Metopic suture in fetuses with trisomy 21 at 11 + 0 to 13 + 6 weeks of gestation

C. FARO*, P. WEGRZYN*, B. BENOIT†, R. CHAOUI‡ and K. H. NICOLAIDES*

*Harris Birthright Research Centre for Fetal Medicine, King’s College Hospital Medical School, London, UK, †Maternite, Hospital Princesse Grace, Monaco and ‡Centre for Prenatal Diagnosis and Human Genetics, Berlin, Germany

KEYWORDS: 3D ultrasound; craniosynostosis, first trimester; metopic suture; trisomy 21

ABSTRACT

Objective To investigate the development of the frontal bones and metopic suture in fetuses with trisomy 21 at 11 + 0 to 13 + 6 weeks of gestation.

Methods Three-dimensional (3D) ultrasound was used to measure the height of and gap between the frontal bones in 75 fetuses with trisomy 21 and these were compared to the measurements in 200 normal fetuses at 11 + 0 to 13 + 6 (median, 12 + 6) weeks of gestation.

Results In the fetuses with trisomy 21, compared to the normal fetuses, there was no significant difference in either the height of the frontal bones (mean difference 0.16 SD, range −1.78 to 2.17 SD; P = 0.369) or the gap between them (mean difference 0.012, 95% CI −0.073 to 0.097; P = 0.780). Additionally, within the group of trisomy 21 fetuses there were no significant differences in the development of the frontal bones and metopic suture between those with absent (n = 46) and those with present (n = 29) nasal bone.

Conclusions In trisomy 21 the development of the frontal bones and metopic suture is as normal and is independent from the development of the nasal bones. Copyright © 2005 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Three-dimensional (3D) ultrasound can provide useful information on the normal and abnormal development of the fetal cranial bones and sutures1–3. In a previous study of nine fetuses with holoprosencephaly at 11 + 0 to 13 + 6 weeks of gestation, we found that the height of the frontal bones was significantly greater and the gap between them was smaller than those in 200 normal fetuses4.

The development of the facial and frontal bones is intimately related to the migration of neuroectodermal cells from the crest of the neural tube. Cells arising from different regions of the neural tube migrate forwards and downwards towards, firstly, the mandible, secondly, the maxilla, and thirdly, the frontonasal region5–7. Many facial abnormalities are thought to be the consequence of impaired migration or inadequate function of neural crest cells6.

The aim of this 3D ultrasound study was to investigate the development of the frontal bones and metopic suture in fetuses with trisomy 21 at 11 + 0 to 13 + 6 weeks. We postulate that the impaired development of the nasal bones and the maxilla, observed in fetuses with trisomy 218–11, may be due to deficient migration and/or function of the neural crest cells8. The development of the frontal bones is altered.

METHODS

The height of the frontal bones and the gap between them were measured as previously described9. The frontal bones were examined from the 3D volumes of the fetal face that were acquired at 11 + 0 to 13 + 6 weeks of gestation in 75 fetuses with trisomy 21 and the values were compared to those in 200 singleton pregnancies with no obvious fetal brain or other abnormalities4. All patients attended our center for first-trimester screening for trisomy 21 by a combination of maternal age and measurement of fetal nuchal translucency thickness. The 3D volumes were obtained with the fetuses in the mid-sagittal plane, the transducer being parallel to the direction of the nose. The 3D examinations were carried out transabdominally or transvaginally.
transvaginally using a RAB 4-8L transabdominal probe or a RIC 5-9H four-dimensional (4D) transvaginal probe (Voluson 730 Expert, GE Medical Systems, Milwaukee, WI, USA) by sonographers with extensive experience in 3D ultrasound.

The 3D volume was first displayed in the three orthogonal planes that compose the multiplanar mode of image postprocessing. The left and right frontal bones were identified in the respective parasagittal views, their vertical height was measured and the average of the two measurements was calculated (Figure 1). For the analysis of the gap between the frontal bones we used the volume contrast imaging (VCI) static postprocessing mode with 100% transparent maximum mode of display. We used the transverse image and scrolled it along the metopic suture area to measure the smallest visible gap (Figure 1). The sequence of transverse views was also used to confirm the presence or absence of the nasal bones12. Every measurement was done offline after the scan by the same operator.

Statistical analysis

In the 200 normal fetuses, regression analysis was used to determine the significance of the association between height and gap of the frontal bones with crown–rump length (CRL)4. The Kolmogorov–Smirnov test demonstrated that the data for the height of the frontal bones were not normally distributed and therefore they were log-transformed to achieve a normal distribution. Each measurement of the log-transformed height was then expressed as a deviation in SD from the expected normal mean for gestation (delta value). Unpaired *t*-test was used to determine the significance of differences in the delta values between the normal and trisomy 21 groups, and within the trisomy 21 group between those with and those without a nasal bone.

In the case of the gap between the frontal bones in the normal fetuses the Kolmogorov–Smirnov test showed that the data were normally distributed4. The Shapiro–Wilks’ W test demonstrated that the data were also normally distributed in trisomy 21 group and in subgroups with absent and present nasal bone, respectively. Therefore, the unpaired *t*-test was used to determine the significance of differences in observed values between the normal and trisomy 21 groups, and within the trisomy 21 group between those with and those without a nasal bone.

The analyses were performed with SPSS 11.5 (SPSS, Chicago, Illinois, USA). *P* < 0.05 was considered to be statistically significant.

RESULTS

In the normal group, the height of the frontal bones increased significantly with gestation from a mean of 2.5 mm (5th and 95th centiles: 1.9 mm and 3.3 mm, respectively) at a CRL of 45 mm to 6.1 mm (5th and 95th centiles: 4.6 mm and 8.1 mm, respectively) at a CRL of 13 weeks of gestation (a) and the measurement of the frontal bones height (b) and transverse gap (c).

![Fetal face in coronal view using volume contrast imaging-static with transparent maximum mode of display of a fetus with trisomy 21 at 13 weeks of gestation (a) and the measurement of the frontal bones height (b) and transverse gap (c).](image-url)
of 84 mm (ln height = 0.023 × CRL in mm −0.125, \( r = 0.788, \ P < 0.0001 \))\(^4\). The gap between the two frontal bones did not change significantly with gestation (mean: 1.5 mm; 5\(^{th}\) centile: 1.0 mm; 95\(^{th}\) centile: 2.0 mm; \( r = 0.076, \ P = 0.282 \))\(^4\). In five (2.5\%) cases both nasal bones were absent and in 195 cases both bones were present.

In the fetuses with trisomy 21, the median maternal age was 38 (range, 24–46) years and the median fetal CRL was 69 (range, 50–84) mm. In 42 cases both nasal bones were absent, in four cases one bone was absent, and in 29 cases both bones were present. In the fetuses with trisomy 21, compared to the normal fetuses, there was no significant difference in either the height of the frontal bones (mean difference SD 0.16; range, SD −1.78 to 2.17; \( P = 0.369 \)) or the gap between them (normal group: mean 1.50 mm, SD 0.32 mm; trisomy 21: mean 1.49 mm, SD 0.30 mm; mean difference 0.012, 95\% CI −0.073 to 0.097; \( P = 0.780 \)) (Figure 2). Additionally, within the group of trisomy 21 fetuses there were no significant differences between those with absence and those with present nasal bones. The finding that in 61\% of the fetuses with trisomy 21 there was unilateral or bilateral absence of the nasal bones is compatible with the results of previous two-dimensional and 3D studies\(^10,12\).

We have previously described that the height of the frontal bones increases with gestation in normal fetuses at 11 + 0 to 13 + 6 weeks, which is compatible with data from histological and radiological studies that ossification of the frontal bones, which starts at around 9 weeks of gestation in the middle of each supraorbital region, spreads radially towards the coronal and metopic sutures\(^13,14\).

The cranium consists of various regions with different origins and they are malformed to a varying extent in different congenital malformations. Essentially, there are two developmental fields, one behind the sella turcica, which arises around the notochord, and one in front of the sella turcica, which arises in part from the introverted mesoderm, and in part from the neural crest cells. In the anterior field, there are three different

**DISCUSSION**

The findings of this study demonstrate that, contrary to our expectation, the development of the frontal bones and metopic suture in fetuses with trisomy 21 at 11 + 0 to 13 + 6 weeks is not significantly different from normal. Additionally, within the group of trisomy 21 fetuses there were no significant differences between those with absent and those with present nasal bones. The finding that in 61\% of the fetuses with trisomy 21 there was unilateral or bilateral absence of the nasal bones is compatible with the results of previous two-dimensional and 3D studies\(^10,12\).

We have previously described that the height of the frontal bones increases with gestation in normal fetuses at 11 + 0 to 13 + 6 weeks, which is compatible with data from histological and radiological studies that ossification of the frontal bones, which starts at around 9 weeks of gestation in the middle of each supraorbital region, spreads radially towards the coronal and metopic sutures\(^13,14\).

The cranium consists of various regions with different origins and they are malformed to a varying extent in different congenital malformations. Essentially, there are two developmental fields, one behind the sella turcica, which arises around the notochord, and one in front of the sella turcica, which arises in part from the introverted mesoderm, and in part from the neural crest cells. In the anterior field, there are three different
areas, the frontonasal, maxillary and mandibular. The frontonasal is the one affected in holoprosencephaly, where, in addition to the mid-facial abnormalities, there is associated premature closure of the metopic suture.

The findings in trisomy 21 fetuses suggest that if absence of the nasal bones is a consequence of defective migration and/or function of the neural crest cells, such a deficit is confined to the development of the nasal bones and does not affect the development of the frontal bones and metopic suture. The development of the nasal and frontal bones may be dependent on different groups of neural crest cells that are differentially affected by trisomy 21.

ACKNOWLEDGMENT

This study was supported by a grant from The Fetal Medicine Foundation (Charity No. 1037116).

REFERENCES