Diagnosis of fetal defects in twin pregnancies at routine ultrasound examination at 11–13 weeks' gestation

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Short title: First-trimester diagnosis of defects in twins

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CONTRIBUTION

What are the novel findings of this work?

The study demonstrates that first, in twins, as in singleton pregnancies, fetal defects essentially fall into three categories in relation to detectability at the 11-13 weeks scan: always detectable, never detectable or sometimes detectable, and second, some major fetal defects are more common in monochorionic than in dichorionic twins.

What are the clinical implications of this work?

In twin pregnancies a routine scan at 11-13 weeks' gestation, carried out according to a standardized protocol, can identify many major fetal defects.

ABSTRACT

Objective To examine the performance of the routine 11-13 weeks scan in detecting fetal defects in twin pregnancies and to examine if in pregnancies with fetal defects, compared to those with normal fetuses, there is increased incidence of nuchal translucency (NT) thickness ≥95th and ≥99th percentiles or intertwin discordance in crown-rump length (CRL) ≥10% and ≥15%.

Methods This was a retrospective analysis of prospectively collected data in twin pregnancies undergoing routine ultrasound examination for fetal anatomy, according to standardized protocols, at 11-13 weeks' gestation between 2002 and 2019. Pregnancies with known chromosomal abnormalities were excluded. The final diagnosis of fetal defects was based on the results of postnatal examination in the case of livebirths and on the findings of the last ultrasound examination in the cases of pregnancy termination, miscarriage or stillbirth. The performance of the 11-13 weeks scan in the detection of fetal defects was determined.

Results The study population of 6,366 twin pregnancies with two live fetuses at 11-13 weeks' gestation, included 4,979 (78.2%) dichorionic (DC) and 1,387 (21.8%) monochorionic (MC) twin pregnancies. The main findings were: first, the overall incidence of fetal defects was higher in MC than DC twins (2.8% vs. 1.3%); second, the proportion of defects diagnosed in the first-trimester was higher in MC than in DC twins (52.6% vs. 27.1%); third, the pattern of defects in relation to detectability at the 11-13 weeks scan, always detectable, sometimes detectable and never detectable, was similar to that previously reported in singleton pregnancies; fourth, always detectable defects included acrania, alobar holoprosencephaly, encephalocele, pentalogy of Cantrell, exomphalos, body stalk anomaly, TRAP sequence and conjoined twins; fifth, the incidence of fetal NT ≥95th percentile was higher in those with than without defects (16.5% vs. 4.5% in DC twins and 19.2% vs. 5.9% in MC twins) and this was also true for NT ≥99th percentile (8.3% vs. 1.0% in DC twins and 15.4% vs. 2.0% in MC twins); and sixth, the incidence of CRL discordance ≥10% was higher in those with than without defects (20.2% vs. 7.9% in DC twins

and 33.8% vs. 9.3% in MC twins) and this was also true for CRL discordance ≥15% (10.1% vs. 1.9% in DC twins and 28.2% vs. 2.8% in MC twins).

Conclusions First, fetal defects are more common in MC than in DC twin pregnancies, second, first-trimester detection of fetal defects in DC twin pregnancies is similar to that in singleton pregnancies, third, detectability of defects in MC twins is higher than in DC twins, fourth, in twin pregnancies with fetal defects there is a higher intertwin discordance in CRL and incidence of high NT, but the predictive performance of screening by these markers is poor.

INTRODUCTION

Ultrasound examination at 11-13 weeks' gestation is widely used for assessment of gestational age,[1] diagnosis of multiple pregnancies and chorionicity,[2] screening for fetal aneuploidies[3-6] and diagnosis of fetal non-chromosomal defects.[7-11] Two studies in a combined total of 146,188 singleton pregnancies, examined between 2006 and 2019, reported that a routine scan for fetal anatomy at 11-13 weeks' gestation can identify about one fourth of all defects and that defects can essentially be divided into first, those that should be always detectable, such as acrania and exomphalos, second, those that are potentially detectable, such as major cardiac defects and spina bifida, and third, those that are undetectable; the latter group includes, first, those that develop during the second or third trimester of pregnancy, such as fetal tumors, second, the phenotypic expression of the abnormality becomes apparent in later pregnancy as a result of physiological changes in the fetus, such as increased fetal swallowing unmasking a bowel obstruction, or third, they evolve with advancing gestational age, such as short limbs in achondroplasia or pulmonary and aortic stenosis.[10,11]

Previous studies on fetal defects in twin pregnancies fall into three categories: first, those that reported the management of pregnancies discordant for specific major fetal abnormalities, such as dichorionic (DC) twins discordant for major trisomies, DC and monochorionic (MC) twins discordant for anencephaly or MC twins with twin reversed arterial perfusion (TRAP) sequence;[12-15] second, studies examining the association between intertwin discordance in crown-rump length (CRL) and incidence of fetal anomalies;[16,17] and third, screening studies for fetal defects. Sperling *et al.*, reported a multicentre study in 421 DC and 74 MC twin pregnancies; fetal defects were identified in 24 (1.9%) cases and 13% of these were detected in the first-trimester scan.[18] D'Antonio *et al.*, examined 820 DC and 264 MC twin pregnancies and reported than in 42 (3.9%) pregnancies one or more fetuses had structural defects, 27% of which were detected in the first-trimester scan; increasing discordance in CRL and nuchal translucency (NT) thickness were associated with fetal defects but their predictive performance was only moderately good.[19]

The objectives of this study of 6,366 twin pregnancies undergoing a routine examination of the fetal anatomy is to investigate further the performance of the 11-13 weeks scan in first, the detection of fetal defects, and second, to examine if in pregnancies with fetal defects, compared to those with normal fetuses, there is increased incidence of NT ≥95th and ≥99th percentile or higher intertwin discordance in CRL.

METHODS

Study population

This was a retrospective analysis of prospectively collected data obtained from women with twin pregnancies undergoing routine ultrasound examination at 11-13 weeks' gestation at King's College Hospital and the Fetal Medicine Centre, London (January 2002 – February 2019), Medway Maritime Hospital, Gillingham (February 2007 – February 2019) or Southend University Hospital, Essex (March 2009 – February 2019), England, UK. The three participating hospitals are maternity units and offer routine ultrasound examination in all patients. The Fetal Medicine Centre is a private outpatient clinic of self-referred patients that deliver in many different hospitals. The inclusion criteria for this study were DC and MC twin pregnancies with two live fetuses at 11-13 weeks' gestation and known pregnancy outcome; we included pregnancies with TRAP sequence in which the pump twin was alive and there was demonstrable blood flow in the recipient. We excluded pregnancies that were referred from other hospitals for assessment and those with chromosomal defects diagnosed prenatally or postnatally. This study did not require ethics committee approval.

Ultrasound examination at 11-13 weeks

In the 11-13 weeks visit we recorded maternal characteristics and performed an ultrasound scan to first, determine gestational age from the measurement of CRL of the larger twin,[1] second, determine chorionicity from the number of placentas and the presence or absence of the lambda sign at the inter-twin membrane-placental junction,[2] third, measure fetal NT thickness as part of screening for trisomies 21, 18 and 13,[5,6,20] and fourth, diagnose any fetal defects.[11]

All ultrasound examinations were carried out according to standardized protocols by sonographers that had obtained the Fetal Medicine Foundation Certificate of Competence in ultrasound examination for fetal defects or by trainees under the supervision of certified sonographers. The ultrasound examinations were performed transabdominally, using 3-7.5 MHz

curvilinear transducers, but in 2-3% of cases when there were technical difficulties to obtain adequate views a transvaginal scan (3-9 MHz) was also carried out. The time allocated for the ultrasound examination of twin pregnancies was 60 minutes. All cases of suspected fetal defects were examined, usually on the same day, by a fetal medicine specialist. Likewise, all cases of suspected fetal cardiac defects were examined by a fetal cardiologist.

At 11-13 weeks it was aimed to obtain a transverse section of the head to demonstrate the skull, midline echo and the choroid plexuses, a mid-sagittal view of the face to demonstrate the nasal bone, sagittal section of the spine to demonstrate kyphoscoliosis, and transverse and sagittal sections of the trunk and extremities to demonstrate the stomach, bladder, abdominal insertion of the umbilical cord, all the long bones, hands and feet. In 2006 the protocol was expanded to include Doppler for assessment of blood flow across the tricuspid valve and in the ductus venosus.[21-24] In 2009 we added use of color Doppler to assess the 4-chamber view of the heart and outflow tracks, transverse views of the face to demonstrate orbits, upper lip and palate, midsagittal view of the head to demonstrate the midbrain and brain stem and sagittal section of the spine to demonstrate the spine and overlying skin. Examination of the posterior fossa was included in the protocol only after 2011 and this was based on visual assessment rather than measurements of the brain stem and brain stem to occipital bone diameter.[25-28] Fetal echocardiography by a cardiologist was carried out at 11-13 weeks in all cases of fetal NT above the 99th percentile for CRL and at 20 weeks in those with NT between the 95th and 99th percentiles or regurgitation across the tricuspid valve or abnormal flow in the ductus venosus at 11-13 weeks.

Second and third trimester scans

At King's College Hospital the routine first trimester scan was offered to all women booked in this hospital for routine pregnancy care from 1992. In the UK the 11-13 weeks scan was offered routinely to all pregnant women only after 2007; before this time, several hospitals referred all their patients to King's for a routine first trimester scan but carried out all subsequent second and third trimester scans. Similarly, most patients who had their 11-13 weeks scan at the Fetal

Medicine Centre had follow-up scans in their own hospitals.

In the second trimester scans in the four participating units it was aimed to obtain the following views: transverse section of the head at the level of the septum cavum pellucidum and lateral ventricles, sub-occipito-bregmatic view to examine the midbrain, cerebellum and vermis, mid-sagittal view of face to examine the nasal bone and exclude micrognathia, transverse views of the orbits, upper lip and palate, sagittal, coronal and transverse views of the spine, sweep through heart in transverse plane to include 4-chamber view, outflow tracts and 3-vessel view, transverse and sagittal sections of the thorax and abdomen to examine the lungs, diaphragm, liver, stomach and bowel, umbilical cord insertion and kidneys, bladder and ureters, systematic examination of upper and lower limbs for length and shape of each bone, position and movement of each joint and examination of both hands and feet, including the digits. Examination of the genitalia was not a compulsory part of the protocol. The third trimester scans were primarily aimed at assessing fetal growth, amniotic fluid volume and Doppler measurements in the umbilical and middle cerebral arteries; in MC twins we also examined flow in the ductus venosus. The sonographers were instructed to assess the fetal anatomy in the same systematic way as in the second trimester, but it was accepted that depending on the fetal position examination of the fetal face, sacrum and extremities may not be possible.

Outcome measures

Data on pregnancy outcome were collected from computerized records of delivery wards and neonatal units or the patient general practitioners or the patients themselves and all prenatal and postnatal findings were recorded in a Fetal Database.

The final diagnosis of fetal defects was based on the results of postnatal examination in the case of livebirths and on the findings of the last ultrasound examination in the cases of pregnancy termination, miscarriage or stillbirth, because in these cases postmortem examination was not performed systematically. All babies in our hospitals are examined in the neonatal period by a pediatrician, but certain asymptomatic internal defects are inevitably missed. For example,

ventricular septal defects or coarctation of the aorta with patent arterial duct may be missed by early neonatal examination, which does not include echocardiography.

Ventriculomegaly was included only if the atrial width during the second or third trimesters was ≥ 15 mm. Hydronephrosis was considered to be present if there was pelvicalyceal dilatation with an anteroposterior diameter ≥ 10 mm in the 2nd trimester or ≥15 mm in the 3rd trimester. We wanted to consider only severe ventriculomegaly and hydronephrosis because the incidence of milder degrees is much higher, and their clinical consequences are questionable. In cases of exomphalos with a sac containing only bowel, megacystis, ventriculomegaly and hydronephrosis a follow up scan was carried out and the cases with spontaneous resolution of the abnormality were considered to be normal. Polydactyly was considered to be present if the extra digit contained bone and talipes was considered to be present if the baby required postnatal treatment.

We included all cases of defects of the heart and great vessels but excluded cases of persistent left superior vena cava and aberrant right subclavian artery because these are variants of normal rather than true defects. Cases with coarctation of the aorta, aortic arch hypoplasia and interrupted aortic arch were classified as arch defects. Cases with at least two different major heart defects were classified as complex.

Association of fetal defects with high NT thickness and high CRL discordance

The incidence of fetal NT ≥95th and ≥99th percentiles for CRL in each fetus with defects was determined and compared to that in fetuses without defects using Chi-square with Yates' correction for large sample sizes.[29,30] Similarly, the incidence of CRL discordance ≥10% and ≥15% in pregnancies with at least one abnormal fetus was compared to that in pregnancies with two normal fetuses.[31]

RESULTS

Study population

The study population of 6,366 twin pregnancies with two live fetuses at 11-13 weeks' gestation and known pregnancy outcome, was composed of 4,979 (78.2%) DC and 1,387 (21.8%) MC twin pregnancies, including 67 (4.8%) that were monochorionic-monoamniotic (MCMA). The median maternal age was 33.7 (IQR 29.8-37.2) years, the median weight was 67.6 (IQR 60.0-77.1) Kg, the racial origin of the women was White in 5,242 (82.3%), Black in 660 (10.4%), South Asian in 273 (4.3%), East Asian in 91 (1.4%) and mixed in 100 (1.6%). At the time of the first trimester scan the median fetal CRL of the larger twin was 65.3 (IQR 60.2-71.2) mm and median gestational age was 12.9 (IQR 12.5-13.3) weeks.

Termination of the whole pregnancy because of fetal defects or miscarriage before 20 weeks' gestation occurred in 119 of pregnancies. In the remaining 6,247 pregnancies follow-up scans were carried out in our four participating units in 69.0% (4,308/6,247) of cases.

Fetal defects

Fetal defects were identified either prenatally or postnatally in 1.7% (211/12,732) twins, including 2.8% (78/2,774) of MC twins, which was higher than in DC twins (1.3%, 133/9,958; $p<0.0001$).

In the 131 of 4,979 DC twin pregnancies with fetal defects one fetus was affected in 129 and both were affected in two; in the 71 of 1,387 MC twin pregnancies with fetal defects one fetus was affected in 64 and both were affected in seven. In the 11-13 weeks scan we diagnosed 36.5% (77/211) of the defects, including 27.1% (36/133) of the defects in the fetuses from DC twin pregnancies and 52.6% (41/78) in the fetuses from MC twin pregnancies (Table 1).

At 11-13 weeks we diagnosed first, all cases of acrania, alobar holoprosencephaly and encephalocele, and 40% of cases of open spina bifida, but none of severe ventriculomegaly,

absent corpus callosum, hypoplastic cerebellum and / or vermis; second, 33% of cases of cleft lip and palate, but none of cleft lip only; third, 50% of cases of congenital diaphragmatic hernia, but none of congenital pulmonary airways malformation; fourth, 52% (14/27) of tetralogy of Fallot, hypoplastic left heart syndrome, arch defects, tricuspid atresia or complex heart defects, but none of atrioventricular or ventricular septal defects, transposition of great arteries, aortic or pulmonary stenosis/atresia, double or right aortic arch, arrythmias or rhabdomyomas; fifth, all cases of exomphalos, but none of duodenal atresia or bladder exstrophy; sixth, 71% of cases of lower urinary tract obstruction, but none of the other urogenital defects; seventh, 67% (6/9) of cases of lethal skeletal dysplasia, fetal akinesia deformation sequence or amputations of extremities, but none of cases of hemivertebra, defects of digits, deformities of wrists or talipes; and eighth, all cases of body stalk anomaly, pentalogy of Cantrell, TRAP sequence and conjoined twins, but none of lymphangioma or sacrococcygeal teratoma.

Association of fetal defects with high NT thickness

In the total population of 12,732 fetuses there were 638 (5.0%) with fetal NT ≥95th percentile and 172 (1.4%) with NT ≥99th percentile. In fetuses from both DC and MC twin pregnancies the incidence of NT ≥95th and NT ≥99th percentile was higher in those with than those without defects (Table 2). In the total population of fetuses from twin pregnancies the percentage with fetal defects was 5.8% (37/638) in those with NT ≥95th percentile and 1.4% (174/12,094) for NT <95th (relative risk 4.031, 95% CI, 2.853-7.902; P<0.0001). The percentage with fetal defects was 13.4% (23/172) in those with NT ≥99th percentile and 1.5% (188/12,560) for NT <99th (relative risk 8.934 (95% CI, 5.953-13.407; P<0.0001).

Association of fetal defects with high intertwin CRL discordance

In all twin pregnancies the median intertwin discordance in CRL was 3.3% (IQR 1.4%-6.0%); the intertwin discordance in CRL was ≥10% in 8.7% (557/6,366) of pregnancies and ≥15% in 2.5% (162/6,366). In both DC and MC twin pregnancies the incidence of CRL discordance ≥10% and ≥15% was higher in those with than those without defects (Table 2). In the total population of twin

pregnancies the percentage with fetal defects was 9.0% (50/557) in those with CRL discordance ≥10% and 2.6% (150/5,809) for CRL discordance <10% (relative risk 3.476, 95% CI, 2.555-4.730; P<0.0001). The percentage with fetal defects was 20.4% (33/162) in those with CRL discordance ≥15% and 2.7% (167/6,204) for CRL discordance <15% (relative risk 7.568 (95% CI, 5.390-10.624; P<0.0001).

DISCUSSION

Main findings of the study

This study of 6,366 twin pregnancies with two live fetuses at 11-13 weeks' gestation and known pregnancy outcome involved systematic examination of the fetal anatomy according to standardized protocols and allocated period of 60 minutes; however, the protocol evolved over the years with the requirement for examination of addition structures. Fetuses with transient anomalies, including exomphalos with a sac containing only bowel, megacystis, ventriculomegaly and hydronephrosis, were considered to be normal. The main findings of the study are: first, the overall incidence of fetal defects was higher in MC than DC twins (2.8% vs. 1.3%); second, the proportion of defects diagnosed in the first-trimester was higher in MC than DC twins (52.6% vs. 27.1%); third, the pattern of defects in relation to detectability at the 11-13 weeks scan, always detectable, sometimes detectable and never detectable, was similar to that previously reported in singleton pregnancies;[10,11] fourth, always detectable defects included acrania, alobar holoprosencephaly, encephalocele, pentalogy of Cantrell, exomphalos, body stalk anomaly, TRAP sequence and conjoined twins; fifth, the incidence of fetal NT ≥95th percentile was higher in those with than without defects (16.5% vs. 4.5% in DC twins and 19.2% vs. 5.9% in MC twins) and this was also true for NT ≥99th percentile (8.3% vs. 1.0% in DC twins and 15.4% vs. 2.0% in MC twins); and sixth, the incidence of CRL discordance ≥10% was higher in those with than without defects (20.2% vs. 7.9% in DC twins and 33.8% vs. 9.3% in MC twins) and this was also true for CRL discordance ≥15% (10.1% vs. 1.9% in DC twins and 28.2% vs. 2.8% in
MC twins).

Comparison with findings of previous studies

In the 11-13 weeks scan we diagnosed 36.5% of the defects, including 27.1% of the defects in fetuses from DC twin pregnancies and 52.6% in fetuses from MC twin pregnancies. In two previous studies in 495 and 1,084 twin pregnancies the proportion of defects detected in the

first-trimester was 13% and 27%, respectively.[18,19] In relation to the types of defects that are detected at 11-13 weeks, the results are consistent with those of our previous studies in singleton pregnancies, which highlighted that defects can essentially be divided into those that should be always detectable, those that are potentially detectable, and those that are undetectable.[10,11] The higher detectability of defects in MC than DC twin pregnancies is to a great extent the consequence of first, TRAP sequence and conjoined twins which are unique to MC twinning and accounted for 24% of defects in such pregnancies, and second, easily detectable defects that were more common in MC than in DC twins, such as acrania, exomphalos, lower urinary tract obstruction and body stalk anomaly. Successful first-trimester diagnosis of the potentially detectable defects depends on first, the objectives set for such a scan and consequently the time allocated for the fetal examination, the expertise of the sonographer and the quality of the equipment used, and second, the presence of an easily detectable marker for an underlying abnormality, such as increased NT or abnormal flow across the tricuspid valve and in the ductus venosus for cardiac defects and posterior fossa defects for open spina bifida.

We found that in pregnancies with fetal defects there is a higher intertwin discordance in CRL and incidence of high NT, but the predictive performance of screening by CRL discordance of ≥10% or ≥15% or fetal NT ≥95th or ≥99th is poor. These findings are consistent with the results of previous smaller studies. Kalish *et al.*, examined 159 DC twin pregnancies at 11-14 weeks' gestation, including 9 with fetal structural or chromosomal defects, and reported that the incidence of CRL discordance >10% was higher in those with than without defects (22.2% vs 2.8%).[16] Harper *et al.*, examined 594 DC twin pregnancies at 7-14 weeks' gestation, including 111 with fetal defects, and reported that the incidence of CRL discordance ≥11% was higher in those with than without defects (27.3% vs. 17.4%).[17] D'Antonio *et al.*, examined 820 DC and 264 MC twin pregnancies at 11-14 weeks' gestation, including 42 with fetal structural defects, and reported that increased intertwin discordance in either CRL or NT was associated with increased risk for fetal defects, but their predictive accuracy was only moderately good (CRL discordance: detection rate 76%, false positive rate 45%; NT discordance: detection rate 71%, false positive rate 40%).[19]

Strengths and limitations of the study

The main strength of our study is the examination of a large number of twin pregnancies attending for routine first-trimester scan using standardized protocols and appropriately trained sonographers in units with expertise in fetal medicine and fetal cardiology. However, the overall number of cases is still small for meaningful conclusions to be drawn concerning detectability of individual defects. This problem of small numbers of individual defects cannot be overcome by reporting overall detection rates because these are inherently dependent on the distribution of different types of defects within a given study population. During the study, which spanned over a period of 17 years, there has been an evolution in the detail of the first-trimester ultrasound scan and incorporation of new easily recognizable markers of underlying defects.

The main limitation of this and most previous studies investigating the effectiveness of routine ultrasound examination in the prenatal diagnosis of fetal defects relates to ascertainment of such defects. For example, although in our participating centers all neonates are examined by pediatricians it is possible that asymptomatic defects of internal organs could be missed. Similarly, we assumed that all morphologically normal neonates were chromosomally normal and in the cases of pregnancy termination, miscarriage or stillbirth we assumed that the findings of the last ultrasound examination were correct because in these cases postmortem examination was not performed systematically. Furthermore, in this study about 30% of the patients delivered in hospitals other than the ones where the first-trimester scan was carried out.

Conclusions

First, fetal defects are more common in MC than in DC twin pregnancies, second, first-trimester detection of fetal defects in DC twin pregnancies is similar to that in singleton pregnancies, third, detectability of defects in MC twins is higher than in DC twins, fourth, in twin pregnancies with high intertwin discordance in CRL and high NT the incidence of fetal defects is increased, but the predictive performance of screening by these markers is poor.

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Table 1. Diagnosis of fetal defects.

Defect	Singleton pregnancies*		Fetuses in twin pregnancies					
			All (n=12,732)		Dichorionic (n=9,958)		Monochorionic (n=2,774)	
	Prevalence	DR 11-13 w	Prevalence	DR 11-13 w	Prevalence	DR 11-13 w	Prevalence	DR 11-13 w
Central nervous system	**1 in 437**	**47.6**	**26 (1 in 490)**	**15 (57.7)**	**18 (1 in 553)**	**9 (50.0)**	**8 (1 in 347)**	**6 (75.0)**
Acrania	1 in 2104	100	10 (1 in 1273)	10 (100)	5 (1 in 1992)	5 (100)	5 (1 in 555)	5 (100)
Encephalocele	1 in 6733	100	2 (1 in 6366)	2 (100)	1 (1 in 9958)	1 (100)	1 (1 in 2774)	1 (100)
Spina bifida	1 in 1712	59.3	5 (1 in 2546)	2 (40.0)	5 (1 in 1992)	2 (40.0)		
Alobar holoprosencephaly	1 in 10100	100	1 (1 in 12732)	1 (100)	1 (1 in 9958)	1 (100)		
Agenesis of the corpus callosum	1 in 3885	0	2 (1 in 6366)		2 (1 in 4979)			
Ventriculomegaly severe	1 in 5611	0	1 (1 in 12732)				1 (1 in 2774)	
Hypoplastic cerebellum / vermis	1 in 6733	13.3	5 (1 in 2546)		4 (1 in 2490)		1 (1 in 2774)	
Face	**1 in 962**	**18.1**	**13 (1 in 979)**	**3 (23.1)**	**6 (1 in 1660)**	**2 (33.0)**	**7 (in 396)**	**1 (14.3)**
Cleft lip and palate	1 in 1942	34.6	9 (1 in 1415)	3 (33.3)	4 (1 in 2490)	2 (50.0)	5 (1 in 555)	1 (20.0)
Cleft lip only	1 in 3607	0	4 (1 in 3183)		2 (1 in 4979)		2 (1 in 1387)	
Thorax	**1 in 1403**	**9.7**	**11 (1 in 1157)**	**2 (18.2)**	**9 (1 in 1106)**	**1 (11.0)**	**2 (1 in 1387)**	**1 (50.0)**
CPAM	1 in 2349	0	7 (1 in 1819)		6 (1 in 1660)		1 (1 in 2774)	
Congenital diaphragmatic hernia	1 in 4208	29.2	4 (1 in 3183)	2 (50.0)	3 (1 in 3319)	1 (33.3)	1 (1 in 2774)	1 (100)
Heart	**1 in 260**	**30.1**	**58 (1 in 220)**	**14 (24.1)**	**38 (1 in 262)**	**11 (29.0)**	**20 (1 in 139)**	**3 (15.0)**
Tetralogy of Fallot	1 in 3607	39.3	8 (1 in 1592)	3 (37.5)	3 (1 in 3319)	1 (33.3)	5 (1 in 555)	2 (40.0)
Transposition of great arteries	1 in 6733	13.3	2 (1 in 6366)		1 (1 in 9958)		1 (1 in 2774)	
Hypoplastic left heart	1 in 2525	92.5	7 (1 in 1819)	6 (85.7)	7 (1 in 1423)	6 (85.7)		
Atrioventricular septal defect	1 in 9182	90.9	2 (1 in 6366)		2 (1 in 4979)			
Ventricular septal defect	1 in 743	0	11 (1 in 1157)		6 (1 in 1660)		5 (1 in 555)	

Arch abnormalities	1 in 2658	31.6	7 (1 in 1819)	3 (42.9)	5 (1 in 1992)	3 (60.0)	2 (1 in 1387)	
Double/right aortic arch	1 in 3156	15.6	7 (1 in 1819)		6 (1 in 1660)		1 (1 in 2774)	
Tricuspid atresia	1 in 14428	100	2 (1 in 6366)	1 (50.0)	1 (1 in 9958)		1 (1 in 2774)	1 (100)
Pulmonary atresia	1 in 9182	100	2 (1 in 6366)		2 (1 in 4979)			
Pulmonary stenosis	1 in 10100	0	2 (1 in 6366)		1 (1 in 9958)		1 (1 in 2774)	
Aortic stenosis	1 in 16833	0	1 (1 in 12732)		1 (1 in 9958)			
Complex heart defect	1 in 4040	60	3 (1 in 4244)	1 (33.3)	1 (1 in 9958)	1 (100)	2 (1 in 1387)	
Rhabdomyomas	1 in 16833	0	1 (1 in 12732)		1 (1 in 9958)			
Arrhythmia	1 in 33666	0	3 (1 in 4244)		1 (1 in 9958)		2 (1 in 1387)	
Gastrointestinal / Abdominal wall	**1 in 727**	**63.3**	**8 (1 in 1592)**	**6 (75.0)**	**5 (1 in 1992)**	**4 (80.0)**	**3 (1 in 925)**	**2 (66.7)**
Exomphalos with bowel or liver	1 in 2295	100	6 (1 in 2122)	6 (100)	4 (1 in 2490)	4 (100)	2 (1 in 1387)	2 (100)
Bladder exstrophy	1 in 50499	0	1 (1 in 12732)				1 (1 in 2774)	
Duodenal atresia	1 in 11222	0	1 (1 in 12732)		1 (1 in 9958)			
Urogenital	**1 in 196**	**8.4**	**30 (1 in 424)**	**5 (16.7)**	**22 (1 in 453)**	**2 (9.0)**	**8 (in 347)**	**3 (37.5)**
Lower urinary tract obstruction	1 in 1942	71.2	7 (1 in 1819)	5 (71.4)	4 (1 in 2490)	2 (50.0)	3 (1 in 925)	3 (100)
Hydronephrosis severe	1 in 1278	0	2 (1 in 6366)		2 (1 in 4979)			
Polycystic kidneys bilateral	1 in 7214	7.1	1 (1 in 12732)		1 (1 in 9958)			
Multicystic kidneys bilateral	1 in 25249	0	1 (1 in 12732)		1 (1 in 9958)			
Multicystic kidney unilateral	1 in 1741	0	5 (1 in 2546)		4 (1 in 2490)		1 (1 in 2774)	
Renal agenesis bilateral	1 in 7769	15.4	1 (1 in 12732)		1 (1 in 9958)			
Pelvic kidney/agenesis unilateral	1 in 814	2.4	6 (1 in 2122)		4 (1 in 2490)		2 (1 in 1387)	
Duplex kidney	1 in 1161	0	4 (1 in 3183)		2 (1 in 4979)		2 (1 in 1387)	
Dilated ureter unilateral	1 in 16833	0	1 (1 in 12732)		1 (1 in 9958)			
Hypospadias	1 in 3885	0	1 (1 in 12732)		1 (1 in 9958)			
Ambiguous genitalia	1 in 20199	0	1 (1 in 12732)		1 (1 in 9958)			
Skeleton / Extremities	**1 in 449**	**29.8**	**35 (1 in 364)**	**6 (17.1)**	**29 (1 in 343)**	**5 (17.0)**	**6 (1 in 462)**	**1 (16.7)**

Skeletal dysplasia lethal	1 in 7214	71.4	2 (1 in 6366)	1 (50.0)	2 (1 in 4979)	1 (50.0)		
Fetal akinesia deformation sequence	1 in 9182	18.2	3 (1 in 4244)	2 (66.7)	2 (1 in 4979)	1 (50.0)	1 (1 in 2774)	1 (100)
Absent hand, arm, leg or foot	1 in 4208	75	4 (1 in 3183)	3 (75.0)	4 (1 in 2490)	3 (75.0)		
Hemivertebra	1 in 8416	33.3	1 (1 in 12732)		1 (1 in 9958)			
Abnormal digits	1 in 1712	42.4	4 (1 in 3183)		4 (1 in 2490)			
Deformity of wrists			3 (1 in 4244)		1 (1 in 9958)		2 (1 in 1387)	
Talipes	1 in 1086	2.2	18 (1 in 707)		15 (1 in 664)		3 (1 in 925)	
Other	**1 in 449**	**29.8**	**24 (1 in 531)**	**22 (91.7)**	**3 (1 in 3319)**	**1 (33.0)**	**21 (1 in 132)**	**21 (100)**
Body stalk anomaly	1 in 6312	100	2 (1 in 6366)	2 (100)			2 (1 in 1387)	2 (100)
Pentalogy of Cantrell	1 in 50499	100	1 (1 in 12732)	1 (100)	1 (1 in 9958)	1 (100)		
Lymphangioma	1 in 25249	0	1 (1 in 12732)		1 (1 in 9958)			
Sacrococcygeal teratoma	1 in 50499	50	1 (1 in 12732)		1 (1 in 9958)			
TRAP sequence	-	-	13 (1 in 979)	13 (100)			13 (1 in 213)	13 (100)
Conjoined twins	-	-	6 (1 in 2122)	6 (100)			6 (1 in 462)	6 (100)
Multiple	**1 in 12625**	**25.0**	**6 (1 in 2122)**	**4 (66.7)**	**3 (1 in 3319)**	**1 (33.0)**	**3 (1 in 925)**	**3 (100)**
CoA, Clenched hands, Talipes	-	-	1 (1 in 12732)		1 (1 in 9958)			
CoA, Multicystic kidneys bilateral	-	-	1 (1 in 12732)	1 (100)			1 (1 in 2774)	1 (100)
Dandy Walker malformation, Micrognathia, Cleft palate	-	-	1 (1 in 12732)		1 (1 in 9958)			
Dextrocardia, Phocomelia, Renal agenesis bilateral	-	-	1 (1 in 12732)	1 (100)			1 (1 in 2774)	1 (100)
HLHS, Exomphalos bowel	-	-	1 (1 in 12732)	1 (100)	1 (1 in 9958)	1 (100)		
Spina bifida, Bladder exstrophy	-	-	1 (1 in 12732)	1 (100)			1 (1 in 2774)	1 (100)
Total			**211 (1.7)**	**77 (36.5)**	**133 (1.3)**	**36 (27.1)**	**78 (2.8)**	**41 (52.6)**

DR = Detection rate; CPAM = Congenital pulmonary airway malformation; CoA = Coarctation of the aorta
* These data are from our previous study in singleton pregnancies.[11]

Table 2. Incidence of high NT and high CRL discordance in DC and MC twin pregnancies with and without defects.

	No fetal defects	Fetal defects	p
NT ≥95th percentile			
Dichorionic	4.5%, 441/9,825	16.5%, 22/133	<0.0001
Monochorionic	5.9%, 160/2,696	19.2%, 15/78	<0.0001
NT >99th percentile			
Dichorionic	1.0%, 96/9,825	8.3%, 11/133	<0.0001
Monochorionic	2.0%, 53/2,696	15.4%, 12/78	<0.0001
CRL discordance ≥10%			
Dichorionic	7.9%, 384/4,850	20.2%, 26/129	<0.0001
Monochorionic	9.3%, 123/1,316	33.8%, 24/71	<0.0001
CRL discordance ≥15%			
Dichorionic	1.9%, 92/4,850	10.1%, 13/129	<0.0001
Monochorionic	2.8%, 37/1,316	28.2%, 20/71	<0.0001