DOI: 10.1002/pd.2938

ORIGINAL ARTICLE

Nasal bone assessment in fetuses with trisomy 21 at 16–24 weeks of gestation by three-dimensional ultrasound

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ABSTRACT

Objective This study aims to investigate the length and shape of the nasal bones in fetuses with trisomy 21 at 16–24 weeks' gestation.

Method We acquired three-dimensional volumes of the fetal profile from 41 fetuses with trisomy 21. The multiplanar mode was used to measure nasal bone length in the exact midsagittal plane and in parasagittal and oblique views of the fetal face and to examine the nasal bones in the coronal plane.

Results There was bilateral absence of the nasal bones in 11 (26.8%) cases and unilateral absence in one (2.4%). In 29 (70.7%) cases with present nasal bones, there was progressive over-estimation of nasal bone length when measured in parasagittal and oblique views compared to measurements taken in the exact midsagittal plane. In the coronal plane, in 18 of 29 (62.1%) fetuses with trisomy 21, the nasal bones were divergent, whereas in 131 of 135 (97.0%) euploid fetuses, the bones were entirely fused in the midline.

Conclusion Parasagittal and oblique scanning planes may produce over-estimation of nasal bone length in trisomy 21 fetuses because they often have divergent nasal bones. Consequently, it is essential that measurement of nasal bone length is carried out in the exact midsagittal plane of the face. © 2012 John Wiley & Sons, Ltd.

Funding Sources: This study was supported by a grant from the Fetal Medicine Foundation (UK charity number 1037116).
Conflicts of interest: None declared

INTRODUCTION

Nasal bone absence is a common phenotypic feature of fetuses with trisomy 21, and it is detectable by ultrasound both in the first and the second trimesters of pregnancy.[1,2] Previous two-dimensional (2D) ultrasound studies showed that in second trimester fetuses with trisomy 21, the nasal bone is absent in about 30% of cases and short in a further 30%.[3] However, the prevalence of short nasal bone varied among the different studies, ranging between 20% and 100%, with significant variations in the reported normal ranges and differences in the definition of nasal bone hypoplasia. We have recently demonstrated, by using the multiplanar mode of three-dimensional (3D) ultrasound, that in euploid fetuses at 16–24 weeks' gestation, parasagittal and oblique scanning planes may produce different degrees of under-estimation or over-estimation of nasal bone length compared with measurements systematically taken in the exact midsagittal plane of the fetal face and that inclusion of the vomeral bone in the definition of such plane could substantially improve the reproducibility of measurements of nasal bone length.[4]

The aims of this study are firstly, to investigate the effect of deviations from the exact midsagittal plane on the measurement of nasal bone length in fetuses with trisomy 21 at 16–24 weeks' gestation and secondly, to examine the appearance of the nasal bones in the coronal plane by use of the multiplanar mode of 3D ultrasound.

METHODS

Nasal bone length was measured by using stored 3D volumes of the fetal face, which had been acquired from 41 fetuses with trisomy 21 confirmed by chorionic villous sampling or amniocentesis, which were carried out because of a high risk for aneuploidies. In 24 (58.5%) cases, the maternal age was 35 years or more, and in 29 (70.7%) cases, there was at least one fetal abnormality or sonographic marker of chromosomal defect, including mild ventriculomegaly (n = 5), nuchal edema (n = 11), cardiac defect (n = 12), intracardiac echogenic focus (n = 5), hyperechogenic bowel (n = 4), duodenal atresia (n = 2), mild hydronephrosis (n = 3), short femur (n = 4), talipes (n = 2), and clinodactyly (n = 2). In each case, transabdominal ultrasound (RAB 4-8 L probe, Voluson 730 Expert, GE Medical Systems, Milwaukee, WI, USA) was carried out by sonographers with previous experience in 3D ultrasound.[5,4] A 3D volume of the fetal head had been acquired in the midsagittal plane of the face with an angle between the transducer and the long axis of the nose close to 45°.[3]

The 3D volumes were examined off-line by using the multiplanar mode to verify the exact midsagittal plane and to make minor corrections from the original acquisition plane when necessary. The exact midsagittal plane was defined by the presence of the nose, upper and lower lips, the maxilla (primary palate), and the chin anteriorly and by the presence of the secondary palate with the overlying vomeral bone posteriorly [6]; Figure 1). Tomographic ultrasound imaging and the multiplanar mode were used, by having as a reference on the tranverse plane a point below the nasal bridge at the level of the orbits, to produce parasagittal views of the profile at a distance of 1 and 2 mm from the midline (Figure 2) and oblique views obtained by rotation of the transverse plane around the midline by (a) 10° along the z-axis, (b) 20° along the z-axis, (c) a combination of 20° rotation along the z-axis and 10° along the y-axis (Figure 3). On-screen calipers were used to measure the length of the nasal bone in each of the profiles.

In addition, a coronal view of the nasal bones was obtained by aligning the long axis of the nasal bone displayed in the exact midsagittal plane to a vertical line and ensuring that the point of intersection between the three orthogonal planes is placed centrally in the thickness of the nasal bone (Figure 4). The appearance of the nasal bones in the corresponding coronal plane was examined and compared with that obtained from 135 euploid fetuses at 16–24 weeks of gestation from our previous study.[4] Assessment of the shape of the nasal bones was carried out by two sonographers independently (N.P. and F.M.).

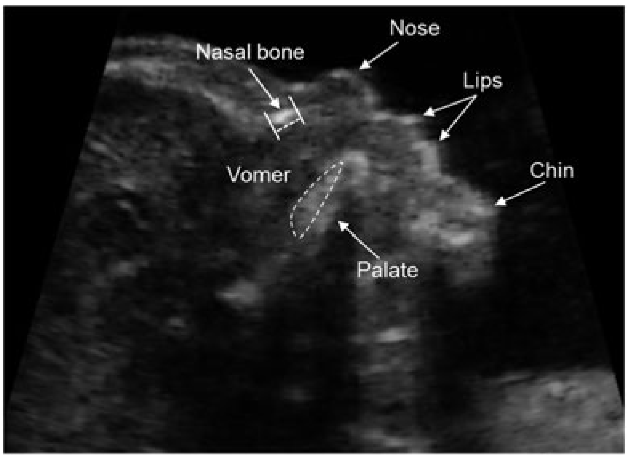

Figure 1 Ultrasound picture from a trisomy 21 fetus at 20 weeks demonstrating the exact midsagittal plane of the face with its sonographic landmarks and measurement of nasal bone length

Statistical analysis

To compare nasal bone length measured in parasagittal and oblique views with measurements taken in the exact midsagittal plane of the face, the mean differences between nasal bone length from each of the different planes and that from the midsagittal plane and their 95% confidence intervals (CI) were calculated.[7] Paired samples t-test was used to evaluate the differences between means of nasal bone length measured in left and right parasagittal planes. The data were analyzed by using the statistical software SPSS 12.0 (Chicago, Illinois, USA) and Excel for Windows 2003 (Microsoft Corp., Redmond, WA, USA).

RESULTS

The median maternal age was 37 (range 20–44) years, and the median gestational age was 19.9 (range 16–24) weeks. Maternal racial origin was Caucasian in 35 (85.4%) cases, African in 4 (9.8%), South Asian in 1 (2.4%), and East Asian in 1 (2.4%).

The nasal bones were bilaterally absent in 11 (26.8%) cases, there was unilateral absence in 1 (2.4%) case and both nasal bones were present in 29 (70.7%) cases.

There was no significant difference between left and right parasagittal measurements at 1 mm from the midsagittal plane (mean difference = 0.087, 95% CI [−1.618 (−1.869 to −1.367) to 1.791 (1.540 to 2.042)], p = 0.589) and between left and right measurements at 2 mm from the midsagittal plane (mean difference = 0.026, 95% CI [−2.529 (−2.905 to −2.153) to 2.581 (2.204 to 2.957)], p = 0.918). Therefore, the average of the left and right measurements at a given distance from the midline was used for subsequent analysis.

The mean difference and 95% CIs for measurements undertaken in parasagittal and oblique planes compared with nasal bone length measured in the midsagittal plane are shown in Table 1. When the measurements were taken in parasagittal and oblique views of the profile, there was a progressive overestimation of nasal bone length for each step of deviation from the midline compared with measurements performed in the midsagittal plane. The variation in the difference between two measurements increased with the distance and degree of deviation from the midline, with consequent widening of the 95% CIs.

There was complete agreement between the operators in the assessment of the appearance of the nasal bones in the coronal view, which was classified as normal, when two parallel bones were visualized (Figure 5a), and bifid, when the two nasal

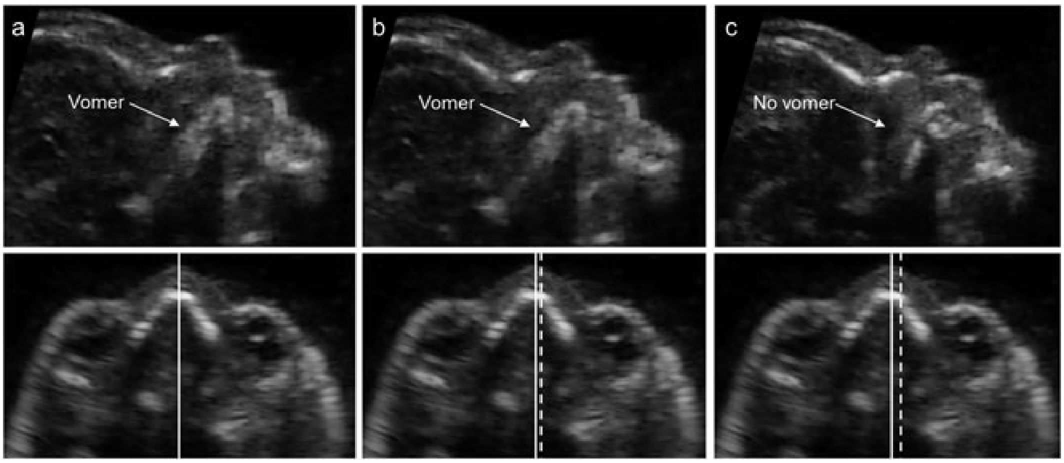

Figure 2 Ultrasound images from a trisomy 21 fetus obtained with the use of tomographic ultrasound imaging demonstrating the sagittal and the corresponding transverse plane of the fetal head at the level of the two eye sockets in the exact midsagittal plane (a) and in parasagittal planes at a distance of 1 (b) and 2 mm (c) from the midline

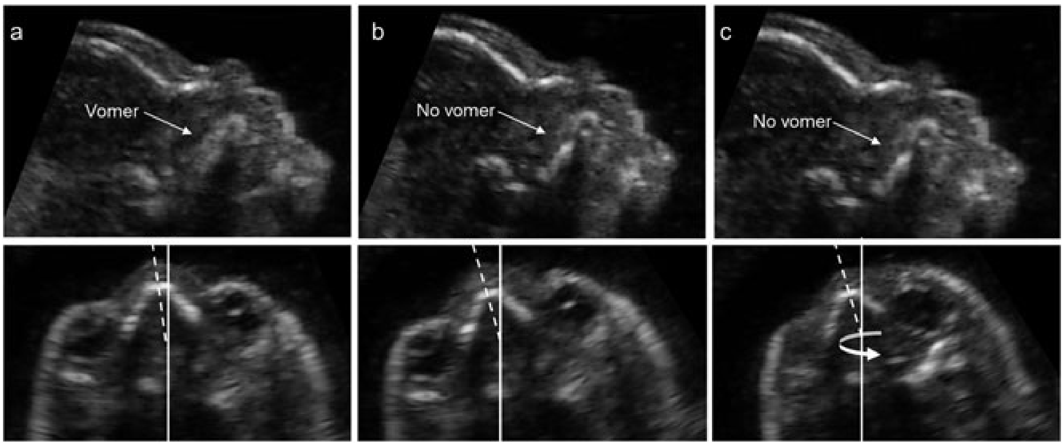

Figure 3 Ultrasound images from a trisomy 21 fetus demonstrating the sagittal and the corresponding transverse plane of the fetal head after rotation away from the exact midsagittal plane around a point placed below the nasal bridge, at the level of the two eye sockets, by 10° along the *z*-axis (a), 20° along the *z*-axis (b), a combination of 20° rotation along the *z*-axis, and 10° along the *y*-axis (c)

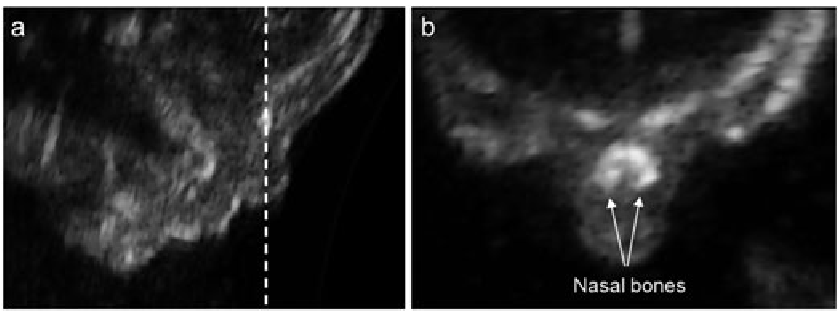

Figure 4 Ultrasound images from a trisomy 21 fetus demonstrating the sagittal (a) and the corresponding coronal view (b) of the nasal bones

Table 1 Mean difference, 95% confidence intervals, and standard deviation of the difference for nasal bone length measured in parasagittal and oblique planes compared with measurements performed in the exact midsagittal plane

Scanning plane	Mean and 95% confidence interval of the differences
Parasagittal	
1 mm from the midline	−0.323 [−1.298 (−1.442 to −1.155) to 0.651 (0.508 to 0.795)]
2 mm from the midline	−0.306 [−1.955 (−2.198 to −1.712) to 1.344 (1.101 to 1.586)]
Oblique (rotation from the midline)	
10° along the *z*-axis	−0.420 [−1.167 (−1.277 to −1.057) to 0.327 (0.217 to 0.437)]
20° along the *z*-axis	−0.910 [−1.965 (−2.121 to −1.810) to 0.145 (−0.010 to 0.301)]
20° along the *z*-axis and 10° along the *y*-axis	−1.210 [−2.155 (−2.295 to −2.016) to −0.265 (−0.404 to −0.125)]

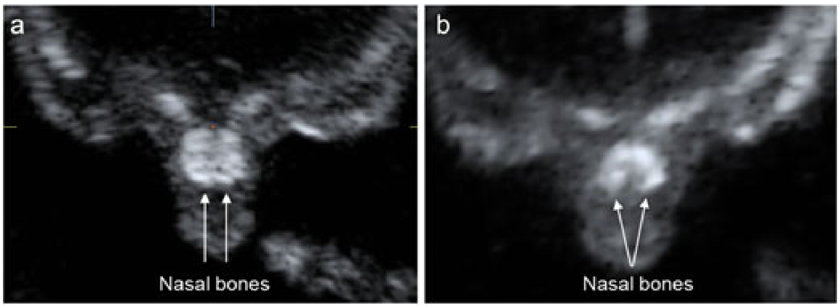

Figure 5 Ultrasound images from a chromosomally normal fetus (a) at 20 weeks demonstrating the two paired nasal bones fused on the midline in the coronal view and from a fetus with trisomy 21 (b) with divergent nasal bones (bifid)

bones diverged laterally and were not fused in the midline throughout their length (Figure 5b). The nasal bones were normal in 11 (37.9%) of 29 fetuses with trisomy 21 and bifid in the remaining 18 (62.1%) cases. Bifid nasal bones were found in 4 (2.9%) of the 135 euploid fetuses from our previous study.[4]

Table 2 shows the proportion of trisomy 21 fetuses with nasal bone length below the fifth and the first percentile of our previously published normal range[4] according to the different scanning planes.

Table 2 Proportion of trisomy 21 fetuses with nasal bone length below the fifth and the first percentile of the normal reference range from our previous study[4]

Scanning plane	< Fifth percentile	< First percentile
Midsagittal	22/29 (75.8%)	18/29 (62.0%)
Parasagittal		
1 mm from the midline	22/29 (75.8%)	15/29 (51.7%)
2 mm from the midline	20/29 (68.9%)	13/29 (44.8%)
Oblique (rotation from the midline)		
10° along the *z*-axis	19/29 (65.5%)	13/29 (44.8%)
20° along the *z*-axis	15/29 (51.7%)	9/29 (31.0%)
20° along the *z*-axis and 10° along the *y*-axis	10/29 (34.5%)	6/29 (20.7%)

DISCUSSION

This study shows firstly, that parasagittal and oblique scanning planes of the fetal profile in fetuses with trisomy 21 produce progressive over-estimation of nasal bone length compared with measurements systematically taken in the exact midsagittal plane and secondly, that a high proportion of trisomy 21 fetuses at 16–24 weeks have divergent nasal bones in the coronal plane.

Our results confirm that nasal bone absence is found in about one third of fetuses with trisomy 21. Unilateral absence of the nasal bone was found in one case, where the bone was not visible in the exact midsagittal plane but was detected in parasagittal views of the profile. Unilateral absence of the nasal bone has been previously reported both in the first and the second trimesters of pregnancy.[8,9] Its clinical significance remains uncertain because of the small number of cases identified, but it is likely to be part of the spectrum of ossification disorders in trisomy 21, which range from hypoplasia to bilateral absence of the nasal bones.

A pre-requisite for incorporation of nasal bone length into screening policies is high reproducibility of the measurements. In a study of euploid fetuses at 16–24 weeks' gestation, we have demonstrated that the nasal bone is shorter when measurements are taken in parasagittal views and longer in oblique views of the profile compared with measurements taken in the exact midsagittal plane.[4] The results from the present study show that in fetuses with trisomy 21, the nasal bone is shorter in the exact midsagittal plane compared with both parasagittal and oblique views. The likely explanation for these findings is that a high proportion of trisomy 21 fetuses had divergent nasal bones that were not entirely fused on the midline. Sandikcioglu *et al.*[10] have shown that the nasal bones develop as two separate ossification centers, which subsequently fuse in the midline and progressively increase in length and width as the pregnancy advances. A disorder in this ossification pattern could be responsible for different degrees of nasal bone dysplasia and consequent bifid appearance in the coronal plane.

The difference between measurements of the nasal bones taken in parasagittal and oblique views and those taken in the exact midsagittal plane could potentially produce significant variations in the detection rate of nasal bone hypoplasia in screening for trisomy 21. As shown in Table 2, if the measurements are all taken in the exact midsagittal plane, the detection rate, at fixed false positive rates of 5% and 1%, would be 76% and 62%, respectively. In contrast, measuring nasal bone length in oblique views would produce a reduction in detection rate to 35% and 21%, respectively. These data support the importance of measuring nasal bone length in the exact midsagittal plane to improve the performance of this marker in screening for trisomy 21. The sonographic landmarks commonly used to define such plane include the nose, upper and lower lips, and the maxilla and the chin, which are also visible in parasagittal and oblique sections of the profile. In our previous study, we suggested that inclusion of the vomeral bone may be useful to ensure that nasal bone length is systematically measured in the exact midsagittal plane of the fetal face.[4]

Examination of the nasal bones in the coronal plane requires 3D ultrasound because this view cannot be easily obtained with 2D sonography. However, divergent nasal bones will result in smaller measurements in the exact midsagittal plane on 2D ultrasound, thus allowing correct identification of fetuses with nasal bone hypoplasia/dysplasia.

WHAT'S ALREADY KNOWN ABOUT THIS TOPIC?

- Nasal bone hypoplasia is an important sonographic feature of trisomy 21 fetuses in the second trimester of pregnancy.

WHAT DOES THIS STUDY ADD?

- To improve the performance of second trimester screening for trisomy 21, the nasal bone length should be measured in the exact midsagittal plane of the fetal face.

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