Frontomaxillary facial angle in trisomy 21 fetuses at 16–24 weeks of gestation

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ABSTRACT

Objectives To establish a normal range for the frontomaxillary facial (FMF) angle by three-dimensional (3D) ultrasound imaging and to examine the FMF angle in trisomy 21 fetuses at 16–24 weeks of gestation.

Methods We measured the FMF angle using 3D volumes of the fetal profile obtained with the transducer parallel to the long axis of the nose and at 45° to the palate, which had been acquired from 150 normal fetuses and 23 fetuses with trisomy 21.

Results In the normal group there was no significant association between the FMF angle and gestational age; the mean FMF angle was 83.9° (range, 76.9–90.2°) and the 95th centile was 88.5°. In 15 (65.2%) of the fetuses with trisomy 21 the FMF angle was greater than 88.5°.

Repeatability studies demonstrated that in 95% of cases the difference between two measurements of FMF angle by the same operator and different operators was less than 5°.

Conclusions In the majority of second-trimester fetuses with trisomy 21 the FMF angle is increased. Copyright © 2008 ISUOG. Published by John Wiley & Sons, Ltd.

METHODS

We measured the FMF angle using 3D volumes of the fetal face, which had been successfully acquired in the mid-sagittal plane of the face from two groups of patients. The first group comprised 150 singleton pregnancies with appropriately growing fetuses and no sonographic evidence of fetal abnormality. These patients were attending our fetal medicine centers for routine ultrasound examination at 16–25 weeks and for this study we prospectively recruited 15 consecutive cases per gestational week. The
second group comprised 23 fetuses with trisomy 21 confirmed by chorionic villus sampling or amniocentesis carried out because of a high risk of a chromosomal defect. In 13 (56.5%) cases the maternal age was 35 years or more, and in all but one case there was at least one fetal abnormality or sonographic marker of a chromosomal defect, including mild ventriculomegaly \( (n = 5) \), nuchal edema \( (n = 8) \), absent nasal bone \( (n = 6) \), cardiac defect \( (n = 8) \), intracardiac echogenic focus \( (n = 4) \), hyper-echogenic bowel \( (n = 2) \), collapsed stomach \( (n = 2) \), duodenal atresia \( (n = 1) \), mild hydronephrosis \( (n = 3) \), short femur \( (n = 4) \), talipes \( (n = 1) \) and clinodactyly \( (n = 1) \).

In each case transabdominal ultrasound examination (RAB 4-8L probe, Voluson 730 Expert, GE Medical Systems, Milwaukee, WI, USA) was carried out by sonographers with extensive experience in 3D ultrasound imaging. A 3D volume of the fetal head had been acquired in the mid-sagittal plane of the face with the transducer parallel to or within 30° of the long axis of the nose and 45° to the palate. In this plane, the palate is visualized as an echogenic line, with a downwards diagonal direction from the maxillary bone anteriorly towards the basilar portion of the occipital bone posteriorly (Figure 2). Care was taken to distinguish between the palate and the overlying vomeral bone, which is less echogenic and has an irregular convex shape on the top. The vomeral bone courses diagonally from the maxilla anteriorly towards the sphenoid bone posteriorly.

Figure 1 Ultrasound images of a normal fetal profile at 12 weeks (a), 16 weeks (b) and 20 weeks (c) of gestation. At 12 weeks the palate (P) and vomer (V) appear as a single hyperechogenic rectangular structure, but in the second trimester there are two echogenic structures. The inferior one, which is directed towards the basilar portion of the occipital bone posteriorly, represents the palate. The vomer is the superior one, with an irregular convex shape on the top, and is directed towards the sphenoid bone posteriorly.

Figure 2 Ultrasound image of a normal fetal profile at 20 weeks demonstrating the measurement of the frontomaxillary facial angle.

The FMF angle measurements were made independently by two sonographers who were not aware of the fetal karyotype. Intraobserver variability in measurements was assessed based on FMF angle measurements by two observers in 100 cases. Intraobserver variability was assessed by one sonographer measuring 50 randomly selected cases on two occasions.

Statistical analysis

Regression analysis was used to determine the significance of the association between the FMF angle and gestational age. Mann–Whitney U-test was used to compare the FMF angle between the normal group and the trisomy group.
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21 fetuses, and between those with and without common defects (ventriculomegaly, nuchal edema, absent nasal bone, cardiac defect) within the trisomy 21 group.

Bland–Altman analysis was used to examine the measurement agreement and bias for a single examiner and between two examiners. The data were analyzed using the statistical software SPSS 12.0 (Chicago, IL, USA) and Excel for Windows 2000 (Microsoft Corp., Redmond, WA, USA). \( P < 0.05 \) was considered statistically significant.

RESULTS

In the group of 150 normal fetuses the median maternal age was 32 (range, 16–44) years and the median gestational age was 21 (range, 16–25) weeks. The maternal ethnicity was Caucasian in 97 (64.7%), Afro–Caribbean in 39 (26.0%), Indian or Pakistani in eight (5.3%), and Chinese or Japanese in six (4.0%). There was no significant association between the FMF angle and gestational age \( (r = 0.002, P = 0.981) \) (Figure 3). The mean FMF angle was 83.9° (range, 76.9–90.2°). The Kolmogorov–Smirnov test confirmed the normality of the distribution, and the 5th and 95th percentiles were 79.3° and 88.5°, respectively.

In the 23 fetuses with trisomy 21 the median maternal age was 35 (range, 20–44) years and the median gestational age was 20 (range, 16–24) weeks. There was no significant association between the FMF angle and gestational age \( (r = 0.189, P = 0.387) \). The mean FMF angle was 89.4° (range, 83.1–95.6°) and was significantly larger than that in the normal fetuses \( (P < 0.001) \). The measurement was above the 95th centile of the normal range in 15 (65.2%) of the trisomy 21 fetuses (Figure 3). There was no significant difference in mean FMF angle between those with and without ventriculomegaly \( (90.9° \text{ vs. } 89.1°, P = 0.491) \), with and without nuchal edema \( (90.1° \text{ vs. } 88.4°, P = 0.294) \), or with and without cardiac defect \( (89.4° \text{ vs. } 89.3°, P = 0.946) \). The mean FMF angle was significantly higher in those with an absent rather than present nasal bone \( (92.0° \text{ vs. } 88.6°, P = 0.036) \) and it was above the 95th centile in all six cases with an absent nasal bone.

The mean difference and 95% limits of agreement (with their 95% CI) between paired measurements by the same observer were \(-0.06° (-2.57° \text{ to } -2.25) \) to \( 2.45° (2.13–2.57) \) and the respective values in paired measurements by the two different observers were \(-0.321° (-2.70° \text{ to } -2.96 \text{ to } -2.52) \) to \( 2.10° (1.88–2.31) \).

DISCUSSION

The data in this prospective 3D ultrasound study confirm our observations from a previous retrospective 2D ultrasound study that the FMF angle during the second trimester in fetuses with trisomy 21 is substantially bigger than that in normal fetuses. We established that the FMF angle does not change between 16 and 25 weeks of gestation in normal fetuses, and that the 95th centile is 88.5°. However, in about 65% of fetuses with trisomy 21 the FMF angle is above this value. The measurement of the FMF angle in the second and third trimesters is reproducible, and in 95% of the cases the difference between two measurements by the same operator and different operators is less than 5°.
When measuring the FMF angle it is important to appreciate that the palate and vomer appear as a single rectangular structure in the scan performed at 11 to 13 + 6 weeks, whereas in the second and third trimesters the two structures are joined anteriorly at the maxilla but diverge posteriorly to produce two separate echogenic lines. In a previous second-trimester study we drew the first ray of the FMF angle in the upper part of the vomer and reported that the FMF angle decreases with gestation. In the present study we used the palate rather than the vomer because the upper surface of the former is straight whereas that of the vomer is usually convex.

The wide FMF angle in fetuses with trisomy 21 could explain the flat face, which is a common phenotypic expression characteristic of this chromosomal defect. Farkas et al. examined 120 patients with trisomy 21 at 7 months to 36 years of age, and reported an abnormally short distance between the nostril and ear in 62% of the cases. 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. Shapiro et al. examined 153 patients with trisomy 21 at 7–66 years of age and reported that the length of the palate was below the 2.5th centile of the normal range in 95%.

In this study all cases of trisomy 21 had been identified by previous screening through maternal age, second-trimester serum biochemistry or routine ultrasound examination, and in 22/23 cases there was a fetal abnormality or sonographic marker of a chromosomal defect. However, there was no significant association between the FMF angle and any of the commonly detected defects. It is therefore reasonable to assume that our findings concerning the FMF angle are representative of all fetuses with trisomy 21.

In the first trimester of pregnancy effective screening for trisomy 21 is provided by a combination of fetal nuchal translucency thickness and maternal serum free beta-human chorionic gonadotropin and pregnancy-associated transcucency thickness and maternal serum free beta-trisomy 21 is provided by a combination of fetal nuchal findings concerning the FMF angle are representative of defects. It is therefore reasonable to assume that our between the FMF angle and any of the commonly detected defects. However, there was no significant association abnormality or sonographic marker of a chromosomal defect.

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REFERENCES