalos sac and in 17 (24%) of the 72 with liver, heart or bladder in the sac. One (3%) of the 30 fetuses with isolated exomphalos had an abnormal karyotype; in contrast, 41 (48%) of the 86 fetuses with additional malformations were found to be chromosomally abnormal (table 1).

Karyotype	Out-come	Ge weeks	Diagnosis
47,XX+18	IUD	30	oesophageal atresia
47,XX+18	IUD	34	oesophageal atresia
47,XX+18	TOP	37	oesophageal atresia
47,XX+18	IUD	32	oesophageal atresia
47,XX+18	IUD	35	oesophageal atresia
47,XX+18	TOP	23	oesophageal atresia
47,XY+18	TOP	25	oesophageal atresia
47,XY+18	TOP	24	oesophageal atresia
47,XY+18	IUD	42	oesophageal atresia
47,XX+18	TOP	26	oesophageal atresia
47,XY+18	TOP	20	oesophageal atresia
47,XY+18	IUD	32	oesophageal atresia
47,XY+18	TOP	23	small stomach
47,XY+18	IUD	39	normal GIT
47,XY+18	TOP	24	no post-mortem
47,XY+18	IUD	40	no post-mortem
47,XY+18	IUD	33	no post-mortem
46,XX	NND	36	no post-mortem
46,XY	TOP	21	no post-mortem
46,XX	alive	37	normal GIT
47,XY+21	IUD	29	compression
46,XX	IUD	32	compression
46,XX	NND	38	arthrogryposis
46,XX	NND	36	arthrogryposis

IUD = Intra-uterine death; TOP = termination of pregnancy; NND = neonatal death.

In the chromosomally abnormal group (n = 42), there were 40 (95%) deaths, due to elective termination of pregnancy (n = 30), intrauterine (n = 6) or neonatal death (n = 4); 2 infants survived, 1 with Klinefelter's syndrome and another with a deletion of the short arm of chromosome 5. In the chromosomally normal group (n = 74), there were 28 elective terminations of pregnancy, 3 intrauterine and 7 neonatal deaths; 36 (33%) infants are alive and 2 pregnancies are continuing.

Gastroschisis

The mean gestational age at referral to our unit was 23 (range 16–35) weeks. In all cases (n = 26), the amniotic fluid volume was normal. In 2 pregnancies, there was evisceration of both bowel and liver; in all the other cases, only bowel was involved. Additional malformations were found in 8 fetuses; 5 had a short femur, 1 had a facial cleft and unilateral anophthalmia, 1 had bilateral mild hydronephrosis, and 1 had facial cleft, digital amputations, scoliosis, talipes and evisceration of both liver and bowel which were attributable to amniotic band syndrome. The fetal karyotype was normal in all cases. Similarly, in an additional 18 cases of antenatally diagnosed gastroschisis, where the parents chose not to have fetal karyotyping, the infants did not have any dysmorphic features that would raise the suspicion of a chromosomal abnormality.

In the total group of 44 cases with gastroschisis, the male to female ratio was 23:21. In 3 cases, among which 2 with evisceration of both bowel and liver, pregnancies were elec-

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tively terminated. Additionally, there was 1 unexplained intra-uterine death at 36 weeks gestation. All the other babies were live-born at 32–39 (mean = 36) weeks gestation; 25 babies were born vaginally, and 16 by elective (n = 10) or emergency (n = 6) caesarean section. Successful surgery was carried out in all cases, but 3 babies died 1–9 days after birth. In 16 (36%) cases, the birthweight was below the 5th centile of the normal range for gestation [28].

Absent Stomach Bubble

The antenatal findings and outcome in the cases with polyhydramnios and absent fetal stomach bubble (n = 24) are shown in table 4. In the 20 fetuses with the presumptive diagnosis of oesophageal atresia, there were 17 (80%) with trisomy 18, and in 5 of these, oesophageal atresia was associated with exomphalos. Only 1 of these 20 fetuses survived, and the infant had a normal gastro-intestinal tract. Permission for post-mortem examination was obtained from 14 of the remaining 19 parents; in 12 cases, the diagnosis of oesophageal atresia was confirmed, in 1 case, the gastro-intestinal tract was apparently normal and in another, the stomach was small but there was no oesophageal atresia.

In 2 cases, the lack of a visible stomach bubble could be attributed to no swallowing due to arthrogryposis; both these fetuses were chromosomally normal but the infants died in the neonatal period because of pulmonary hypoplasia. In an additional 2 cases, the lack of a visible stomach could be attributed to oesophageal compression due to cystic adenomatoid malformation of the lung and pleural effusion, respectively; the former had a normal female karyotype, and the latter had trisomy 21.

Duodenal Atresia

The antenatal findings and outcome of these fetuses are shown in table 5 (n = 23). There were 10 (43%) fetuses with trisomy 21, and 13 with a normal karyotype. Additional malformations, mainly cardiac, were found in 9 (90%) of the trisomic and in 8 (62%) of the chromosomally normal fetuses. At presentation, the amniotic fluid volume was increased in all but 2 cases; 1 fetus had obstructive uropathy and in the other, duodenal atresia was diagnosed at 20 weeks gestation. In the latter case, the fetus was thought to have a genetic syndrome because, in addition to duodenal atresia, there were hydrocephalus, pelvic kidney, radial aplasia and absence of thumbs; similar abnormalities had been diagnosed in a previous pregnancy of the same family. Survival in the chromosomally normal group was 77% (10 of 13), and in the trisomic group 30% (3 of 10).

Dilated Bowel

The antenatal findings and outcome of these fetuses are shown in table 6 (n = 24). There were 14 cases of small bowel obstruction due to an atresic segment in the jejunum or ileum, 6 cases of large bowel obstruction, and 4 cases where the dilated bowel was subsequently found to be due to megacystis microcolon intestinal hypoperistalsis syndrome or myotonia dystrophica. The karyotype was normal in all but 1 case, in which the fetus had multiple abnormalities. There were 3 elective terminations of pregnancy, 2 intra-uterine, 5 neonatal and 2 infant deaths; 12 (50%) infants survived.

Abdominal Cysts

The antenatal findings and outcome of these fetuses are shown in table 7 (n = 27). There were 5 cases with a mesenteric cyst, 5 cases with an ovarian cyst, 1 with a hepatic cyst, and 4 with adrenal cysts. In 2 of the latter

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Table 5. Findings in 23 fetuses with duodenal atresia including maternal age (Age), gestation at referral (GA), amniotic fluid volume (AF), growth retardation (IUGR) and/or additional malformations including relative shortening of the femur (head circumference to femur length ratio > 97.5th centile), karyotype, outcome, mode of delivery (MD) and gestation at delivery (Ge)

Case No.	Age years	GA weeks	AF	Additional malformations	Karyotype	Outcome	MD	Ge weeks
1	24	27	P		46,XX	alive	V	39
2	23	33	P	short femur, IUGR	46,XX	alive	Em	36
3	37	34	P		46,XX	alive	V	36
4	35	32	P	brachycephaly	46,XX	alive	El	36
5	22	33	P		46,XX	alive	V	35
6	24	30	P		46,XX	alive	V	38
7	22	32	P	IUGR	46,XX	alive	Em	38
8	25	34	I	hydrocephalus, radial aplasia, pelvic kidney, IUGR	46,XX	IUD	V	36
9	26	20	N	hydrocephalus, radial aplasia, pelvic kidney, IUGR	46,XX	TOP	V	20
10	32	34	P	brachycephaly	46,XY	alive	V	37
11	21	32	P		46,XY	alive	V	32
12	34	36	I	cardiac defect, ventriculomegaly	46,XY	IUD	V	36
13	27	27	P	sandal gap	46,XY	alive	V	31
14	38	30	P		47,XX+21	alive	Em	34
15	24	23	P	cardiac defect, clinodactyly, macroglossia	47,XX+21	TOP	V	24
16	33	33	I	nuchal edema, macroglossia	47,XX+21	alive	V	38
17	34	21	I	nuchal edema	47,XX+21	TOP	V	22
18	31	35	I	brachycephaly	47,XY+21	alive	V	37
19	30	32	P	cardiac defect, short femur	47,XY+21	IUD	V	37
20	24	31	D	cardiac defect, moderate hydronephrosis, IUGR, short femur	47,XY+21	NND	V	37
21	30	27	P	clinodactyly	47,XY+21	TOP	V	27
22	35	33	P	mild hydronephrosis, short femur	47,XY+21	IUD	V	33
23	23	25	I	cardiac defect, nuchal edema	47,XY+21	TOP	V	25

P = Polyhydramnios; I = increased; N = normal; D = decreased; TOP = termination of pregnancy; IUD = intra-uterine death; NND = neonatal death; V = vaginal; Em = emergency caesarean section; El = elective caesarean section.

cases, the fetuses had the Beckwith-Wiedemann syndrome, and in addition to the multiple adrenal cysts, they had hepatosplenomegaly and enlarged hyperechogenic pancreas. In 6 cases, the nature of the cysts is uncertain because they resolved antenatally and there were no pathological findings at postnatal examination. In 3 cases with a large central abdominal cyst, postnatal surgery demonstrated a 'hydronephrotic sac' that was excised. In another case, a large tubular prehepatic cyst was found to be a dilated umbilical vein, and postnatally, this was found to be associated with aortic valve stenosis.

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Table 6. Findings in 24 fetuses with bowel obstruction including age (Age), gestation at referral (GA), amniotic fluid volume (AF), growth retardation and/or additional malformations including relative shortening of the femur (head circumference to femur length ratio > 97.5th centile), karyotype, outcome, mode of delivery (MD) and gestation at delivery (Ge)

Case No.	Age years	GA weeks	AF	Additional malformations		Karyo-type	Out-come	MD	Ge weeks	Diag-nosis
				bowel	other					
1	34	28	N	SO	short femur	46,XY	alive	El	34	1
2	22	31	N	SO	growth retardation, short femur	46,XX	alive	El	35	1
3	25	32	N	SO		46,XX	alive	V	40	1
4	27	33	N	SO		46,XY	alive	V	35	1
5	27	29	N	SO		46,XY	alive	V	37	1
6	35	33	I	SO		46,XY	alive	V	40	1
7	37	35	I	SO		46,XX	alive	V	37	1
8	33	32	N	SO	growth retardation	46,XY	ID	V	35	1
9	24	30	rD	SO	growth retardation, short femur	46,XX	NND	Em	30	1
10	26	32	N	SO	brachycephaly	46,XY	alive	V	38	2
11	24	36	I	SO		46,XY	alive	V	36	2
12	29	33	I	SO	growth retardation	46,XX	NND	V	35	2
13	33	26	I	SO	growth retardation, duplex kidney, rocker-bottom feet	46,XX	NND	V	31	2
14	31	27	N	SO	edema	46,XY	NND	V	30	2
15	27	29	I	SO		46,XY	ID	V	35	3
16	34	30	I	SO	hydronephrosis	46,XY	alive	V	37	4
17	25	18	I	SO	hydronephrosis	46,XX	TOP	V	19	4
18	40	26	N	LO	hydronephrosis, two-vessel cord, echogenic lung	46,XX	NND	V	34	4
19	28	25	rD	LO	multicystic kidney	46,XY	alive	V	38	5
20	32	24	N	LO	hydronephrosis, growth retardation	46,XX	IUD	V	24	6
21	32	34	rD	LO	growth retardation, OF, clinodactyly, short femur	46,XY,t4,15	IUD	V	35	7
22	26	23	rD	LO	hydronephrosis	46XY	TOP	V	27	8
23	26	23	rD	LO	hydronephrosis, growth retardation, short femur	46XY	TOP	V	24	9
24	30	22	N	LO		46XY	alive	V	40	10

N = Normal; I = increased; D = decreased; SO = small bowel obstruction; LO = large bowel obstruction; OF = overlapping fingers; ID = infant death; NND = neonatal death; IUD = intra-uterine death; TOP = termination of pregnancy; V = vaginal; Em = emergency caesarean section; El = elective caesarean section.

Diagnosis: 1 = ileal atresia; 2 = jejunal atresia; 3 = myotonia dystrophica; 4 = megacystis microcolon intestinal hypoperistalsis syndrome; 5 = imperforate anus, rectovesical fistula; 6 = imperforate anus, trachco-oesophageal fistula, phocomelia; 7 = anal atresia; 8 = imperforate anus, bladder extrophy; 9 = agenesis of distal colon, rectum and anus; 10 = no gastrointestinal defect postnatally.

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In 1 of the fetuses with Beckwith-Wiedemann syndrome, the karyotype was 46,XX/46,XX,dup(11p15). All other fetuses had a normal karyotype. There were 3 neonatal deaths; 1 was due to pulmonary hypoplasia in an infant with a large mesenteric cyst and generalized oedema, the second was in an infant with Beckwith-Wiedemann syndrome, the third in the infant with aortic valve stenosis. The remaining 22 (88%) infants are alive.

Liver Nodules

In 2 fetuses, referred to our unit at 21–22 weeks gestation, there were 2–3 hyperechogenic nodules (1–3 mm in diameter) in the liver. In 1 case, there was nuchal oedema and digital abnormalities, and the karyotype was 47,XY+21. The pregnancy was terminated, and at post-mortem examination, the hepatic nodules could not be identified. In the second fetus, there were no other abnormalities and the karyotype was normal (46,XX); the infant was born at term, and postnatal X-ray examination demonstrated areas of calcification at the origin of the right hepatic vein.

Discussion

This study of antenatally diagnosed abdominal wall and gastro-intestinal defects has demonstrated that (1) the prognosis for fetuses with exomphalos, oesophageal atresia, or large bowel obstruction is poor, because the majority of cases have associated lethal malformations and chromosomal abnormalities; (2) the prognosis for fetuses with gastroschisis, small bowel obstruction, or abdominal cysts is excellent and these defects are almost invariably isolated, and (3) in duodenal atresia, approximately half of the fetuses have other abnormalities and do not survive.

In exomphalos, the findings of this study confirm those from previous ones (table 2) that (1) the incidence of associated abnormalities is higher and the prognosis poorer than the reported incidences in the pediatric literature [1–13]; (2) the indicence of associated chromosomal abnormalities is higher in older mothers in the presence of multisystem fetal malformations [17, 21] in male than female fetuses [17] and when the exomphalos sac contains bowel rather than liver [21, 22]. Furthermore, the patterns of the additional malformations are related to the type of associated chromosomal abnormality. For example, in trisomy 13, the most commonly encountered defects are holoprosencephaly, facial cleft, cardiac defects and abnormalities of the hands and feet. In trisomy 18, associated malformations include strawberry-shaped skull, choroid plexus cysts, facial cleft or micrognathia, heart defects, overlapping fingers and talipes. The differences between exomphalos and gastroschisis in the incidence of both chromosomal abnormalities and associated malformations further reinforce the need to distinguish between these two abdominal wall defects by ultrasonography.

In gastro-intestinal tract obstruction, the incidence and types of chromosomal abnormalities and the pattern of other malformations were related to the level of the obstruction. Thus, in oesophageal atresia, the commonest chromosomal abnormality was trisomy 18, whereas in duodenal atresia the commonest abnormality was trisomy 21 and consequently, the associated defects were more subtle and included nuchal oedema, macroglossia, sandal gap and clinodactyly.

In this study, all fetuses with confirmed oesophageal atresia had trisomy 18. In contrast, associated chromosomal abnormalities were reported in only 3–4% of live births with oesophageal atresia [29, 30]. One possible explanation for this apparent discrepancy, and for the finding that in more than 90% of infants with oesophageal atresia there is an associated

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tracheo-oesophageal fistula [31], is that trisomic fetuses are more likely to die in utero, due to other malformations and intra-uterine growth retardation, but also to be born at previable gestations due to the polyhydramnios, because their oesophageal atresia develops in the absence of tracheo-oesophageal fistula.

Duodenal atresia is usually sporadic, although in some cases, as found in one family in this series, there is an autosomal recessive mode of inheritance. The small difference in the incidence of trisomy 21 between antenatally (43%) and postnatally (20–30%) [32, 33] diagnosed duodenal atresia is compatible with the reported difference in the maternal age-related risk for trisomy 21 at the time of second-trimester amniocentesis and in live births.

Table 7. Findings in 25 fetuses with abdominal cysts including maternal age (Age), gestation at referral (GA) antenatal findings, outcome, gestation at delivery (Ge), sex, diagnosis and comments on antenatal (AN) or postnatal (PN) treatment

Case No.	Age years	GA weeks	Abdominal cyst			Outcome	Ge weeks
			position	septae	size		
1	20	20	central	–	16×21×29	alive	42
2	31	25	central	–	44×47×52	alive	38
3	41	34	central	–	65×70×80	NND	35
4[1]	29	34	central	–	70×81×90	alive	38
5	37	20	central	–	13×28×36	alive	29
6	27	35	central-left	+	47×42×33	alive	36
7	21	33	central-left	–	37×37×60	alive	37
8	40	33	central-left	–	23×23×30	alive	38
9	21	33	central-left	+	30×30×30	alive	37
10	24	37	central-left	–	35×47×53	alive	37
11	30	37	central-right	–	22×23×35	alive	39
12	18	20	upper-anterior	+	20×20×28	alive	42
13	29	21	central	–	20×20×20	alive	39
14	26	23	central	–	20×20×25	alive	39
15	19	35	central	–	26×30×34	alive	37
16	35	38	central	+	25×30×40	alive	41
17	19	28	central	–	90×99×100	alive	39
18	28	29	central	–	65×70×100	alive	38
19	21	34	central	–	70×72×80	alive	39
20	34	23	suprarenal	+	18×18×20	alive	40
21	23	26	suprarenal	+	16×18×21	alive	38
22[2]	35	23	suprarenal	+	25×25×58	TOP	24
23[2]	30	30	suprarenal	+	45×45×50	NND	30
24	23	33	hepatic	–	40×40×60	alive	35
25[4]	27	21	pre-hepatic	–	11×24×28	NND	32

TOP = Termination of pregnancy; NND = neonatal death.

[1] Megacystis and bilateral hydronephrosis.

[2] Beckwith-Wiedemann syndrome; enlarged liver, spleen, kidneys, tongue and echogenic pancreas.

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Jejuno-ilial atresias, thought to be the consequence of vascular impairment during embryogenesis, are not usually associated with extra-intestinal abnormalities. Although none of the fetuses in the present series had chromosomal abnormalities, in a combined series of 589 affected infants, there were 5 cases of Down's syndrome [34]. This risk is relatively small, but still higher than the widely accepted level of risk at which karyotyping by amniocentesis is offered either on the basis of advanced maternal age or 'abnormal' maternal serum triple biochemistry. Unlike small bowel obstruction, anorectal malformations are associated with other abnormalities, mainly renal, and reduced amniotic fluid volume; furthermore, they have a poor prognosis.

The findings of bilateral moderate hydronephrosis, megacystis, and dilated bowel in the presence of normal or increased amniotic fluid volume should raise the suspicion that the underlying diagnosis is the megacystis microcolon intestinal hypoperistalsis syndrome which, unlike urethral obstruction, is more common in females than in males.

Ovarian cysts are the most common fetal abdominal cysts. They present in the third trimester of pregnancy, presumably because at earlier gestations there is insufficient hormonal stimulation, and they usually regress spontaneously either before or after delivery. Both in this study and in previous series, the cysts were not associated with other abnormalities [35–37]. Similarly, mesenteric or omental cysts and hepatic cysts have not been found to be associated with other abnormalities. Although an abdominal cyst due to severe hydronephrosis should theoretically be easy to distinguish from other abdominal cysts, this is not necessarily the case, as demonstrated in this study. The hydronephrosis can grow larger anteriorly to present as a central abdominal cyst with a thin wall; the compressed adrenal is presumably mistaken for a normal kidney.

Echogenic nodules in the liver have been reported in association with congenital infection and ischaemic hepatic necrosis [38, 39]. The possible association with trisomy 21 and the underlying mechanism remain to be determined. Adrenal cysts, presenting as multicystic perirenal cysts, in association with macroglossia and hepatosplenomegaly should raise the suspicion of the Beckwith-Wiede-

Sex	Diagnosis	Comment
F	mesenteric	PN resolving at 9 months
M	mesenteric	PN surgery
M	mesenteric	no details available
M	mesenteric	PN surgery
F	mesenteric	PN surgery
F	ovarian	PN surgery
F	ovarian	PN resolved by day 7
F	ovarian	PN resolved by day 5
F	ovarian	PN surgery
F	ovarian	PN resolved at 6 months
F	uncertain	AN resolved by 40 weeks
M	uncertain	AN resolved by 24 weeks
M	uncertain	AN resolved by 32 weeks
F	uncertain	AN resolved by 24 weeks
F	uncertain	AN resolved by 37 weeks
F	uncertain	AN resolved by 41 weeks
M	left renal	PN surgery
M	left renal	PN surgery
M	right renal	PN surgery
M	adrenal	PN resolved by 30 days
M	adrenal	PN resolving at 7 months
F[3]	adrenal	
F	adrenal	
F	hepatic	PN surgery
M	umbilical vein	

[3] Karyotype: 46,XX/46,XX dup(11p15).
[4] Nuchal oedema, aortic valve stenosis.

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mann syndrome; karyotyping is indicated because some cases may be due to duplication of the short arm of chromosome 11.

This study has confirmed the need for both detailed sonographic examination and karyotyping of malformed fetuses [16]. Furthermore, it demonstrates that chromosomal abnormalities are usually associated with multisystem malformations.

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