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Ear length in trisomy 21 fetuses at 11–14 weeks of gestation

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KEYWORDS: chromosomal defect; ear length; first trimester; nuchal translucency; screening; trisomy 21

ABSTRACT

Objective *To determine the value of measuring fetal ear length at 11–14 weeks of gestation in screening for chromosomal defects.*

Methods *The fetal ear length was measured in 450 fetuses immediately before chorionic villus sampling for karyotyping at 11–14 weeks of gestation.*

Results *The median gestational age was 12 (range, 11–14) weeks. The fetal ear was successfully examined in all cases. The fetal karyotype was normal in 409 cases and abnormal in 41, including 32 cases of trisomy 21. In the chromosomally normal group the fetal ear length increased significantly with crown–rump length from a mean of 3.7 mm at 45 mm to 6.9 mm at 84 mm. In the trisomy 21 fetuses the median ear length was significantly below the normal mean for crown–rump length by 0.45 mm* ($P = 0.013$) *but it was below the 5*th *centile of the normal range in only two (6.3%) of the cases. There was no significant association between the delta score of ear length and delta nuchal translucency in either the chromosomally normal* ($r = -0.015$, $P = 0.753$) *or the trisomy 21 fetuses* ($r = -0.014$, $P = 0.94$).

Conclusions *At 11–14 weeks of gestation the ear length in trisomy 21 fetuses is significantly reduced but the degree of deviation from normal is too small for this measurement to be useful in screening for trisomy 21.*

INTRODUCTION

Patients with trisomy 21 have short ears. Aase *et al.* reported that the mean ear length of 25 affected neonates was 21% lower than that of normal controls and that the length was below the 3rd centile of the normal range in 21 (84%) of the cases[1]. The authors concluded that short ears constitute the most consistent clinical characteristic, aside from hypotonia, in making the clinical diagnosis of trisomy 21. Farkas *et al.*, examined 124 patients with trisomy 21 between 7 months and 36 years of age and reported that the ear length was abnormally short in 72% of cases[2].

Several sonographic studies have examined the potential value of measuring fetal ear length at 14–36 weeks of gestation in prenatal screening for trisomy 21 and report contradictory results, with sensitivities from 26 to 78% and false-positive rates of 1.2–8.0% (Table 1)[3–6].

The aim of this study was to examine the potential value of measuring fetal ear length at 11–14 weeks of gestation in screening for trisomy 21.

METHODS

We measured the fetal ear length at the routine ultrasound scan, which was being carried out before fetal karyotyping by chorionic villus sampling in 450 consecutively examined fetuses at 11–14 weeks of gestation. There were 436 singleton pregnancies and seven twin pregnancies, in which each fetus was examined. The study was carried out in our center during a 3-month period (October to December 2002). In all cases there had been prior screening for chromosomal defects by a combination of maternal age and fetal nuchal translucency thickness and the patients included in this study were those that after counseling elected to have invasive testing[7].

The fetal ears were visualized in a coronal view and the maximal length was measured with calipers on the screen (Figure 1). In each case two measurements were obtained and the mean value was used. The magnification of the image was such that each increment in the distance between calipers was only 0.1 mm and therefore the fetal head, neck and thorax occupied the whole image. The fetal nuchal translucency thickness and crown–rump length were also measured and the fetal profile was examined for presence or absence of the nasal bone[8]. Examination

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Table 1 Comparison of published studies reporting on ear length in trisomy 21 fetuses at 14–36 weeks of gestation

Study	*Gestational age (weeks)*	*Definition of short ears*	*Number (%) with short ears*	
			Trisomy 21 fetuses	*Normal fetuses*
Lettieri *et al.* (1993)[3]	14–25	$< 10^{th}$ centile	7/9 (78)	33/410 (8.0)
Awwad *et al.* (1994)[4]	20–28	Observed/expected < 0.8	3/4 (75)	5/408 (1.2)
Shimizu *et al.* (1997)[5]	18–38	$< 5^{th}$ centile	3/4 (75)	– (5.0)
Chitkara *et al.* (2002)[6]	16–36	$< 10^{th}$ centile	5/19 (26)	87/1263 (6.9)

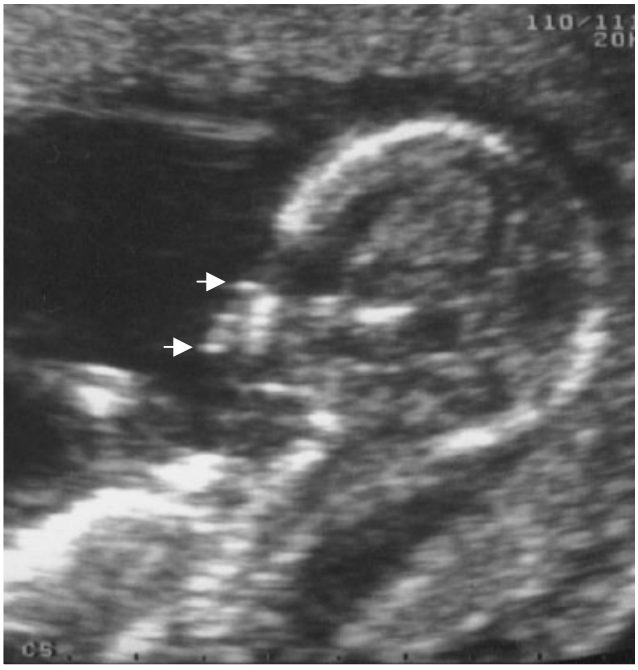

Figure 1 Ultrasound image of a 12-week fetus demonstrating measurement of ear length.

of the fetal ears was successfully achieved in all cases and this added 1–3 min to the overall time of about 15 min for the 11–14-week scan.

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

Statistical analysis

In the chromosomally normal group, regression analysis was used to determine the significance of the association between ear length and crown–rump length. Each measurement of ear length was then expressed as a difference from the expected mean for crown–rump length (delta value) and the Mann–Whitney *U*-test was used to determine the significance of difference in the delta values between the chromosomally normal and the trisomy 21 fetuses. Regression analysis was used to determine the significance of the association between delta ear length and delta nuchal translucency thickness both

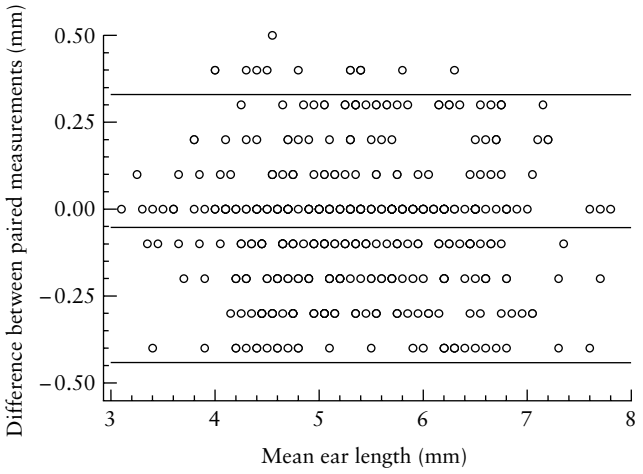

Figure 2 Bland–Altman plot of the difference against the average between the paired measurements in ear length.

in the chromosomally normal and the trisomy 21 fetuses. The Mann–Whitney *U*-test was used to determine the significance of difference in the delta ear length between the trisomy 21 fetuses with nasal bone present and absent. A Bland–Altman plot (difference between the two paired measurements plotted against the average between the two) was constructed and the 95% tolerance interval for paired observations was calculated[9].

RESULTS

The median maternal age was 37 (range, 18–46) years, the median fetal crown–rump length was 65 (range, 45–84) mm and the median gestational age was 12 (range, 11–14) weeks. The maternal ethnic group was Caucasian in 412 (91.5%) cases, Afro-Caribbean in 14 (3.1%) cases, Asian in 11 (2.4%) cases, Oriental in 7 (1.5%) cases and mixed in 6 (1.3%) cases. The fetal ears were successfully examined in all cases. The fetal karyotype was normal in 409 cases and abnormal in 41, including 32 cases of trisomy 21, four of trisomy 13, three of trisomy 18, one of triploidy and one of Turner syndrome. In the Bland–Altman plot the mean difference between paired measurements was 0.15 mm and the 95% limits of agreement were − 0.44 to 0.34 mm (Figure 2). In the chromosomally normal group the fetal ear length increased significantly with crown–rump length from a mean of 3.7 mm at 45 mm to 6.9 mm at 84 mm (ear length = 0.095 + 0.081 × crown–rump length in mm; $r = 0.76$, $P < 0.0001$; Figure 3).

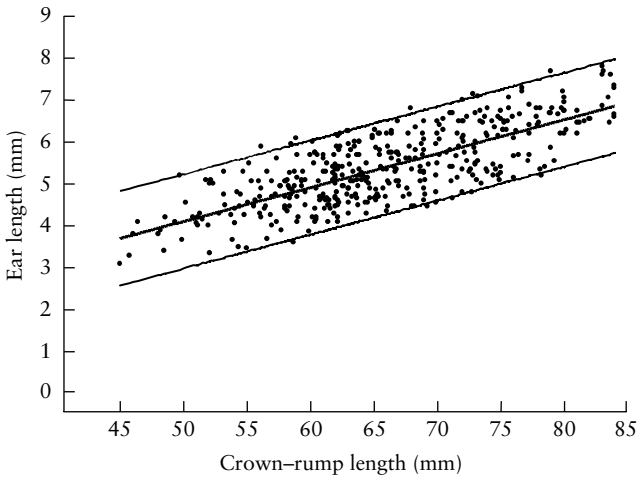

Figure 3 Reference range (mean, 5th and 95th centiles) of ear length against crown–rump length in chromosomally normal fetuses at 11–14 weeks of gestation.

In the trisomy 21 fetuses the median ear length was significantly below the normal mean for crown–rump length by 0.45 mm ($P = 0.013$) but it was below the 5th centile of the normal range in only two (6.3%) of the cases (Figure 4). The ear length was above the 5th centile in all nine fetuses with chromosomal defects other than trisomy 21.

There was no significant association between the delta score of ear length and delta nuchal translucency in either the chromosomally normal ($r = -0.015, P = 0.753$) or the trisomy 21 fetuses ($r = -0.014, P = 0.94$). The nasal bone was absent in 22 (68.8%) of the trisomy 21 fetuses, in two (22.2%) of those with other chromosomal defects and in eight (1.95%) of the chromosomally normal fetuses. In the trisomy 21 fetuses there was no significant difference in median delta ear length between those with absent and those with present nasal bone (median difference, $P = 0.12$).

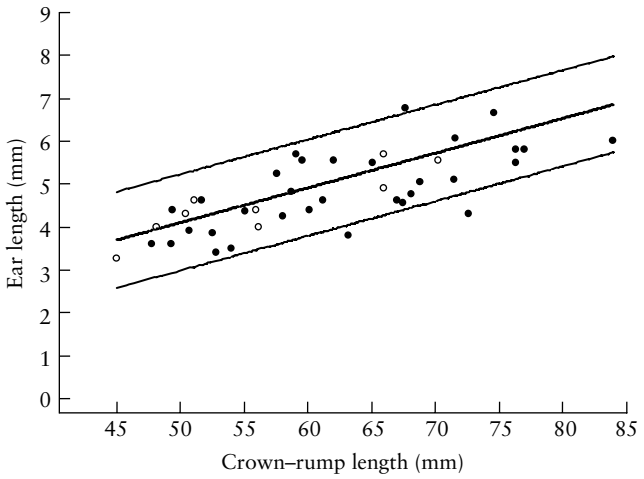

Figure 4 Fetal ear length in fetuses with trisomy 21 (●) and those with other chromosomal defects (○) plotted on the reference range (mean, 5th and 95th centiles) against crown–rump length of chromosomally normal fetuses.

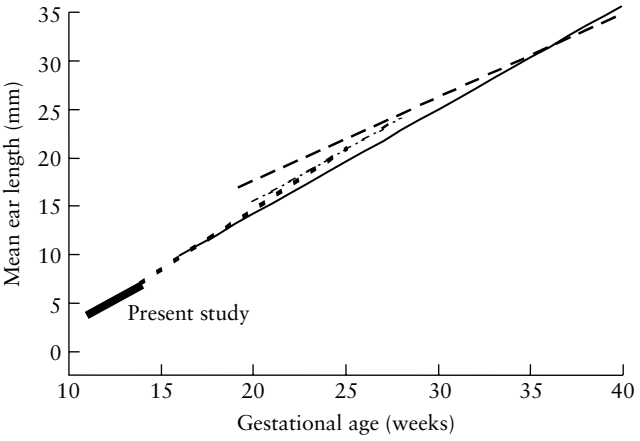

Figure 5 Comparison of results of this study (——) with those of published studies reporting on ear length in normal fetuses at 14–36 weeks of gestation: Lettieri *et al.*[3] (— —), Awwad *et al.*[4] (— - - -), Shimizu *et al.*[5] (— —) and Chitkara *et al.*[6] (——).

DISCUSSION

This study has demonstrated the feasibility of measuring fetal ear length at 11–14 weeks of gestation. The ears were successfully visualized and measured in all fetuses and in 95% of cases the difference between two consecutive measurements was < 0.45 mm.

Fetal ear length increased linearly with gestational age. This is compatible with the results of previous studies that reported measurements for the second and third trimesters of pregnancy and our values are in clear continuity with those from two of the studies (Figure 5)[3–6].

The finding that in trisomy 21 fetuses at 11–14 weeks of gestation the ear length was significantly reduced is compatible with the well described association of trisomy 21 and short ears both in postnatal studies and in prenatal sonographic data from the second and third trimesters of pregnancy[1–6]. Furthermore, shortening of ear length was independent of the other characteristic features of trisomy 21 at 11–14 weeks, thus there was no significant association between the degree of ear shortening and increased nuchal translucency thickness or the incidence of absent nasal bone. However, the degree of deviation from normal was too small for this measurement to be useful in screening for trisomy 21.

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