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Umbilical cord diameter at 11–14 weeks of gestation: relation to chromosomal defects

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KEYWORDS: chromosomal defect; first trimester; screening; trisomy 21; umbilical cord diameter

ABSTRACT

Objective *To determine the potential value of measuring umbilical cord diameter (UCD) at 11–14 weeks of gestation in screening for chromosomal defects.*

Methods *The UCD was measured in 1323 fetuses immediately before chorionic villus sampling for karyotyping at 11–14 weeks of gestation. In the group of chromosomally normal fetuses, regression analysis was used to determine the association between UCD and crown–rump length (CRL). UCD was compared in normal fetuses and those with chromosomal abnormalities.*

Results *The median gestation was 12 (range, 11–14) weeks. The UCD was successfully measured in all cases. The fetal karyotype was normal in 1150 pregnancies and abnormal in 173, including 97 cases of trisomy 21. In the chromosomally normal group the UCD increased significantly with CRL from a mean of 2.9 mm at a CRL of 45 mm to 4.4 mm at a CRL of 84 mm. The UCD in the group of fetuses with trisomy 21 was significantly smaller than normal. Conversely, there were no significant differences from normal in the UCD of fetuses with other chromosomal abnormalities.*

Conclusion *At 11–14 weeks of gestation the UCD of fetuses with trisomy 21 is significantly smaller than normal but the magnitude of the difference is too small for useful inclusion of this measurement in screening. Copyright © 2004 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

In a recent study by Ghezzi *et al.*[1] the umbilical cord diameter (UCD) was examined at 10–14 weeks of gestation in 645 fetuses. In the study there were 14 fetuses with chromosomal defects, including five cases of trisomy 21, two of trisomy 18, two of Turner syndrome, one of trisomy 13, one of Klinefelter syndrome and three cases of confined placental mosaicism. The UCD was above the 95th centile for gestation in four (including two cases of Turner syndrome, one of trisomy 21 and one of trisomy 13) of the 14 cases (28.6%) with a chromosomal defect, compared to 5.5% (35/631) of the fetuses with normal karyotype. The authors suggested that in chromosomally abnormal fetuses the UCD may be increased and that this could help in identifying more fetuses with chromosomal abnormalities[1].

The aim of the present study was to investigate further the potential value of measuring UCD in screening for chromosomal abnormalities.

METHODS

The UCD was measured at the routine scan carried out before fetal karyotyping, by chorionic villus sampling, in 1323 fetuses at 11–14 weeks of gestation. There were 1303 singleton pregnancies and 10 dichorionic twin pregnancies in which each fetus was examined. The study was carried out in our center during a 15-month period (October 2001–January 2003). 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[2].

For measurement of the UCD we chose a free loop and obtained a long-axis view, as previously described by Weissman *et al.*[3]. The magnification of the image was such that each increment in the distance between calipers was only 0.1 mm. The beam of the ultrasound transducer was perpendicular to the surface of the umbilical cord and in this sagittal section two vessels were visualized (Figure 1). Six horizontal and parallel echogenic lines were seen. The outer two lines were the margins of the

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cord and the internal four were the walls of two vessels. The intervening gray areas were due to the Wharton's jelly and the translucent areas represented the lumen of the vessels.

The UCD was measured with the calipers placed outer-to-outer so that the Wharton's jelly was also included in the measurement (Figure 1). Two measurements were taken in two different images, and the mean of the two examinations was recorded. In addition, in 50 cases the UCD was measured by two different sonographers. All the scans were performed transabdominally using 5-MHz transducers (Aloka 5000, Aloka, Tokyo, Japan; Toshiba Powervision, Toshiba, Tokyo, Japan).

Demographic characteristics and ultrasound findings were recorded in a fetal database at the time of the examination. Once the fetal karyotype results were made available they were entered in the database also.

Statistical analysis

In the chromosomally normal group, linear regression was used to determine the significance of the association between UCD and crown–rump length (CRL). Each measurement of UCD was then expressed as a deviation from the expected mean for CRL (delta value) and the Mann–Whitney *U*-test was used to determine the significance of differences in the delta values between the chromosomally normal and abnormal groups. In order to assess any possible correlation between UCD and NT, the delta values of UCD were regressed against the delta values of NT. The Bland–Altman plot (the difference between the two paired measurements versus the average of the two measurements) was performed and the 95% tolerance interval for paired observations was calculated to determine intra- and interobserver variability[4].

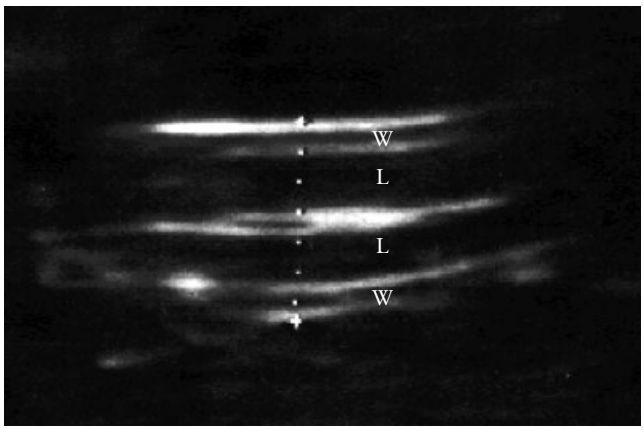

Figure 1 Umbilical cord at 12 weeks of gestation in a normal fetus. The beam of the ultrasound transducer is perpendicular to the surface of the umbilical cord and six parallel echogenic lines are seen. The outer two lines are the margins of the cord and the internal four represent the walls of two vessels. The intervening gray areas are due to the Wharton's jelly (W) and the translucent areas represent the lumen of the vessels (L).

RESULTS

The median maternal age was 37 (range, 16–48) years, the median fetal CRL was 66 (range, 45–84) mm and the median gestation was 12 (range, 11–14) weeks. The UCD was successfully examined in all cases. In the Bland–Altman plot the mean difference between paired measurements by the same sonographer was 0.17 mm and the 95% limits of agreement were −0.44 to 0.45 mm. In the 50 cases with measurements by two sonographers the mean difference between paired measurements was 0.18 mm and the 95% limits of agreement were −0.45 to 0.44 mm.

The fetal karyotype was normal in 1150 pregnancies and abnormal in 173 (Table 1), including 97 cases of trisomy 21, 42 of trisomy 18, 18 of Turner syndrome and 16 with other chromosomal abnormalities. In the chromosomally normal group the UCD increased significantly with CRL from a mean of 2.9 mm at a CRL of 45 mm to 4.4 mm at a CRL length of 84 mm ($UCD = 1.24 + 0.037 \times CRL$, $r = 0.72$, $P < 0.0001$; Figure 2).

Table 1 Mean difference in umbilical cord diameter from the normal mean for crown–rump length in the chromosomally normal and abnormal pregnancies

Karyotype	n	*Mean difference (range)*	*Mann–Whitney U-test P-value*
Normal	1150	0.0005 (−0.75 to 0.76)	
Trisomy 21	97	−0.156 (−0.99 to 0.81)	< 0.0001
Trisomy 18	42	0.131 (−0.91 to 1.23)	0.065
Turner syndrome	18	−0.142 (−0.8 to 0.66)	0.099
Trisomy 13	6	−0.183 (−0.57 to 0.5)	0.171
Triploidy	6	0.298 (−0.47 to 1.01)	0.055
XXY	4	0.055 (−0.08 to 0.18)	0.663
Total	1323		

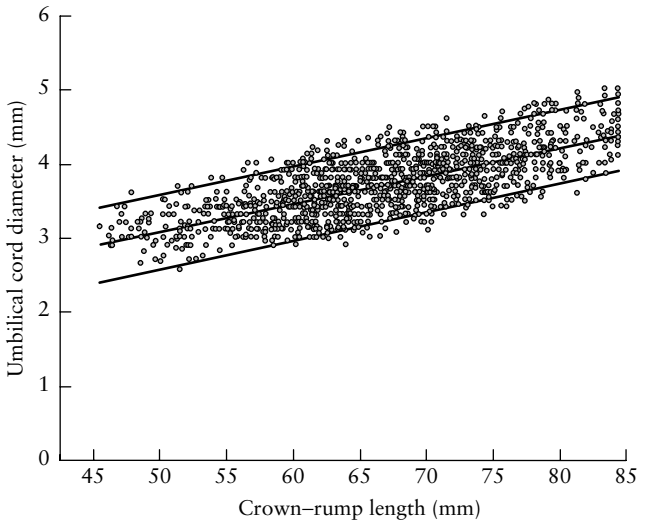

Figure 2 Reference range (mean, 95th and 5th centiles) of umbilical cord diameter with crown–rump length in the chromosomally normal fetuses at 11–14 weeks of gestation.

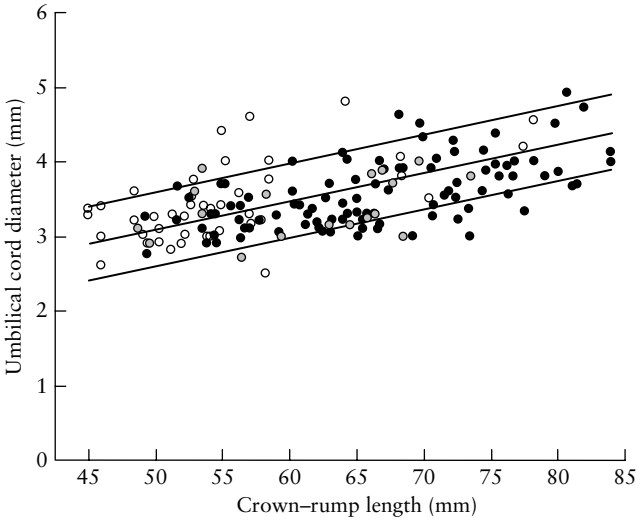

Figure 3 Umbilical cord diameter in trisomy 21 (●), trisomy 18 (○) and Turner syndrome (◎) plotted on the reference range (mean, 95th and 5th centiles) with crown–rump length of the chromosomally normal fetuses.

In the trisomy 21 fetuses the mean UCD was significantly lower than normal ($P < 0.0001$; Figure 3). Furthermore, in the trisomy 21 group there was no significant association between delta UCD and delta fetal NT ($r = -0.189$, $P = 0.064$). There were no significant differences from normal in the UCD of fetuses with other chromosomal abnormalities.

DISCUSSION

This study has confirmed previous observations that the UCD increases with fetal CRL[1,3]. In trisomy 21 fetuses the UCD was significantly lower than normal but the magnitude of the difference was too small for useful inclusion of this measurement in screening. In fetuses with other chromosomal defects there was no significant difference from normal, but in trisomy 18 there was a tendency for increased UCD. A possible explanation for this increase is that in trisomy 18 more than 75% of fetuses have a single umbilical artery[5] and it was previously reported that the umbilical artery diameter in a two-vessel cord is significantly higher than in a three-vessel cord[6]. The methodology used for measurement of UCD in the present study did not permit the diagnosis of a single umbilical artery, which requires the use of color flow mapping of vessels in the fetal pelvis.

There is no obvious physiological explanation for our findings in trisomy 21. Possible causes of the increased NT in chromosomally abnormal fetuses include cardiac dysfunction, altered composition of the extracellular matrix, and abnormal or delayed development of the lymphatic system[7]. However, we found no significant association between NT and UCD. Furthermore, the subcutaneous edema accompanying heart failure is due to extravasation of intravascular fluid through the capillaries and no such mechanism is possible in the umbilical cord because it contains only large vessels and no capillaries. Immunohistochemical and ultrastructural investigation of the umbilical cord in trisomy 21 and normal pregnancies may clarify the possible etiopathological mechanisms of the reduced UCD in trisomy 21 fetuses.

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