

Maxilla–nasion–mandible angle: a new method to assess profile anomalies in pregnancy

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KEYWORDS: cleft alveolus; fetal face; fetal mandible; fetal maxilla; fetal profile; flat face; prenatal diagnosis; retrognathia

ABSTRACT

Objectives To collect normative data and test the feasibility and reproducibility of measurement of the maxilla–nasion–mandible (MNM) angle between 16 and 36 weeks' gestation and its diagnostic ability in a group of pathological cases.

Methods The MNM angle is defined as the angle between the intersection of the maxilla–nasion and mandible–nasion lines in the exact mid-sagittal plane. After assessing reproducibility, the MNM angle was measured in 3D volumes in 241 fetuses cross-sectionally and in 11 fetuses longitudinally. The MNM angle was then tested in 18 pathological cases with facial malformations or syndromes with specific facial features.

Results The MNM angle could be measured in 92.3% of normal fetuses. Intra- and interobserver intraclass correlation coefficient (ICC) variability was 0.92 and 0.81, respectively. The difference between paired measurements performed by one or two observers was less than 2.5° and 3.6°, respectively in 95% of the cases. The mean MNM angle was 13.5° and did not change significantly during pregnancy ($r = -0.08$, $P = 0.25$). The MNM angle was above the 95th centile in all cases of retrognathia and maxillary alveolar ridge interruption. The MNM angle was below the 5th centile in Apert syndrome, thanatophoric dysplasia and in two of the three Down syndrome cases.

Conclusions The feasibility and reproducibility of measurement of the MNM angle is good. The MNM angle can be used to evaluate the convexity of the fetal profile by enabling an objective assessment of the anteroposterior relationship of the jaws and it may therefore be of help in the diagnosis of retrognathia, maxillary alveolar ridge interruption and flat profile. Copyright © 2011 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Important information can be drawn from examination of the fetal profile. As opposed to the adult profile, which is flat, the fetal profile is characterized by a convex form, profoundly influenced by the position of the jaws. Conditions such as retrognathia of the mandible, maxillary hypoplasia or maxillary alveolar ridge interruption can all influence the convexity of the profile. These features are frequently encountered in genetic disorders such as chromosomal abnormalities or syndromes¹. Jaw abnormalities may also be associated with swallowing disorders that may cause polyhydramnios and may affect breathing or feeding after birth^{2,3}. Later in life, jaw abnormalities can result in speech, mastication or orthodontic problems and may cause variable degrees of psychological problems³.

Evaluation of the fetal profile is currently largely dependent on subjective visual interpretation. However, for a correct diagnosis of profile abnormalities it is important to rely upon normative measurements providing standards for classification, documentation, follow-up and comparison.

Previously, we have demonstrated that 3D ultrasound is an essential tool for definition of the exact mid-sagittal profile view⁴. However, an easy and objective method to assess jaw position at prenatal ultrasound is still lacking. This method should be simple and reproducible, with easy to identify superficial landmarks that are not hampered by shadowing of bony structures, and without the need for reference lines or specific insonation angles.

Of all the measurements proposed in the literature, the cephalometric point A–nasion–point B (ANB) angle (nasion is the most anterior point at the intersection of the frontal and nasal bones), used by Riedel to assess the jaw relationship for orthodontic diagnosis, prognosis and treatment planning in 1952, appears promising



Figure 1 Point A–nasion–Point B (ANB) angle measurement on a cephalogram of an adult. The ANB angle is the angle between the lines Point A–nasion and Point B–nasion. Point A is the innermost point on the curvature of the anterior aspect of the maxilla. Point B is the innermost point on the curvature of the anterior aspect of the mandible. N is the nasion, the most anterior point at the intersection of the frontal and nasal bones.

for application during prenatal ultrasound examination (Figure 1)⁵.

In the present study, we collected normative data and determined whether a prenatal version of the ANB angle, renamed the maxilla–nasion–mandible angle (MNM angle), could be a useful tool to establish, by means of 3D ultrasound, the convexity of the profile in the second and third trimesters of pregnancy (Figure 2). We also tested the MNM angle in pathological cases.

PATIENTS AND METHODS

The study was approved by the local ethics committee and all women gave written consent. Study data were obtained from 261, nonsmoking, healthy, low-risk, pregnant Caucasian women with a singleton and uncomplicated pregnancy. Women were recruited at the time of the dating scan or routine second-trimester anomaly scan. They were asked to attend an additional examination at between 16 and 36 weeks' gestation. In addition, 11 healthy Caucasian employees of our hospital attended every 4 weeks, starting at 16 weeks' gestation, for a longitudinal study. Only non-anomalous fetuses were included. Gestational age was determined from the last menstrual period and by a first-trimester dating scan. The examinations were carried out transabdominally, using a Voluson 730 Expert ultrasound system (GE Medical Systems, Zipf, Austria). In the course of the study, the 2–5-MHz transducer was replaced by a 4–8-MHz transducer.

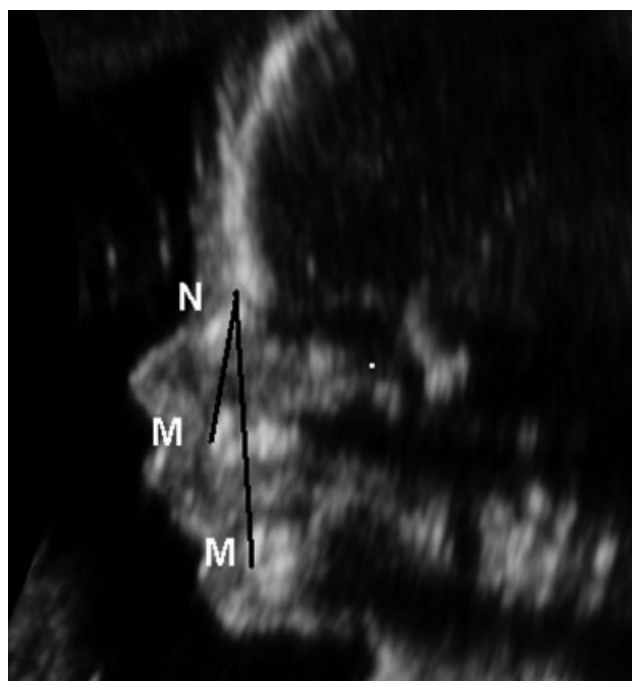


Figure 2 Maxilla–nasion–mandible (MNM) angle measurement on a prenatal ultrasound image. The MNM angle is the angle between the lines maxilla–nasion and mandible–nasion in the exact mid-sagittal plane. The landmarks on the maxilla (upper M) and mandible (lower M) are in the middle of the anterior borders of the jaws. N is the nasion, the most anterior point at the intersection of the frontal and nasal bones.

When the fetus was facing the transducer with closed mouth, 3D volumes of the fetal head were acquired, starting at the mid-sagittal plane. An attempt was made to start at the exact mid-sagittal plane, without a specific insonation angle around the x-axis of the fetus. The ultrasound image of the fetal head was enlarged to at least one third the size of the screen, the render box was placed such that the whole fetal head was included within it and the angle of the volume was adjusted to the size of the fetal head. Volumes were obtained with high-2 or maximum quality depending on the behavioral state of the fetus. A normal frequency range was used in most women, but this was changed to 'resolution' or 'penetration' in case of a slim or obese woman. Except in the longitudinal group, each fetus was investigated only once for the purpose of this study. An attempt was made to collect at least two volumes per investigation.

All examinations were carried out by one experienced ultrasonographer (E.J.P.). The volumes were stored on removable digital media for subsequent analysis on 4D View software version 7.0 (GE Medical Systems). With the multiplanar mode the exact mid-sagittal plane was depicted. The MNM angle was then defined as the angle between the lines maxilla–nasion and mandible–nasion in the exact median plane (Figure 2). The nasion is defined as the most anterior point at the intersection of the frontal and nasal bones. Jaw landmarks were defined as the middle points of the anterior borders of the maxilla and

mandible. Calipers were placed on the outermost borders of the bone.

When there was a gap between the nasal and frontal bones, the landmark nasion was at the point of intersection between the lines tangential to the nasal bone and tangential to the lower part of the frontal bone. When there was a wide metopic suture, the echogenic line representing the future frontal bone was used. When necessary, the marker dot in the B-plane of the multiplanar view was used to identify landmarks on the maxilla or mandible (Figure 3).

Intra- and interobserver variability was assessed by intraclass correlation coefficient (ICC) and Bland–Altman analysis⁶ on paired volumes, acquired using the 4–8-MHz transducer, of 20 patients chosen at random at different gestational ages, with at least 3 days between the two assessments.

In 18 fetuses, the MNM angle was measured on stored 3D volumes after a facial anomaly or syndrome with specific facial features was suspected at ultrasound investigation and before the final diagnosis had been made (by genetic investigation or postpartum examination).

Data were analyzed using the statistical software SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA) and Excel for Windows 2000. Means with ranges or SD were calculated when appropriate. Correlation was determined by Pearson's correlation test. The statistical significance of the difference of the means of two groups was tested with the unpaired Student's *t*-test. To compare means on the same subjects over time, the paired

t-test was used. $P < 0.05$ was considered statistically significant.

RESULTS

The cross-sectional study group included 261 fetuses. In two fetuses, an anomaly was diagnosed: one was excluded from the study (spina bifida) and the other was moved to the pathological group (facial cleft). In 16 fetuses (6.1%), no volume could be obtained because the fetus was facing the maternal spine (15 cases) or had an unfavorable position combined with shadows produced by the arms (one case). These cases were equally distributed over both trimesters: seven in the second trimester, nine in the third trimester. One case was excluded after analysis because of uncertainty over mouth closure. Another was excluded because extreme flexion of the head prevented identification of the mandibular landmark. The MNM angle was thus measured in 241 normal fetuses (92.3%). Fifty-two investigations (22%) were performed with the 2–5-MHz transducer and 189 investigations (78%) with the 4–8-MHz transducer.

Mean BMI of the women before pregnancy was 23.7 (range, 17.4–36.2). The mean amniotic fluid index was 17.0 (range, 7.3–28.3). The presentation of the fetus was cephalic in 67%, breech in 28% and transverse in 5%. The mean birth weight of the babies was 3473 g (range, 1160–4885 g), with 89% of the babies between the 5th and 95th centile. Fifty-four percent of the babies were boys and 46% were girls.

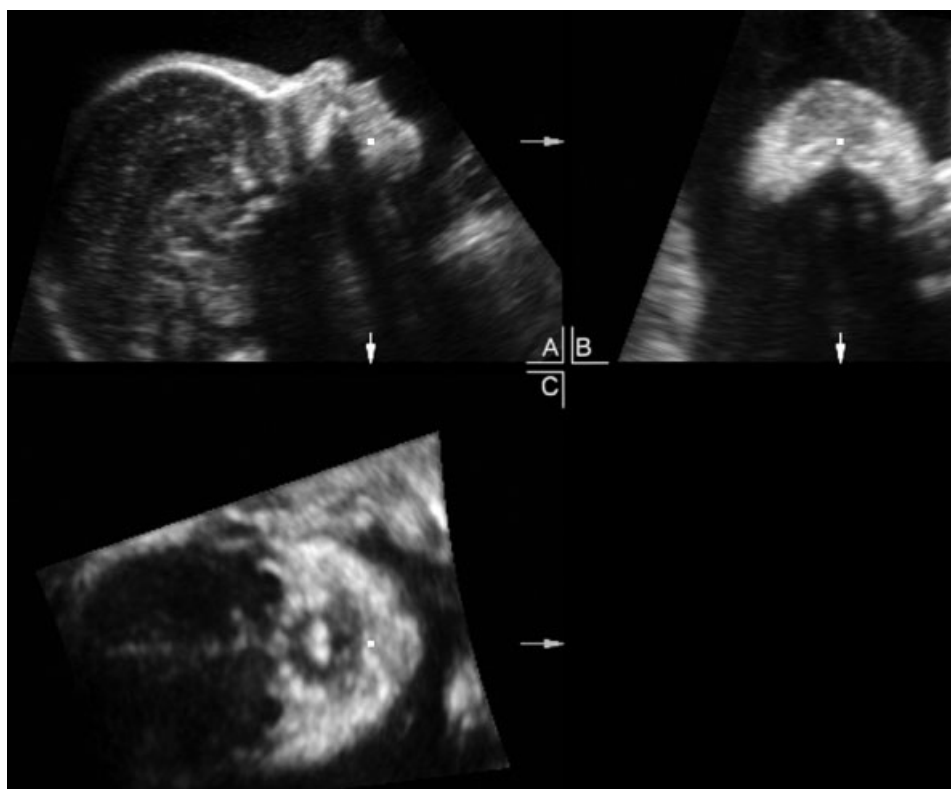


Figure 3 Multiplanar view showing identification of the landmark used for the mandible (i.e. the middle point of the anterior border) with marker dot in the B-plane.

The MNM angle measurements, with corresponding gestational ages, used to assess intra- and interobserver variability are shown in Table S1. The intra- and interobserver ICC variability was 0.92 and 0.81, respectively. For paired measurements performed by one observer, the mean difference and 95% limits of agreement (with their 95% CI) were -0.05° (-2.50° (-3.44° to -1.54°) to 2.40° (1.44° – 3.34°)). For paired measurements performed by two different observers, the respective values were -0.15° (-3.57° (-4.89° to -2.25°) to 3.27° (1.94° – 4.59°)) (Figure 4).

The mean MNM angle of the study population (241 fetuses) was 13.53° (95% CI, 13.28° – 13.78° ; range, 8.96° – 19.58°). No correlation between gestational age and the MNM angle could be demonstrated (Pearson $r = -0.08$, $P = 0.25$). The 5th and 95th centiles were 10.39° and 16.91° , respectively (Figure 5). There was no difference between the MNM angle in boys (mean: 13.45°) and girls (mean: 13.59°) (Student's t -test $P = 0.68$). The MNM angles of the longitudinal study group are presented in Figure 6 (mean MNM angle: 13.81° (range,

10.61° – 16.81°)). The first and last measurements of the longitudinal group were not significantly different (paired t -test $P = 0.52$).

Pathological cases

The pathological group consisted of eight cases in which retrognathia was suspected (CHARGE association, two cases of trisomy 18, campomelic dysplasia, Cri du chat syndrome, Goldenhar syndrome, Goldenhar syndrome with VACTERL association and Pierre–Robin syndrome), three cases with suspicion of a flat profile (Apert syndrome and two cases of thanatophoric dysplasia type 1, without cloverleaf skull), three cases of trisomy 21 and four cases of facial clefts of variable severity. The results are presented in Figure 7 and Table 1.

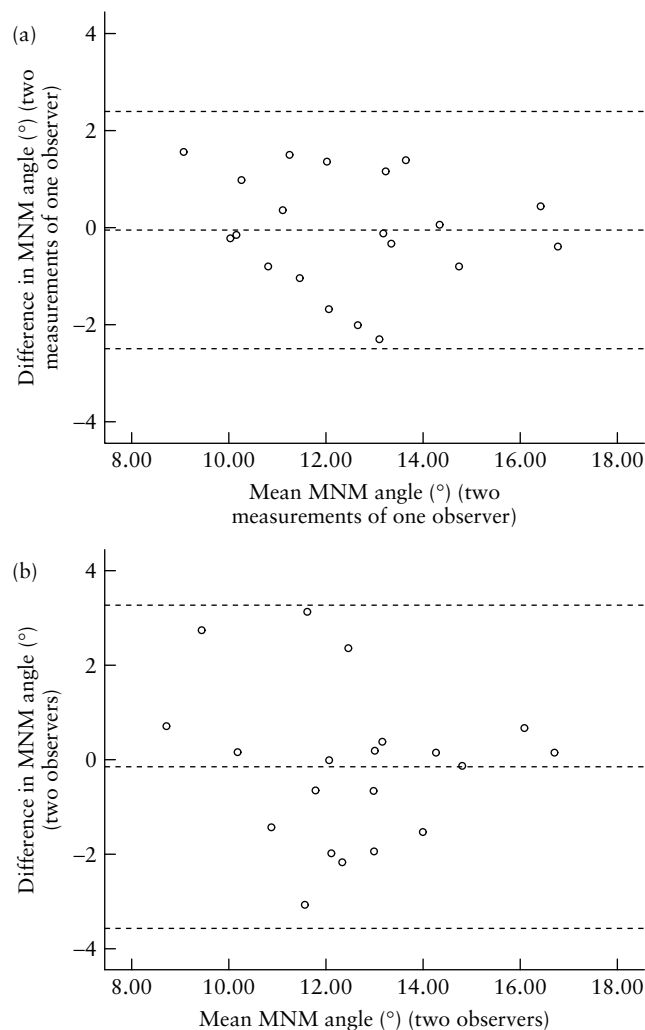


Figure 4 Bland–Altman plots showing mean difference and 95% limits of agreement between paired measurements of the maxilla–nasion–mandible (MNM) angle by (a) the same observer (intraobserver) and (b) two different observers (interobserver).

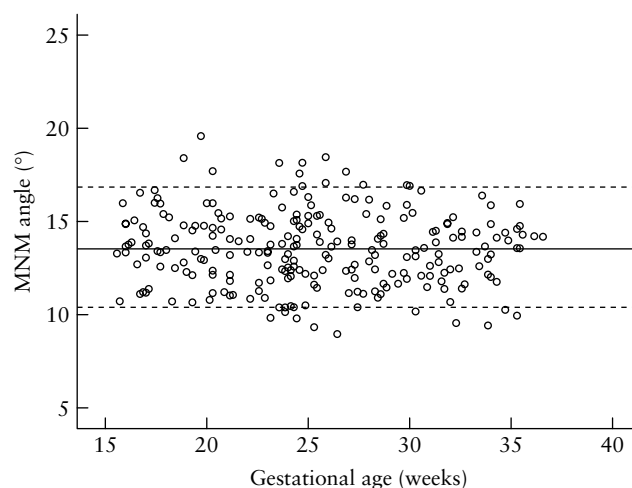


Figure 5 Scatterplot of maxilla–nasion–mandible (MNM) angle against gestational age in 241 healthy fetuses, with mean (—) and 5th and 95th centiles (---).

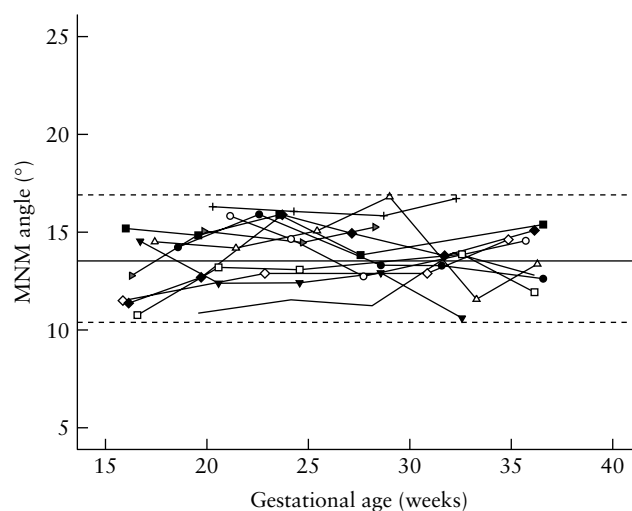


Figure 6 Serial maxilla–nasion–mandible (MNM) angle measurements in 11 healthy fetuses between 16 and 36 weeks' gestation, showing mean (—) and 5th and 95th centiles (---) of the normal cross-sectional population.

Table 1 Summary of pathological cases with maxilla–nasion–mandible (MNM) angle measurements

Abnormality	Genetic confirmation	GA (weeks)	MNM angle (°)	MNM angle classification	Retrognathia*	Cleft alveolus*	Other facial anomalies seen with ultrasound
Thanatophoric dysplasia type I	Yes	19 + 5	9.2	< P5	No	No	Frontal bossing
Thanatophoric dysplasia type I	Yes	20 + 6	6.9	< P5	No	No	Frontal bossing
Apert syndrome	Yes	32 + 1	2.8	< P5	No	No	Frontal bossing
CHARGE association	Yes	28 + 6	12.3	P5–P95	No	No	Hemifacial microsomia, unilateral microphthalmia
Trisomy 18	Yes	20 + 0	16.6	P5–P95	No	No	Small nose
Trisomy 18	Yes	22 + 3	20.0	> P95	Yes	No	—
Campomelic dysplasia	Yes	20 + 5	18.1	> P95	Yes	No	—
Cri du chat syndrome	Yes	28 + 0	23.0	> P95	Yes	No	—
Goldenhar syndrome	No	21 + 4	22.1	> P95	Yes	No	Hemifacial microsomia, unilateral microphthalmia
Goldenhar syndrome + VACTERL	No	21 + 5	22.6	> P95	Yes	No	Hemifacial microsomia
Pierre–Robin syndrome	No	25 + 4	22.8	> P95	Yes	No	—
Trisomy 21	Yes	31 + 5	8.2	< P5	No	No	—
Trisomy 21	Yes	23 + 2	8.8	< P5	No	No	—
Trisomy 21	Yes	30 + 4	11.2	P5–P95	No	No	—
Bi. cleft lip/alveolus and palate (isolated)	No	16 + 0	17.9	> P95	No	Bi.	—
Bi. cleft lip/alveolus and palate (trisomy 13)	Yes	20 + 3	26.6	> P95	No	Bi.	—
Uni. cleft lip/alveolus (isolated)	No	22 + 2	19.6	> P95	No	Uni.	—
Uni. cleft lip and palate (VCF syndrome)	Yes	22 + 0	15.4	P5–P95	No	No	—

*Confirmed after birth. Bi., bilateral; GA, gestational age; P, percentile; Uni., unilateral; VCF, velocardiofacial.

In all six cases with postnatally confirmed retrognathia, the MNM angle was above the 95th centile. The MNM angle was normal in the two cases without retrognathia. The MNM angle was below the 5th centile in Apert syndrome, in both cases of thanatophoric dysplasia and in two of the three trisomy 21 cases. In all three cases of bi- or unilateral interruption of the alveolar ridge, the MNM angle was above the 95th centile. The MNM angle was normal in the case with unilateral cleft lip and palate but intact alveolar ridge. In the case of cleft lip detected in the study group, the subtle interruption of the alveolar ridge was only identified after the enlarged MNM angle (17.9°) prompted a careful reexamination of the volumes (Figure 8).

DISCUSSION

This study proposes measurement of the MNM angle as a new method enabling an objective assessment of fetal jaw abnormalities in the second and third trimesters. The mean angle remains constant at 13.5° and measurements can easily be performed using 3D ultrasound, with good intra- and interobserver reproducibility.

3D ultrasound improves accuracy⁴. Ultrasonographers should be aware of this when using 2D ultrasound. No specific preacquisition insonation angle around the fetal x-axis is required. However, the accuracy of the measurements probably increases when an insonation angle perpendicular to the profile plane is used.

Because racial variations in craniofacial morphology are reflected in a different configuration of alveolar and dental areas, an ethnic variation in the angle is expected^{7,8}. Future studies should therefore investigate the angle in non-Caucasian fetuses also. The MNM angle appears not to be affected by fetal gender, confirming the findings of a postmortem study⁹.

Several second- and third-trimester jaw measurements have been proposed, such as length of mandibular ramus^{10,11}, transverse mandibular diameter^{12–16}, anteroposterior mandibular diameter^{12,13,16}, maxillary length¹⁷ and maxillary width¹⁴, as well as ratios such as anteroposterior mandibular diameter/biparietal diameter (BPD) $\times 100$ ¹³, mandibular width/maxillary width¹⁴, BPD/transverse mandibular diameter¹⁵ and transverse/anteroposterior mandibular diameter¹⁶. These measurements have seldom been used clinically. One

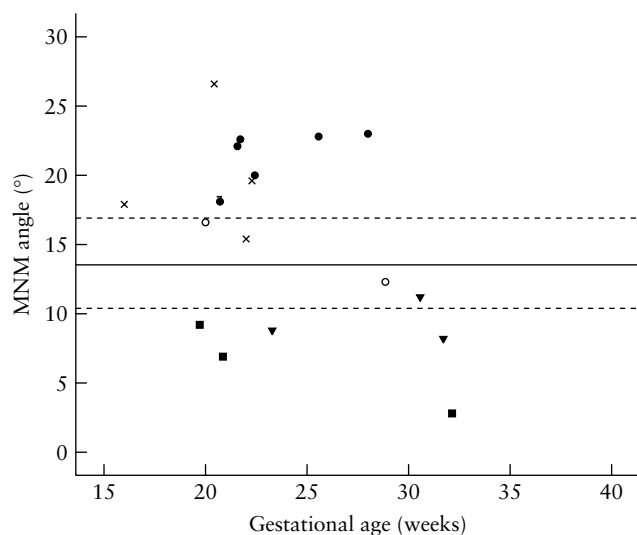


Figure 7 Maxilla–nasion–mandible (MNM) angle measurements in 18 pathological cases plotted against gestational age, with mean (—) and 5th and 95th centiles (---) for normal fetuses. Pathological cases included: Apert syndrome and thanatophoric dysplasia (■); trisomy 21 (▼); facial clefts (×); cases with retrognathia (trisomy 18, campomelic dysplasia, Cri-du-chat syndrome, Goldenhar syndrome, Goldenhar syndrome with VACTERL and Pierre–Robin syndrome) (●); cases without retrognathia (CHARGE association, trisomy 18) (○).

explanation could be that they require visualization of the fetal face in the axial or coronal plane, which are not routinely used^{10–17}. Moreover, difficulty in identifying landmarks located more posteriorly in the head,

and therefore more affected by shadowing, may hamper application of these measurements^{10–14,16,17}.

In this 3D ultrasound study, measurement of the MNM angle was successful whenever the fetus was facing the transducer. Measurement failed in one case in which extreme flexion of the head prevented visualization of the mandibular landmark. When the nasal bone is absent the lowest anterior edge of the frontal bone can be used as a reference point, as for prenasal thickness measurement¹⁸. Because the frontal bones develop independently of the nasal bones, the lowest anterior edge of the frontal bone is not influenced by nasal bone hypoplasia and it is therefore an acceptable alternative for the nasion in such cases¹⁹.

The MNM angle can be derived from two gestational age-independent angular measurements proposed by Roelfsema *et al.*²⁰. The difference between their mean mandibular and maxillary protrusion is 13.8°, which is very close to the 13.5° reported in this study. Two other studies, aimed at improving the diagnosis of retrognathia in the second and third trimesters of pregnancy, also found constant values in angular measurements in the profile view^{14,21}. A limitation of these studies is that the forehead was used as a reference point, implying that malformations like bossing or sloping forehead will influence these measurements. Moreover, both studies used superficial skin landmarks, difficult to identify when there is not sufficient amniotic fluid surrounding the face, and possibly influenced by facial expression.

During fetal life, the maxilla, anatomically fused with the cranium, is pushed forward by the progressive brain

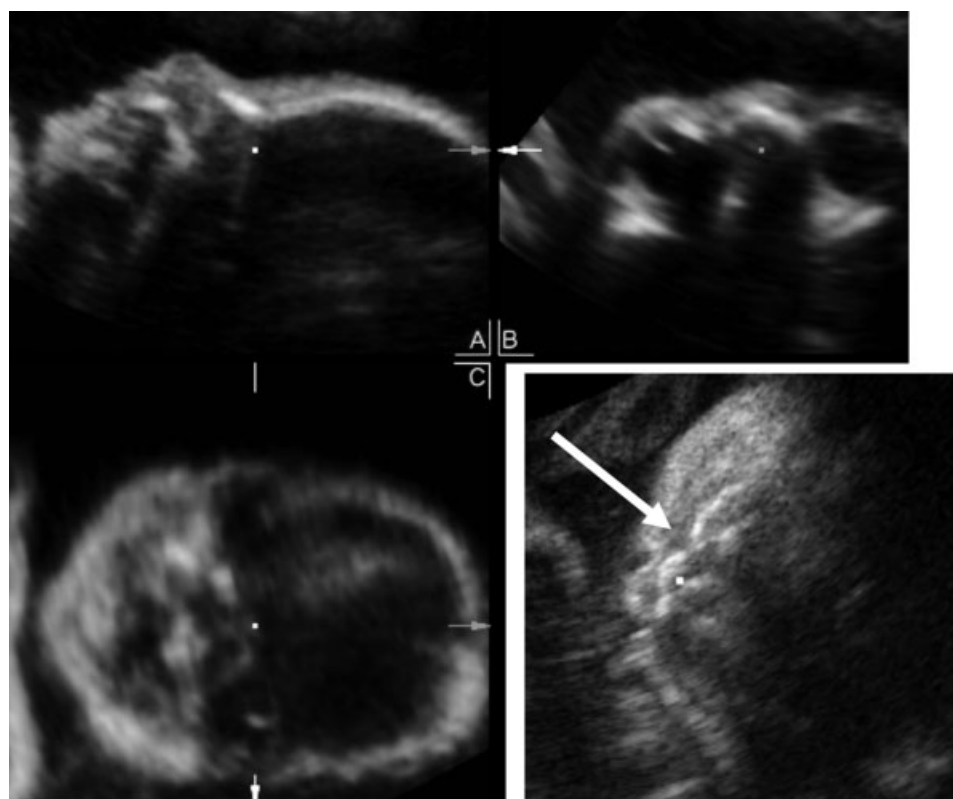


Figure 8 Fetal profile that was subjectively interpreted as normal, shown in multiplanar mode. A small interruption in the alveolar ridge is shown in the axial plane (arrow). This was only noticed after the enlarged maxilla–nasion–mandible angle (17.9°) had alerted the investigator.

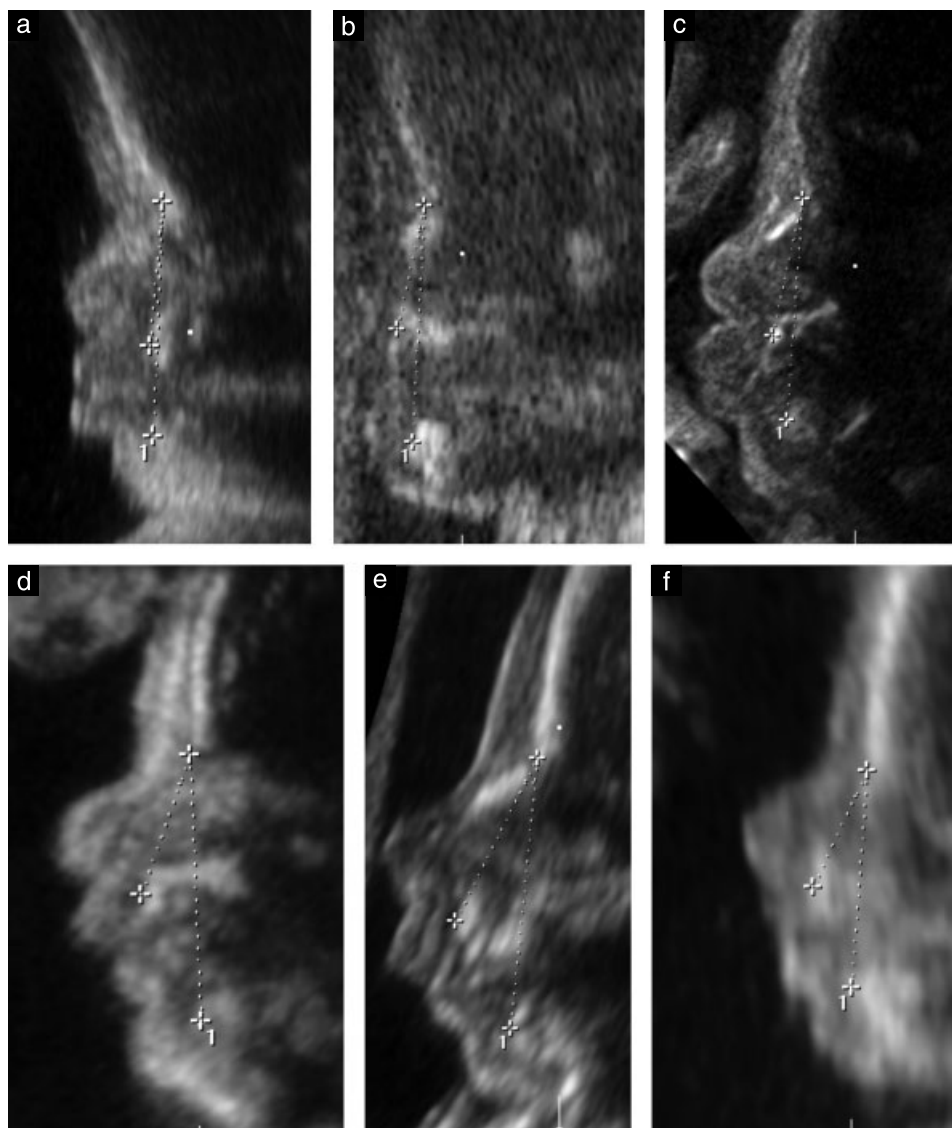


Figure 9 Examples of abnormally small (a–c) and large (d–f) maxilla–nasion–mandible (MNM) angles: (a) Apert syndrome (MNM: 2.8°); (b) thanatophoric dysplasia (MNM: 9.2°); (c) trisomy 21 (MNM: 8.8°); (d) Cri-du-chat syndrome (MNM: 23.0°); (e) Goldenhar syndrome (MNM: 22.6°); (f) alveolar ridge interruption (MNM: 19.6°).

development, while the cranial base flattens. This implies that it is difficult for the mandible, only connected to the skull through the temporomandibular joint and muscles, to catch up with maxillary growth²². Postnatally, facial growth predominates over brain growth and the functional development of chewing and speech further stimulate growth of the mandible²³. This catch-up growth of the mandible results in a change in profile during adolescence from convex to flat. The ANB angle becomes, on average, 2.8° in adulthood⁷.

When the MNM angle is small, the profile is flat (Figure 9a–c). This can be the result of maxillary hypoplasia or forward displacement of the mandible; the latter is a rare finding in prenatal life. When the MNM angle is abnormally large, the fetal profile is exaggeratedly convex (Figure 9d–f). The mandible is then moved backwards or the maxilla forwards, as shown by retrognathia and facial cleft cases. When an abnormally large MNM

angle is encountered, an alveolar ridge interruption or retrognathia is likely. When the MNM angle is negative the profile is concave. This is described postnatally in non-syndromic healthy Caucasian adults, but prenatally this is an extremely rare finding. Owing to the by nature convex fetal profile, this is clearly pathological and will be easy to recognize.

The position of the nasion influences the MNM angle, but the nasion is probably not easily influenced by facial malformations. Backwards or downwards displacement of the nasion should theoretically increase the MNM angle. Nevertheless, both cases of thanatophoric dysplasia, a syndrome known to be associated with small facies and a low nasal bridge, had an abnormally small MNM angle, indicating a flat profile. Further studies are necessary to detect how, for example, midfacial hypoplasia influences the position of the nasion and possibly the MNM angle.

In all six cases with postnatally confirmed retrognathia, the MNM angle was above the 95th centile. Therefore, the MNM angle seems to be an objective method to confirm the subjective suspicion of retrognathia at prenatal ultrasound. Because the anterior border of the mandible is used as landmark in the MNM angle, this may imply that, technically, only retrognathia and not micrognathia could be identified. However, in 11 fetuses with micrognathia, Paladini *et al.*¹³ observed that in this condition the growth deficit is more evident in the sagittal plane than in the coronal plane, implying that micrognathia is often also accompanied by retrognathia. In the facial cleft cases, the MNM angle was above the 95th centile only when the alveolar ridge was not intact, indicating that the MNM angle may be helpful in identifying small alveolar ridge interruptions. The MNM angle may be of diagnostic value in recognizing premaxillary protrusion, recently described as a prognostic factor for lethal aneuploidies associated with bilateral cleft lip and palate²⁴. In the Apert syndrome case, a syndrome characterized by a flat face, the MNM angle was below the 5th centile. Interestingly, the MNM angle was also small in two of the three trisomy 21 cases. However, larger series are needed to establish the exact clinical value of the MNM angle in diagnosing specific facial abnormalities.

In conclusion, the MNM angle is a promising tool to establish the convexity of the fetal profile by enabling an objective assessment of the anteroposterior relationship of the jaws. This method has the potential of assisting in the prenatal recognition and classification of abnormal profile findings.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Maxilla–nasion–mandible (MNM) angle measurements used for assessing intra- and interobserver variability, arranged from lowest to highest gestational age.