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# Frontomaxillary facial angle in chromosomally normal fetuses at 11 + 0 to 13 + 6 weeks

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**KEYWORDS:** fetal maxilla; fetal palate; first-trimester screening; frontomaxillary facial angle; three-dimensional ultrasound

## ABSTRACT

***Objective*** *To establish the normal range of the frontomaxillary facial (FMF) angle at 11 + 0 to 13 + 6 weeks of gestation.*

***Methods*** *In this prospective study, three-dimensional (3D) volumes of the fetal head were obtained from 500 pregnancies before fetal karyotyping by chorionic villus sampling (CVS), after screening by fetal nuchal translucency (NT) thickness and maternal serum free β-human chorionic gonadotropin (β-hCG) and pregnancy-associated plasma protein-A (PAPP-A) at 11 + 0 to 13 + 6 weeks. Only cases with a normal karyotype were included in this study. The FMF angle was measured off-line. In a subgroup of 150 cases the FMF angle was measured using 2D ultrasound before obtaining a 3D volume. In 50 cases the 3D volumes were used to measure the FMF angle by the same examiner twice and by another examiner once.*

***Results*** *The mean FMF angle decreased with crown–rump length (CRL) from 84.3° at CRL 45 mm to 76.5° at CRL 84 mm. There was no significant association between the FMF angle and fetal NT or serum PAPP-A or β-hCG. In the volumes with paired measurements, the difference between two measurements by the same or two sonographers was < 5% in 95% of the cases. In the cases with paired 3D and 2D ultrasound measurements, the difference in FMF angles was < 8% in 95% of the cases.*

***Conclusions*** *At 11 + 0 to 13 + 6 weeks the FMF angle decreases with fetal CRL but is not related to fetal NT or serum biochemistry. The measurement is reproducible and the results obtained by 3D and 2D ultrasound are similar. Copyright © 2007 ISUOG. Published by John Wiley & Sons, Ltd.*

## INTRODUCTION

The frontomaxillary facial (FMF) angle, between the upper surface of the palate and the frontal bone in a midsagittal view of the fetal face, is a recently described sonographic method of defining the relative position of the maxilla to the forehead[1]. In a study of stored three-dimensional (3D) volumes of the fetal face, the FMF angle in 100 fetuses with trisomy 21 at 11 + 0 to 13 + 6 weeks of gestation was significantly greater than that in 300 chromosomally normal fetuses[1]. In the normal group there was a non-significant decrease in FMF angle with crown–rump length (CRL) and the $95^{th}$ centile was 85°. In the trisomy 21 fetuses the FMF angle was above 85° in 69% of cases, suggesting that this measurement is likely to be a useful marker in first-trimester screening for trisomy 21.

The aims of this prospective study in chromosomally normal fetuses at 11 + 0 to 13 + 6 weeks were: first, to establish a normal range of FMF angle with gestation; second, to investigate the possible association between the FMF angle and fetal nuchal translucency (NT) thickness and maternal serum free β-human chorionic gonadotropin (β-hCG) and pregnancy-associated plasma protein-A (PAPP-A), which are also used in first-trimester screening for trisomy 21[2,3]; and third, to compare the measurements of the FMF angle obtained by two-dimensional (2D) ultrasound with those taken by 3D ultrasound.

## METHODS

This was a prospective study in singleton pregnancies at 11 + 0 to 13 + 6 weeks of gestation in which 3D volumes of the fetal head and measurement of the FMF angle were obtained immediately before fetal karyotyping by chorionic villus sampling (CVS). The women chose to

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have CVS after risk assessment by a combination of maternal age, fetal NT thickness and maternal serum free β-hCG and PAPP-A[2,3]. All cases included in this study were subsequently found to have a normal karyotype.

In each case, we attempted within a period of 15 min to obtain a 3D volume of the fetal head in the midsagittal plane of the face, with the transducer being parallel to, or within 30° of, the long axis of the nose[4]. The 3D volumes were examined off-line, using the multiplanar mode to identify 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 tip of the nose anteriorly, the translucent diencephalon in the middle, the nuchal membrane posteriorly and a rectangular shape of the palate[4] (Figures 1 and 2).

The FMF angle was measured between a line along the upper surface of the palate and a line which traverses the upper corner of the anterior aspect of the maxilla, extending to the external surface of the forehead,

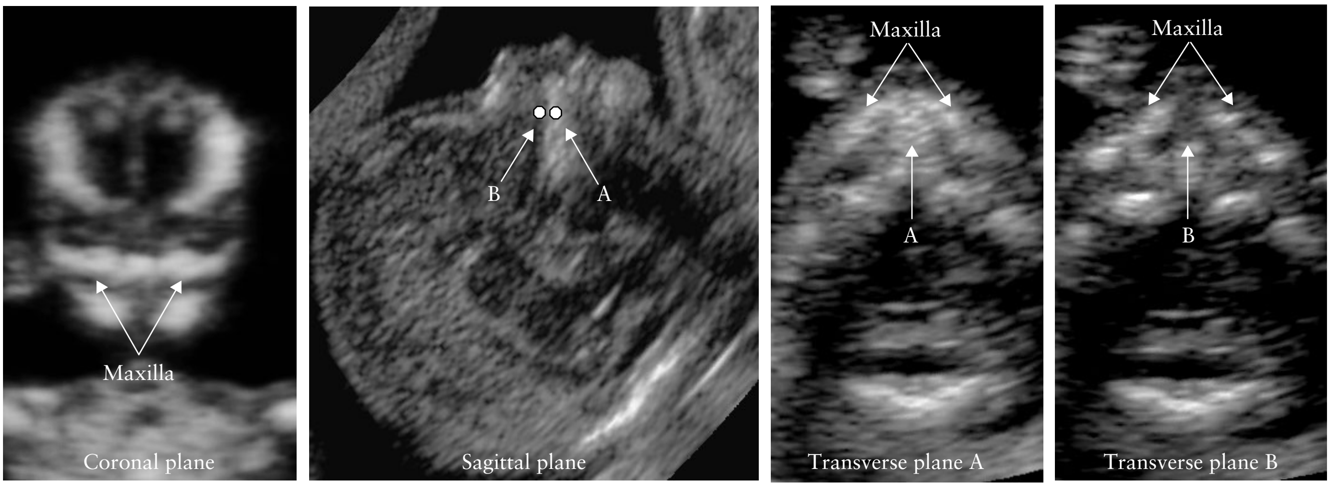


**Figure 1** Multiplanar view of the fetal face, demonstrating the maxilla in the coronal plane and the palate in the sagittal plane and transverse plane A at the level of point A of the sagittal plane. When position B in the sagittal plane is selected, the palate is not visible in the transverse plane B.

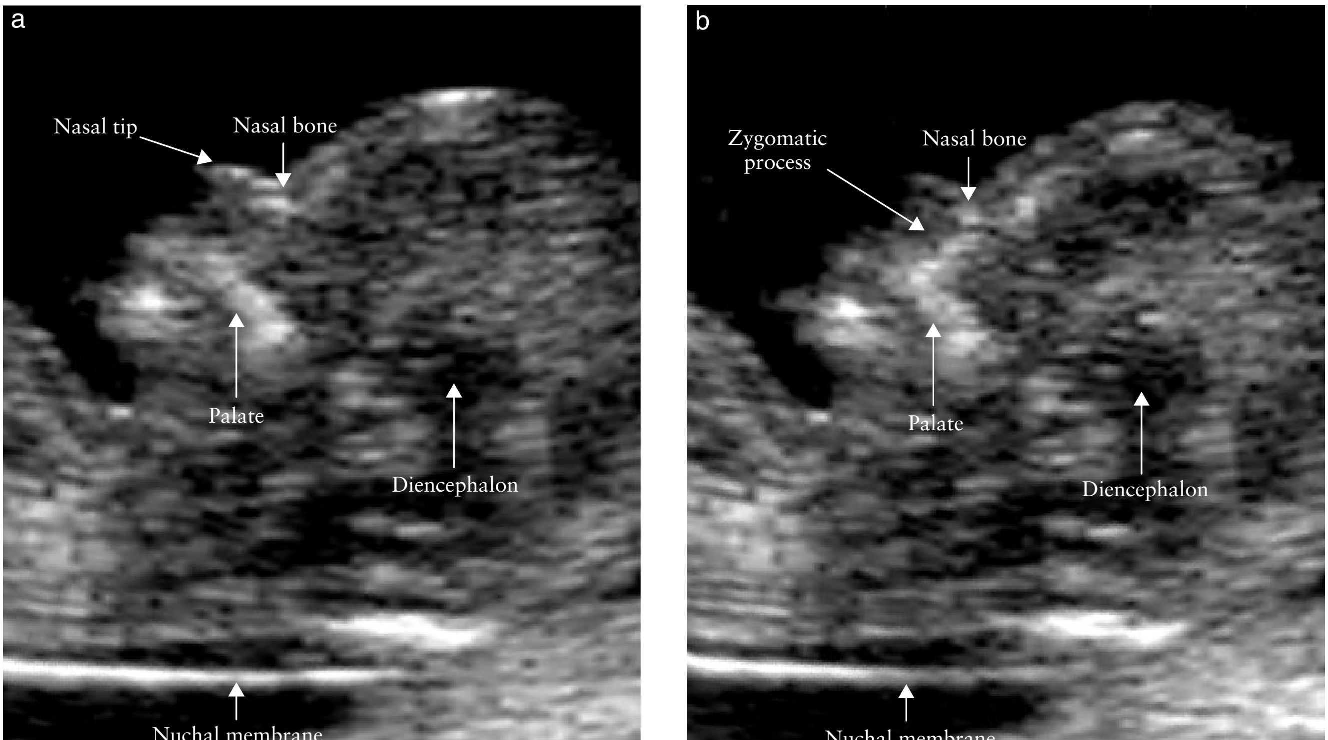


**Figure 2** Midsagittal plane of the fetal profile, demonstrating the tip of the nose, the translucent diencephalon, the nuchal membrane and the rectangularly shaped palate (a). The plane is not midsagittal when the tip of the nose is not visible and the zygomatic process appears (b).

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represented by the frontal bones or an echogenic line under the skin below the metopic suture that remains open[1] (Figure 3).

All examinations were carried out transabdominally (RAB 4-8L probe; Voluson 730 Expert, GE Medical Systems, Milwaukee, WI, USA) by sonographers with extensive experience in first-trimester scanning and 3D ultrasound.

### Repeatability of the measurement

In 50 cases selected by computerized randomization the 3D volumes were used to measure the FMF angle by the same examiner twice, with an interval of 3–5 days between the two measurements, and by another examiner once. These data were used to assess the repeatability of the measurement.

### Comparison of measurements obtained by 2D and 3D ultrasound

In a subgroup of 150 consecutive cases, the FMF angle was prospectively measured using 2D ultrasound immediately before obtaining a 3D volume. In these cases the examiner undertaking the off-line 3D assessment was not aware of the FMF angle measurement obtained by 2D ultrasound. These data were used to compare the measurements obtained by 2D and 3D ultrasound.

### Statistical analysis

Regression analysis was used to determine the significance of the association between the FMF angle and CRL. Each measurement of the FMF angle was expressed as a difference from the expected normal mean for CRL (delta value). The Kolmogorov–Smirnov test was used to confirm the normal distribution of the delta values for the FMF angle. Regression analysis was also used to evaluate the relationship between delta FMF angle and delta fetal NT (difference between observed NT and normal mean for CRL) and maternal serum PAPP-A and β-hCG (expressed as multiples of the median (MoMs) and corrected for fetal CRL and maternal weight, ethnicity and smoking status[3,5–7]). The Mann–Whitney *U*-test was used to determine the significance of differences in mean delta FMF angle between Caucasians and Afro-Caribbeans or Indians/Pakistanis.

In 50 cases with paired measurements of the FMF angle, Bland–Altman[8] analysis was used to compare the measurement agreement and bias for each of two examiners and between the two examiners. Similarly, Bland-Altman[4] analysis was used to compare the measurement agreement and bias for the FMF angle by 2D and 3D ultrasound.

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.

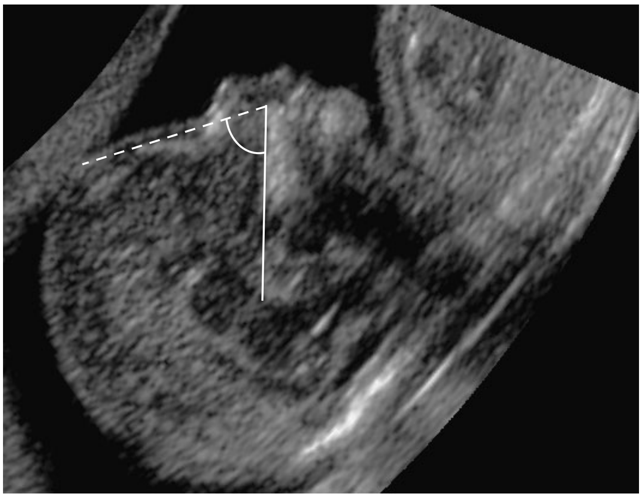

**Figure 3** Ultrasound image demonstrating the measurement of the frontomaxillary facial angle. The angle is defined by a line along the upper surface of the palate and a line from the upper corner of the anterior aspect of the maxilla extending to the external surface of the frontal bone.

## RESULTS

Acquisition of a 3D volume of the fetal head in the appropriate midsagittal plane of the face was successfully obtained in 500 (81.8%) of 611 consecutively examined chromosomally normal fetuses. In 111 cases the fetal position was such that, within the allocated 15 min, it was not possible to image the fetal profile and obtain the appropriate 3D volume. In the 500 selected cases the median maternal age was 35.4 (range 17–50) years, the median CRL was 68.2 (range 46–84) mm and the median gestation was 12 (11 + 0 to 13 + 6) weeks. The ethnic origin of the mother was Caucasian in 456 (91.2%), Afro-Caribbean in 23 (4.6%) and Indian or Pakistani in 21 (4.2%).

The mean FMF angle decreased with CRL from 84.3° at CRL 45 mm to 76.5° at CRL 84 mm (FMF angle = $93.34 - 0.200 \times$ CRL, $r = 0.374$, $P < 0.0001$; Figure 4). The mean delta FMF was 0.0148, 95% CI −0.36 to 0.39. There was no significant association between delta FMF angle and fetal delta NT ($r = 0.007$, $P = 0.875$), maternal serum PAPP-A MoM (0.012, $P = 0.793$) or maternal serum β-hCG MoM ($r = 0.100$, $P = 0.832$). The mean delta FMF angle in Caucasians was −0.02 (95% CI −0.416 to 0.371) and this was not significantly different from the values in Afro-Caribbeans (mean −0.38, 95% CI −2.137 to 1.371, $P = 0.735$) or Indians/Pakistanis (mean 1.264, 95% CI −0.830 to 3.358, $P = 0.286$).

### Repeatability of the measurement

In the 50 volumes with paired measurements of the FMF angle, the mean difference and the 95% limits of agreement between paired measurements by the same sonographer and between paired measurements by the two different observers are shown in Figure 5 and Table 1.

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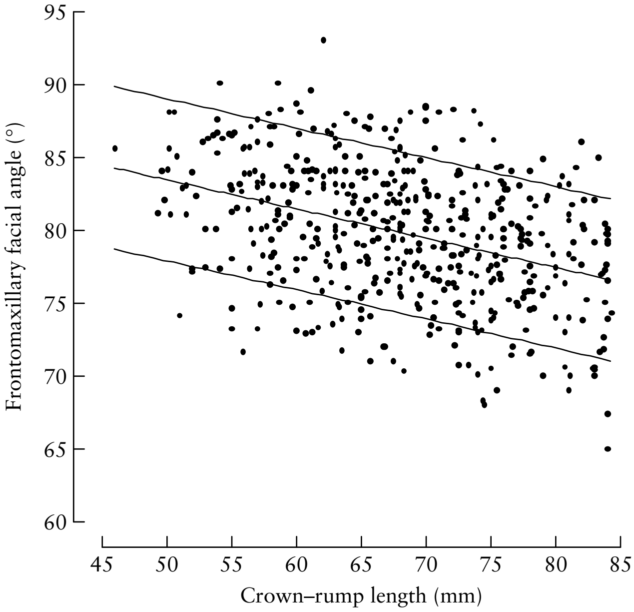


**Figure 4** Frontomaxillary facial angle in 500 chromosomally normal fetuses vs. crown–rump length (mean, 95th and 5th percentiles).

### Comparison of measurements obtained by 2D and 3D ultrasound

An appropriate 2D image of the fetal profile was successfully obtained in 144 (96.0%) of the 150 consecutive cases in which this was attempted. In these 144 cases, the mean difference and the 95% limits of agreement between paired 2D and 3D measurements of the FMF angle are shown in Figure 6 and Table 1.

## DISCUSSION

The findings of this study demonstrate that at $11 + 0$ to $13 + 6$ weeks of gestation the FMF angle decreases with fetal CRL from a mean of about 85° at CRL 45 mm to 75° at CRL 84 mm. The FMF angle provides an objective measurement of the position of the anterior end of the maxilla to the forehead, and the observed decrease in the angle with gestation may be due to a preferential forward growth of the maxilla with respect to the forehead or upward displacement or growth of the palate.

The additional findings of the study are: first, measurement of the FMF angle is reproducible and in 95% of cases the difference between two consecutive measurements by the same or two sonographers is $< 5\%$;

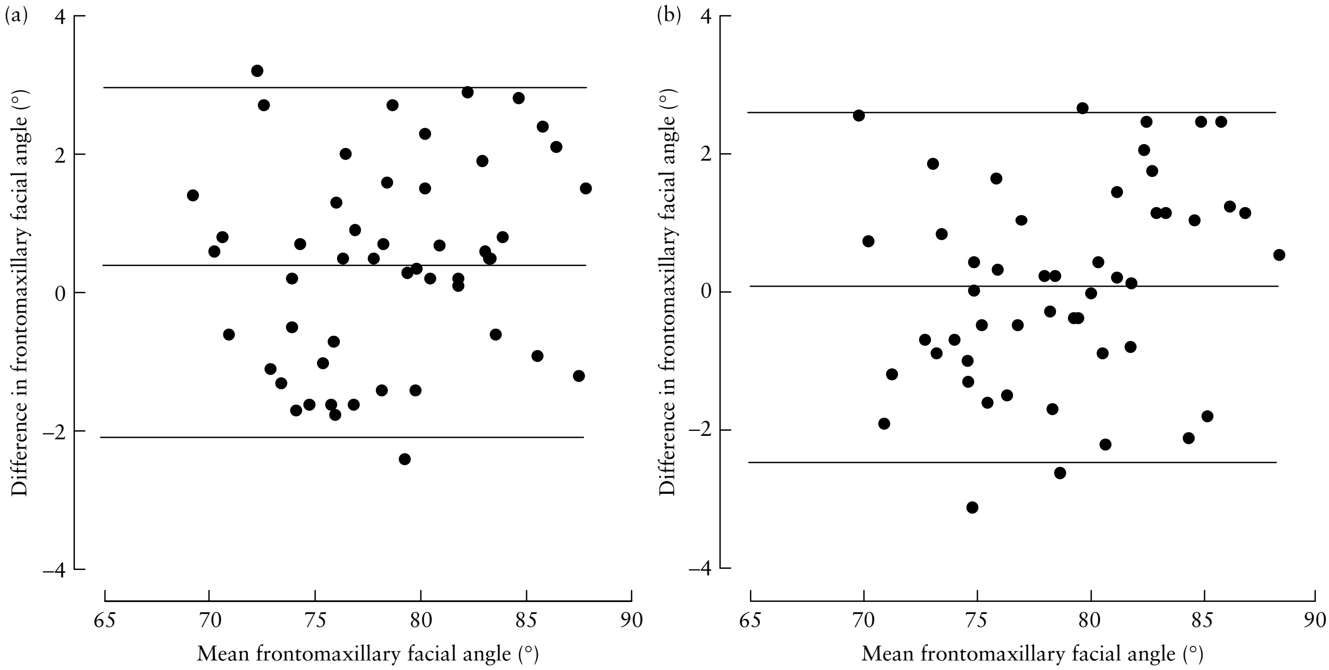


**Figure 5** Mean difference and 95% limits of agreement between paired measurements of the frontomaxillary facial angle by the same observer (a, intraobserver) and between paired measurements by the two different observers (b, interobserver).

**Table 1** Comparison between paired measurements of the frontomaxillary facial angle

| *Comparison* | *Mean difference (95% CI)* |
|---|---|
| Measurements by two- and three-dimensional ultrasound | −0.713 [−6.16 (−6.39 to −5.63) to 4.59 (4.20 to 4.97)] |
| Two measurements by the same observer | 0.402 [−2.44 (−2.80 to −2.08) to 3.24 (2.89 to 3.60)] |
| Measurements by different observers | 0.059 [−2.77 (−3.12 to −2.41) to 2.89 (2.53 to 3.24)] |

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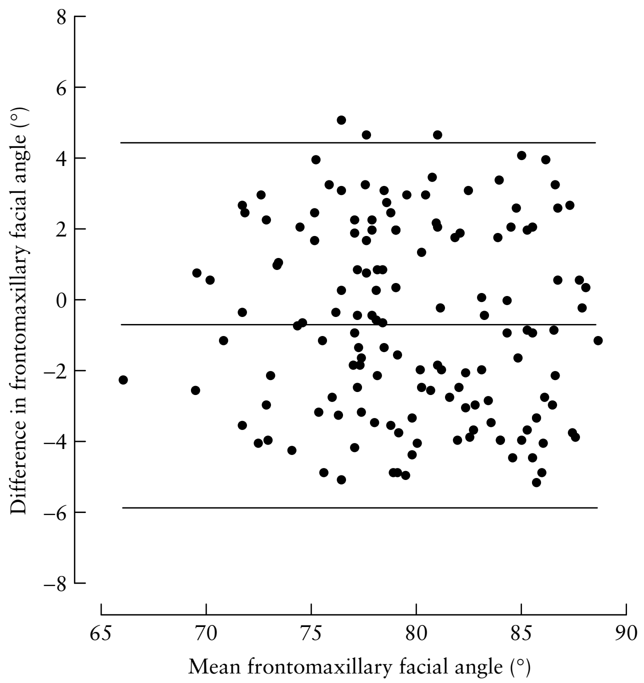


**Figure 6** Mean difference and 95% limits of agreement between paired measurements of the frontomaxillary facial angle by two- and three-dimensional ultrasound.

second, there is no significant association between the FMF angle and fetal NT thickness or maternal serum free β-hCG and PAPP-A; and third, the measurements of the FMF angle obtained by 3D and 2D ultrasound are similar.

Effective first-trimester screening for trisomy 21 is provided by a combination of maternal age, fetal NT thickness and maternal serum free β-hCG and PAPP-A. Using this approach, the detection rate of trisomy 21 is about 90% for a false positive rate of 5%[9]. Preliminary results suggest that the FMF angle measurement is above the 95$^{th}$ centile in > 60% of fetuses with trisomy 21[1]. Our study shows that measurement of the FMF angle is reproducible and that, at least in chromosomally normal fetuses, there is no significant association between the angle size and fetal NT thickness or maternal serum free β-hCG and PAPP-A. Consequently, this measurement is likely to improve the performance of first-trimester sonographic and biochemical screening. However, accurate assessment of the FMF angle necessitates extensive experience in scanning and, as demonstrated in our study, it may not be possible to obtain the exact midsagittal plane of the fetal face within a period of 15 min in up to 20% of cases. It is therefore unlikely that the FMF angle will be incorporated into routine first-trimester sonographic screening for chromosomal abnormalities in all cases. An alternative approach to routine measurement of the FMF angle in all cases is to reserve this examination for the subgroup of pregnancies with an intermediate risk after combined fetal NT and maternal serum free β-hCG and PAPP-A screening, which constitutes only 10-15% of the total population[9].

Measurements of the FMF angle obtained by 3D and 2D ultrasound are similar, provided that they are performed in the exact midsagittal view of the fetal face. In 3D ultrasound the simultaneous display of the three orthogonal planes ensures easy identification of this view. However, the exact midsagittal plane can also be obtained by 2D ultrasound when the sonographers are appropriately trained to recognize the necessary landmarks. These include presence of the echogenic tip of the nose and rectangular shape of the palate anteriorly, the translucent diencephalon in the center and the nuchal membrane posteriorly. Minor deviations from the exact midline plane would cause non-visualization of the tip of the nose and visibility of the zygomatic process of the maxilla[4]. Examination of the exact midsagittal plane is necessary not only for measurement of the FMF angle but also for accurate assessment of the nasal bone and measurement of the fetal NT.

## ACKNOWLEDGMENT

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