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Single umbilical artery at 11–14 weeks' gestation: relation to chromosomal defects

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KEYWORDS: chromosomal defect; color Doppler; first trimester; nuchal translucency; single umbilical artery; trisomy 18

ABSTRACT

Objective *To determine the possible association between single umbilical artery (SUA) at 11–14 weeks of gestation and the incidence of chromosomal abnormalities.*

Methods *Color flow imaging of the fetal pelvis was used to determine the number of umbilical arteries in 717 fetuses immediately before chorionic villus sampling for karyotyping at 11–14 weeks' gestation.*

Results *Single umbilical artery (SUA) was diagnosed in 21/634 (3.3%) chromosomally normal fetuses, in 5/44 (11.4%) with trisomy 21, 14/18 (77.8%) with trisomy 18 and 2/21 (9.5%) with other chromosomal defects. In the chromosomally normal group there was no significant difference in median fetal crown–rump length or nuchal translucency (NT) between those with a single and those with two umbilical arteries. In the 42 fetuses with SUA the expected number of cases of trisomy 21, estimated on the basis of maternal age, gestational age and fetal NT, was 4.7, which was not significantly different from the observed 5. The corresponding numbers for trisomy 18 were 2.0 for expected and 14 for observed (Fisher's exact test* $P = 0.0016$*).*

Conclusion *A SUA at 11–14 weeks' gestation has a high association with trisomy 18 and other chromosomal defects.* *Copyright © 2003 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

A single umbilical artery (SUA) is found in 0.2–1.9% of deliveries[1–5]. The condition is associated with malformations of all major organ systems and chromosomal defects[5,6]. Previous ultrasonographic studies, in the second and third trimesters of pregnancy, reported chromosomal defects in about 10% of fetuses with SUA, most commonly trisomy 18, but in the vast majority of such cases there were other major defects (Table 1)[4,7–23].

In this study we examine the association between SUA and chromosomal abnormalities at 11–14 weeks' gestation. Since the associated chromosomal defects have a high rate of intrauterine lethality[24], we hypothesized that, at this gestation, both the incidence of SUA and the incidence of chromosomal defects would be higher than those reported at birth or in the second trimester of pregnancy.

METHODS

This was a prospective study in 717 consecutively examined singleton pregnancies to determine the incidence of SUA in fetuses undergoing karyotyping by chorionic villus sampling (CVS) at 11–14 weeks' gestation. In all cases there was prior screening for chromosomal defects by a combination of maternal age and fetal nuchal translucency (NT) and the patients included in this study were those that after counseling elected to have invasive testing[25].

An oblique transverse section of the lower fetal abdomen, including the umbilicus and the fetal bladder, was first obtained and color flow mapping was then used to visualize the umbilical arteries on either side of the bladder and in continuity with the umbilical cord insertion to the fetus (Figure 1). All the scans were performed transabdominally using 5-MHz transducers (Aloka 5000, Aloka, Tokyo, Japan; Toshiba Powervision, Toshiba, Tokyo, Japan). The fetal NT and crown–rump length (CRL) were also measured and a systematic search was made for the detection of any major anomalies. Examination of the umbilical arteries was successfully achieved in all cases and this added about 1 min to the overall time of about 15 min for the 11–14-week scan.

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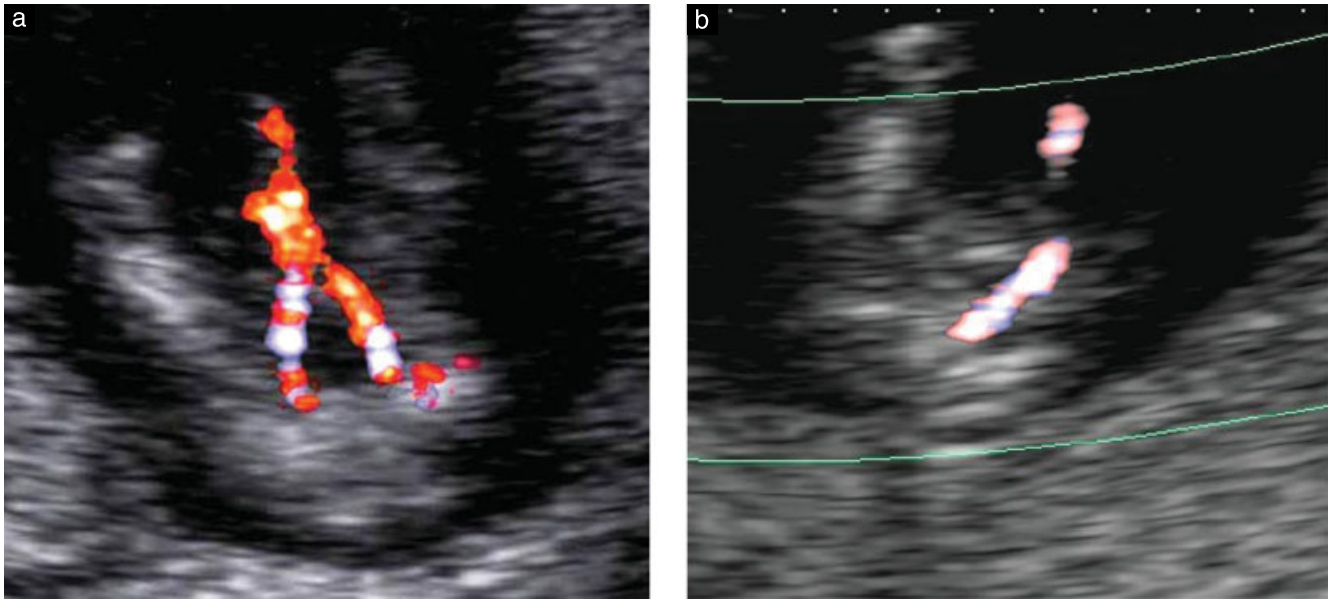

Figure 1 Color flow imaging illustrating visualization of the umbilical (superior vesical arteries) on either side of the bladder at 12 weeks. (a) A normal fetus with two umbilical arteries and (b) a trisomy 18 fetus with a single umbilical artery.

Demographic characteristics and ultrasound findings were recorded in a fetal database at the time of the examination. In all cases CVS was carried out and when the results of fetal karyotype were made available they were also entered in the database.

Statistical analysis

The Mann–Whitney *U*-test was used to compare the median fetal CRL and NT in those with a single and those with two umbilical arteries. Fisher's exact test was used to compare the observed incidence of chromosomal defects to the incidence estimated on the basis of maternal age, CRL and NT.

RESULTS

The median maternal age was 37 (range, 19–49) years, the median fetal CRL was 65 (range, 45–84) mm and the median gestation was 12 (range, 11–14) weeks. The fetal NT was above the 95th centile for CRL in 258/717 (36%) cases. SUA was diagnosed in 42/717 (5.9%) cases. The fetal karyotype was normal in 634 pregnancies and abnormal in 83 (11.6%).

In the chromosomally normal group the incidence of SUA was 3.3% (21/634 cases) and there was no significant difference in median fetal CRL or NT between those with a single and those with two umbilical arteries (62 vs. 66 mm, $P = 0.087$ and 2.3 vs. 2.2 mm, $P = 0.330$, respectively). In the group of 21 fetuses with an SUA there were six (28.6%) fetuses with other major defects detected at the 11–14-week scan (including two with exomphalos, two with diaphragmatic hernia, one with megacystis and one with kyphoscoliosis) and this was significantly higher than in the 613 with two arteries, where there were five fetuses with other defects (0.8%, Fisher's exact test $P < 0.0001$), including two with exomphalos, one with gastroschisis, one with megacystis and one with skeletal dysplasia.

In the chromosomally abnormal group there was an SUA in 5/44 (11.4%) with trisomy 21, 14/18 (77.8%) with trisomy 18 and 2/21 (9.5%) with other defects. In the group of 21 fetuses with an SUA there were 11 (52.4%) fetuses with other major defects detected at the 11–14-week scan (including 10 with exomphalos and one with holoprosencephaly) and this was significantly higher than in the 62 with two arteries, where there were six fetuses with other defects (9.7%, Fisher's exact test $P < 0.0001$), including five with exomphalos and one with megacystis.

In the 18 trisomy 18 fetuses, there were 11 with an abdominal wall defect or megacystis and in nine (81.8%) of these there was an SUA, which was not significantly different than in those without an abdominal wall defect or megacystis (5/7, 71.4%; Fisher's exact test $P = 0.652$).

In the 42 fetuses with SUA the expected number of cases of trisomy 21, estimated on the basis of maternal age, gestational age and fetal NT, was 4.7, which was not significantly different from the observed 5[25,26]. The corresponding numbers for trisomy 18 were 2.0 for expected and 14 for observed (Fisher's exact test $P = 0.0016$)[24,25]. In 17/42 fetuses with SUA there were easily detectable associated major defects. In the remaining 25 fetuses with apparently isolated SUA the expected number of cases of trisomy 18, estimated on the basis of maternal age, gestational age and fetal NT, was 1.06, which was not significantly different from the observed 4 (Fisher's exact test $P = 0.349$).

DISCUSSION

In this study of fetuses at 11–14 weeks' gestation the incidence of SUA was 5.9%, which is substantially

Table 1 Prenatal ultrasonographic studies reporting on the incidence of chromosomal defects

Reference	*Gestation at ultrasound (mean (range) in weeks)*	n	*Chromosomal defects plus single umbilical artery*						
			Total	*Isolated*	*Trisomy 18*	*Trisomy 13*	*Trisomy 21*	*Triploidy*	*Other*
Tortora *et al.* (1984)[7]	— (28–36)	7	1	0/2	1				
Herrmann and Sidiropoulos (1988)[8]	— (23–38)	9	2	0/1				1	1
Nyberg *et al.* (1991)[9]	25 (16–36)	30	6	0/0	4	1		1	
Duerbeck *et al.* (1991)[10]	— (22–38)	13	1	0/8				1	
Gonen *et al.* (1995)[11]	Second trimester	16	0	0/0					
Abuhamad *et al.* (1995)[12]	25 (10–40)	77	6	0/55	4			1	1
Parilla *et al.* (1995)[13]	25 (15–35)	50	0	0/50					
Catanzarite *et al.* (1995)[14]	— (16–39)	82	10	0/45	4	2	1	1	2
Sepulveda *et al.* (1996)[15]	20 (15–36)	55	5	0/55	3	1			1
Ulm *et al.* (1997)[16]	21 (16–41)	103	9	0/74	3	2		2	4
Sener *et al.* (1997)[17]	— (20–37)	15	1	1/10	1				
Blazer *et al.* (1997)[18]	— (14–16)	46	0	0/40					
Chow *et al.* (1998)[19]	29 (16–41)	118	5	0/81	2	2			1
Farrell *et al.* (2000)[20]	— (18–22)	22	0	0/22					
Rinehart *et al.* (2000)[21]	22 (10–34)	27	7	0/9	1	1	2	1	2
Geipel *et al.* (2000)[22]	21 (13–39)	102	10	0/59	5	2			3
Budorick *et al.* (2001)[23]	Second trimester	57	11	0/31	4	3	1		3
Gornall *et al.* (2003)[4]	19 (19–20)	107	5	1/87	1	1	1	1	1
Total		936	79 (8%)	2/629	33	15	5	9	19

higher than the reported birth incidence of 0.2–1.9%[1–5]. Furthermore, the incidence of chromosomal defects in fetuses with SUA (50%) was considerably higher than the 8% reported in second- and third-trimester ultrasonographic studies (8%; Table 1). It is likely that both the observed incidence of SUA and the incidence of associated chromosomal defects are overestimated because our population was preselected for fetal karyotyping by a combination of maternal age, being on average 37 years, and increased fetal NT, which was above the 95th centile for CRL in 36% of our cases. Nevertheless, in the chromosomally normal group the incidence of SUA was 3% and there was no significant difference in median fetal CRL or NT between those with a single and those with two umbilical arteries.

SUAs can be diagnosed prenatally by ultrasonography but in routinely performed mid-trimester scans only 30–67% of cases were identified[3,4,8,20]. Various methods have been suggested in the past to improve the detection of SUAs, including the measurement of transverse umbilical arterial diameter or the umbilical vein to umbilical artery ratio[15,27]. However, these techniques have become obsolete by the introduction of color Doppler imaging, which allows the easy visualization of the arteries along the sides of the fetal bladder[28].

In both the chromosomally normal and abnormal fetuses, those with an SUA had a substantially higher incidence of other major defects than fetuses with two umbilical arteries. The most common major defects at 11–14 weeks were exomphalos and megacystis and the most common chromosomal abnormality was trisomy 18. The high incidence of chromosomal defects (16/22 or 73%) in fetuses with exomphalos or megacystis in this study is compatible with our previous reports[29,30]. In this study we found that in a very high proportion of fetuses with trisomy 18 there was an associated exomphalos or megacystis but the incidence of SUA was not significantly different between those with and those without these abnormalities. Consequently, the high association between trisomy 18 and SUA is not the result of the high association between trisomy 18 and exomphalos or megacystis.

In the second trimester, the finding of an SUA should alert the ultrasonographer to search for the associated malformations and markers of chromosomal defects. In cases of apparently isolated SUA there is no indication for fetal karyotyping because in this group there is no evidence of increased risk of chromosomal defects. Similarly, we found that in first-trimester screening for chromosomal defects by a combination of maternal age and fetal NT the finding of an SUA does not increase the risk of trisomy 21. In contrast, an SUA is associated with a seven-fold increase in risk of trisomy 18. A high proportion of trisomy 18 fetuses have other major defects that are easily detectable at the 11–14-week scan and many other abnormalities that are detectable at 16–20 weeks. It is therefore unlikely that the finding of an SUA *per se* should be an indication for fetal karyotyping. However, this finding should certainly stimulate a more detailed sonographic examination that may well lead to the early detection of defects, such as overlapping fingers, facial cleft, cardiac anomalies or spina bifida, that are not usually detected at a routine 11–14-week scan.

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