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

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KEYWORDS: chromosomal defect; first trimester; maxilla; screening; trisomy 21; ultrasound

ABSTRACT

Objective *To determine the value of measuring maxillary length at 11–14 weeks of gestation in screening for trisomy 21.*

Methods *In 970 fetuses ultrasound examination was carried out for measurement of crown–rump length (CRL), nuchal translucency and maxillary length, and to determine if the nasal bone was present or absent, immediately before chorionic villus sampling for karyotyping at 11–14 weeks of gestation. In 60 cases the maxillary length was measured twice by the same operator to calculate the intraobserver variation in measurements.*

Results *The median gestation was 12 (range, 11–14) weeks. The maxilla was successfully examined in all cases. The mean difference between paired measurements of maxillary length was −0.012 mm and the 95% limits of agreement were −0.42 (95% CI, −0.47 to −0.37) to 0.40 (95% CI, 0.35 to 0.44) mm. The fetal karyotype was normal in 839 pregnancies and abnormal in 131, including 88 cases of trisomy 21. In the chromosomally normal group the maxillary length increased significantly with CRL from a mean of 4.8 mm at a CRL of 45 mm to 8.3 mm at a CRL of 84 mm. In the trisomy 21 fetuses the maxillary length was significantly shorter than normal by 0.7 mm and in the trisomy 21 fetuses with absent nasal bone the maxilla was shorter than in those with present nasal bone by 0.5 mm. In fetuses with other chromosomal defects there were no significant differences from normal in the maxillary length.*

Conclusion *At 11–14 weeks of gestation, maxillary length in trisomy 21 fetuses is significantly shorter than in normal fetuses. Copyright © 2004 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Trisomy 21 is associated with the sonographic findings of increased nuchal translucency (NT) and nasal hypoplasia[1,2]. In the present study we investigated further the original observation of Langdon Down that in individuals with trisomy 21 'the face is flat and broad'[3]. In addition to nasal hypoplasia, a flat face may be the consequence of underdevelopment of the maxilla.

Farkas *et al.* examined 120 patients with Down syndrome at 7 months to 36 years of age and reported abnormally short distance between the nostril and ear in 62% of cases[4]. Several radiological studies reported that individuals with Down syndrome have oligodontia, especially in the maxilla. Lomholt *et al.*, in a study of 70 patients with Down syndrome, reported that the incidence of third molar agenesis was four times greater than in a normal population and that agenesis occurred more often in the maxilla than in the mandible[5]. Shapira *et al.* reported third molar agenesis in 74% of patients with Down syndrome and speculated that the slow rate of cell growth in this syndrome may be responsible for underdevelopment of the upper jaw, delayed dental development and reduction in teeth number and size[6]. Mestrovic *et al.* reported hypodontia in 39% of 112 patients with Down syndrome[7]. Kumasaka *et al.* examined 98 patients with Down syndrome and found that 63% had oligodontia, and in 53% two or more teeth were missing[8]. Russell *et al.* studied 100 patients with Down syndrome and reported that the incidence of tooth agenesis was 10 times greater that in the general population[9]. Allanson *et al.* examined 199 patients with trisomy 21 at 6 months to 61 years of age and reported that maxillary growth was reduced in comparison to mandibular growth[10].

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The aim of this study was to examine if maxillary length at 11–14 weeks' gestation in fetuses with trisomy 21 is reduced.

METHODS

We measured the maxillary length at the routine ultrasound scan carried out before fetal karyotyping, by chorionic villus sampling (CVS), in 970 consecutively examined fetuses at 11–14 weeks of gestation. There were 927 singleton pregnancies, 20 twin pregnancies and one triplet pregnancy in which each fetus was examined. In all cases there was prior screening for chromosomal defects by a combination of maternal age and fetal NT and the patients included in this study were those that after counseling elected to undergo invasive testing[11].

The maxillary length was measured by transabdominal sonography. A mid-sagittal view of the fetal profile was first obtained to determine if the nasal bone was present or absent[2,11]. The transducer was then gently angled laterally so that the both the maxillary bone and mandible, including the ramus and condylar process, could be seen. Maxillary length was then measured with calipers on the screen and care was taken to exclude the ramus and condylar process of the mandible (Figure 1). The magnification of the image was such that each increment in the distance between calipers was only 0.1 mm. The fetal NT and crown–rump length (CRL) were also measured. Examination of the maxilla 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. In 60 cases the maxillary length was measured twice by the same operator to calculate the intraobserver variation in measurements.

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

In the chromosomally normal group, regression analysis was used to determine the significance of the association between maxillary length with CRL. Each maxillary length was then expressed as a difference from the expected mean for CRL (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 trisomy 21 fetuses. Regression analysis was used to determine the significance of the association between delta maxillary length and delta NT both in the chromosomally normal and trisomy 21 fetuses. Furthermore, the Mann–Whitney *U*-test was used to determine the significance of the difference in the delta values between the trisomy 21 fetuses with present and those with absent nasal bone. In the 60 cases with paired measurements, the Bland–Altman plot (difference between the two paired measurements against the average between the two) was performed and the 95% limits of agreement with their 95% CIs were calculated[12].

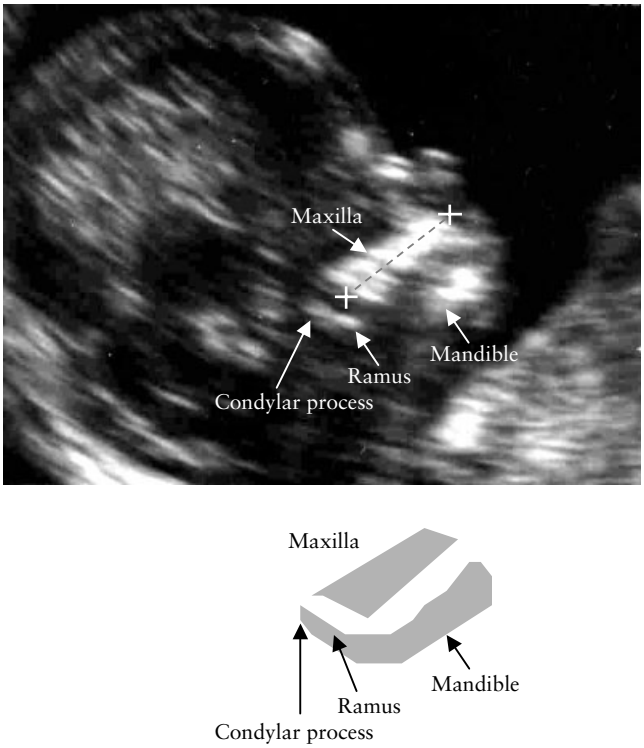

Figure 1 Ultrasound image of a 12-week fetus demonstrating measurement of maxillary length.

RESULTS

The median maternal age was 37 (range, 16–48) years, the median fetal CRL was 64 (range, 45–84) mm and the median gestation was 12 (range, 11–14) weeks. The maternal ethnic group was Caucasian in 923 (95.2%) cases, Afro-Caribbean in 13 (1.3%), Asian in 23 (2.4%), Chinese or Japanese in seven (0.7%) and mixed in four (0.4%). The fetal maxilla was successfully examined in all cases. The fetal karyotype was normal in 839 pregnancies and abnormal in 131, including 88 cases of trisomy 21 and 43 with other abnormalities (18 of trisomy 18, three of trisomy 13, 13 of Turner syndrome, two of Klinefelter syndrome, two of triple X syndrome, one of triploidy and four with autosomal mosaicism).

In the Bland–Altman plot the mean difference between paired measurements of maxillary length was −0.012 and the 95% limits of agreement were −0.42 (95% CI, −0.47 to −0.37) to 0.40 (95% CI, 0.35 to 0.44) mm (Figure 2). In the chromosomally normal group the maxillary length increased significantly with CRL from respective means of 4.8 and 8.3 mm at 45 and 85 mm (maxillary length = $0.708 + 0.090 \times$ CRL (in mm); $r = 0.784$; $P < 0.0001$; Figure 3).

In the trisomy 21 fetuses the median maxillary length was significantly below the normal mean for CRL by 0.7 (range, −2.3 to 0.6) mm ($P < 0.0001$) and it was below the median and the 5th centile of the normal range in 73 (83.0%) and 21 (23.9%) cases, respectively (Figure 4).

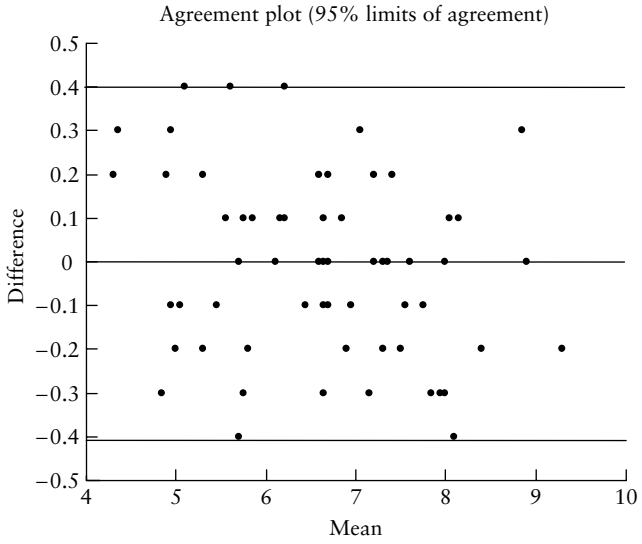

Figure 2 Bland–Altman plot of the difference vs. the mean of paired measurements in maxillary length.

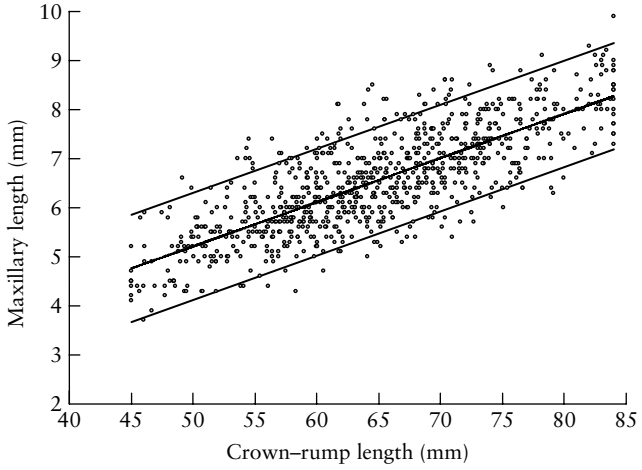

Figure 3 Reference range (mean, 95th and 5th centiles) with crown–rump length in maxillary length in chromosomally normal fetuses at 11–14 weeks of gestation.

In the fetuses with other chromosomal abnormalities the median maxillary length was not significantly different from the normal mean for CRL (mean difference −0.1 (range, −1.4 to 1.6) mm; $P = 0.1284$; Figure 5). In the trisomy 21 fetuses there was a significant association between the delta score of maxillary bone length and delta NT ($r = -0.255$; $P = 0.0167$) and the median delta score was significantly lower in those with an absent compared to a present nasal bone (−0.8 and −0.3, respectively; $P < 0.0001$).

DISCUSSION

The present study has demonstrated the feasibility of measuring maxillary length at 11–14 weeks of gestation. The maxilla was successfully visualized and measured in all fetuses and in 95% of cases the difference between two consecutive measurements was less than 0.47 mm.

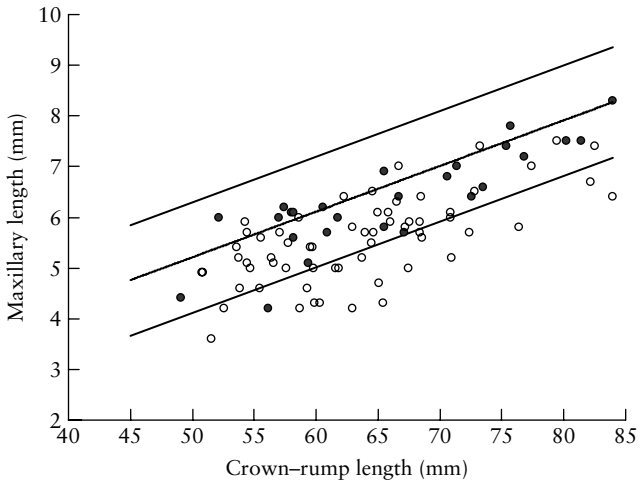

Figure 4 Maxillary length in trisomy 21 fetuses with present (●) and absent (○) nasal bone plotted on the reference range (mean, 95th and 5th centiles) with crown–rump length of the chromosomally normal fetuses.

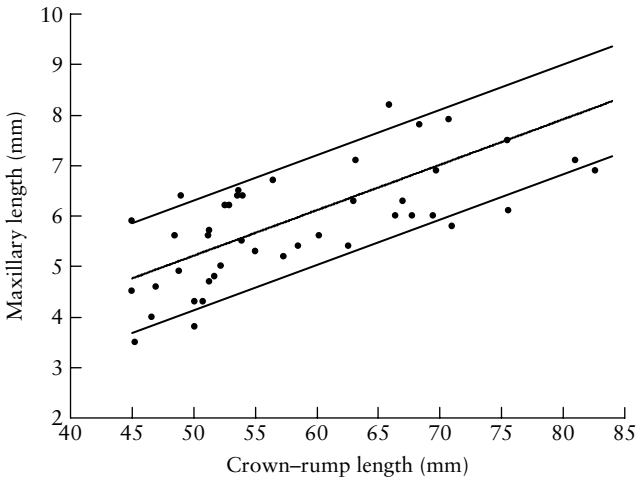

Figure 5 Maxillary length in chromosomal defects other than trisomy 21 plotted on the reference range (mean, 95th and 5th centiles) with crown–rump length of the chromosomally normal fetuses.

Maxillary length increased linearly with gestation by about 0.1 mm for each 1 mm increase in CRL.

The finding that in trisomy 21 fetuses at 11–14 weeks of gestation the maxillary length was significantly reduced is compatible with the well-described findings of impaired maxillary growth and oligodontia in postnatal radiological studies[4–10]. The growth of bone is dependent on the surrounding functional matrix, and immunohistochemical studies of the skin of trisomy 21 fetuses have demonstrated alterations in the composition of the extracellular matrix, which may be attributed to gene dosage effects[13–16].

Short maxilla is a potentially useful first trimester marker for trisomy 21 since the measurement was below the normal median and below the 5th centile of the normal range in 83% and 24% of affected fetuses, respectively. However, there is a significant association

between maxillary bone length and NT, and in fetuses with absent nasal bone the maxilla was shorter than in those with present nasal bone. Consequently, the independent contribution of maxillary length in screening for trisomy 21 remains to be determined.

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