The fetal mandible: a 2D and 3D sonographic approach to the diagnosis of retrognathia and micrognathia

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ABSTRACT

Objective To define parameters that enable the objective diagnosis of anomalies of the position and/or size of the fetal mandible in utero.

Design Fetuses at 18–28 gestational weeks were examined by two- and three-dimensional ultrasound. The study included normal fetuses and fetuses with syndromes associated with known mandible pathology: Pierre Robin sequence or complex (n = 8); hemifacial microsomia (Treacher–Collins syndrome, n = 3); postaxial acrofacial dysostosis (n = 1). Fetuses with Down syndrome (n = 8) and cleft lip and palate without Pierre Robin sequence or complex (n = 18) were also studied. Retrognathia was assessed through the measurement of the inferior facial angle, defined on a mid-sagittal view, by the crossing of: 1) the line orthogonal to the vertical part of the forehead at the level of the synostosis of the nasal bones (reference line); 2) the line joining the tip of the mentum and the anterior border of the more protruding lip (profile line). Micrognathia was assessed through the calculation of the mandible width/maxilla width ratio on axial views obtained at the alveolar level. Mandible and maxilla widths were measured 10 mm posteriorly to the anterior osteous border.

Results In normal fetuses, the inferior facial angle was constant over the time span studied. The mean (standard deviation) value was 65.5 (8.13)°. Consequently, an inferior facial angle value below 49.2° (mean – 2 standard deviations) defined retrognathism. All the fetuses with syndromes associated with mandible pathology had inferior facial angle values below the cut-off value. Using 49.2° or the rounded-up value of 50° as a cut-off point, the inferior facial angle had a sensitivity of 1.0, a specificity of 0.989, a positive predictive value of 0.750 and a negative predictive value of 1.0 to predict retrognathia. In normal fetuses, the mandible width/maxilla width ratio was constant over the time interval studied. The mean (standard deviation) value was 1.017 (0.116). Consequently, a mandible width/maxilla width ratio < 0.785 defined micrognathism. Mandible width/maxilla width ratio values were below this cut-off point in eight and in the normal range in four fetuses with syndromes associated with mandible pathology.

Conclusions Retrognathia and micrognathia are conditions that can be separately assessed. The use of inferior facial angle and mandible width/maxilla width ratio should help sonographic recognition and characterization of fetal retrognathic and micrognathic mandibles in utero.

INTRODUCTION

Mandible anomalies are commonly encountered fetal facial defects. They form part of more than 100 genetic syndromes. Micrognathia is frequently seen in syndromes such as Pierre Robin sequence and hemifacial microsomia (e.g. Treacher–Collins syndrome), and is associated with various chromosomal anomalies such as trisomies 18 and 13, triploidy, and those involving gene deletions or translocations.

Fetuses with mandible anomalies are at risk of acute neonatal respiratory distress syndrome. This is a neonatal emergency since the tongue may obstruct the upper airways and lead to suffocation. Antenatal recognition of mandible anomalies allows the neonatologist to be present in the delivery room to provide immediate care for the infant. Milder cases of the defect should also be diagnosed as there is no strict parallelism between the severity of the anatomical defect and the impairment of respiratory function at birth. The respiratory compromise can be related to an associated defect of the central nervous system or to an associated mechanical defect of the airways.

Mandible anomalies are amenable to antenatal diagnosis by sonography. They are usually defined subjectively,
and various descriptions have been provided: prominent upper lip and small chin; subjective impression of a small jaw or posterior displacement of the mandible; an unusually small mandible resulting in a receding chin. The importance of differentiating anomalies of position, namely recession of the chin (retrognathia), from insufficient size (micrognathia) is recognized; however, the difference is often omitted in published reports, the term micrognathia being the most favored.

Attempts have recently been made to define biometric parameters that would allow objective distinction between normal and abnormal mandibles, but they do not differentiate retrognathia from micrognathia.

In the present study we have defined two indices, one to assess the posterior displacement (retrognathia) and the second to assess the restriction in size (micrognathia). Normative data are provided, together with a study of pathological states.

PATIENTS AND METHODS

Patients

The study design was cross-sectional and each fetus was included in the analysis only once. Not all of the measurements were obtained in each fetus as the second index was introduced later in the study. Normal fetuses were randomly selected from the patients registering for antenatal care at our unit. Fetuses with mandible anomalies were either identified in our unit or referred by colleagues. All the fetuses with a mandible anomaly diagnosed during the study period (1997–2000) were included. All measurements were obtained at 18–28 weeks' gestation.

Normal fetuses

Measurements were obtained in patients referred for routine second-trimester sonographic examination, usually between 22 and 24 gestational weeks. Only singleton pregnancies with morphologically and biometrically normal fetuses whose gestational age was confirmed by a late first-trimester scan were included. In four cases the sonographic report indicated retrognathia. Three newborns were normal, one had isolated clinical retrognathia. Patients with maternal diseases potentially affecting fetal growth (hypertension, diabetes, systemic diseases) were excluded.

Pathological fetuses

The series included 12 fetuses with mandible anomalies (Table 1): isolated Pierre Robin sequence (n = 5), Pierre Robin complex, i.e. Pierre Robin sequence associated with chromosomal anomalies (n = 3), hemifacial microsomia (Treacher–Collins syndrome, n = 3); and one case of postaxial acrofacial dysostosis (PAAFD), a variant of Treacher–Collins syndrome. Eight fetuses with Down syndrome and 18 fetuses with cleft lip and palate without Pierre Robin sequence or complex were also included. All diagnoses were confirmed by a neonatologist in the case of a live birth (n = 6) or at fetopathological postmortem examination in the case of medical termination of pregnancy. The facial defect in the six newborns with mandible anomalies was morphologically severe in all cases. With regard to vital functions, the impairment was mild in two newborns (suction present, few feeding problems, no respiratory impairment), intermediate in two (suction anomalies necessitating gavage, limited respiratory impairment with pCO$_2$ < 50 mmHg), and severe in two (hypoxemia). In cases of Treacher–Collins syndrome and Pierre Robin sequence or complex, the physician diagnosed the presence or absence of retrognathia and/or micrognathia, with or without a complex malformative syndrome.

Sonography

Ultrasound examinations were performed on a Kretz Combison 530 MT ultrasound system (Kretz Technik, Zipf, Austria), equipped with a 5–8-MHz probe. The fetal face was first examined, and the sonographer made a subjective assessment as to the absence of abnormality or the presence of retrognathism. This qualitative examination was completed with the measurements of three parameters: the

<table>
<thead>
<tr>
<th>Case</th>
<th>Syndrome</th>
<th>GA (weeks)</th>
<th>IFA (°)</th>
<th>MD (mm)</th>
<th>MX (mm)</th>
<th>MD/MX</th>
<th>Clinical stage</th>
<th>Associated anomalies</th>
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<td>45</td>
<td>25</td>
<td>23</td>
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<td>III</td>
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<td>40</td>
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<td>30</td>
<td>1.00</td>
<td>III</td>
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<tr>
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<td>Isolated PRS</td>
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<td>18</td>
<td>29</td>
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<td>Isolated PRS</td>
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<td>45</td>
<td>27</td>
<td>36</td>
<td>0.75</td>
<td>I-II</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Isolated PRS</td>
<td>27</td>
<td>45</td>
<td>31</td>
<td>26</td>
<td>1.19</td>
<td>II-II</td>
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<td>46</td>
<td>31</td>
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<td>0.94</td>
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<td>45</td>
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<td>35</td>
<td>20</td>
<td>28</td>
<td>0.71</td>
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<td>28</td>
<td>14</td>
<td>18</td>
<td>0.78</td>
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<td>Treacher–Collins</td>
<td>22</td>
<td>40</td>
<td>17</td>
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<td>37</td>
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<td>Inferior labial cleft, agenesia of left hemimandible</td>
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<td>0.53</td>
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</table>

All twelve cases had cleft lip and palate and the morphological grade for all twelve was ‘severe’. GA, gestational age; IFA, inferior facial angle; MD, mandible width; MX, maxilla width; PRS, Pierre Robin sequence; trs., translocation; PAAFD, postaxial acrofacial dysostosis; NA, not applicable.
inferior facial angle (IFA), the mandible width (MD) and the maxilla width (MX). Three scans were necessary to obtain these three measurements: one mid-sagittal and two axial scans of the palate area. All three scans can be obtained either by direct two-dimensional (2D) scanning or by using three-dimensional (3D) reconstructed views, the latter being the case in the present study. The best 3D reconstructions for analysis of the face were obtained when the 3D volume was acquired starting from a mid-sagittal plane, with all the sagittal planes included. The 3D volume data were displayed on the screen as three orthogonal planar images (sagittal, coronal and axial). One acquisition took less than 2 s. Thanks to the use of 3D reconstruction, no case had to be excluded from the study because the measurements could not be performed. Three-dimensional surface rendered images of the fetal face were also used, mostly to facilitate communication with the parents or pediatric surgeons.

Inferior facial angle (IFA)
The IFA was defined on a sagittal view (Figure 1a) by the crossing of two lines:
1. a line orthogonal to the vertical part of the forehead, drawn at the level of the synostosis of the nasal bones (reference line);
2. a line joining the tip of the mentum and the anterior border of the more protrusive lip (profile line).

The angle could be traced and measured on a photograph using a protractor; with 3D sonography, measurement of the angle is automatic.

Mandible width (MD), maxilla width (MX) and MD/MX ratio
The MD and MX were measured on an axial plane caudal to the base of the cranium, at the level of the alveolus (dental arch). A line orthogonal to the sagittal axis was drawn 10 mm posteriorly to the anterior osteous border (approximately at the level of the canines). Measurements were obtained from one external bone table to the other (Figure 1b and c). The MD/MX ratio was derived from these two measurements.

Statistics
Regression lines for IFA, MD, MX and MD/MX ratio as a function of gestational age were calculated. For variables shown to be independent of gestational age, the mean and standard deviation (SD) were computed. The mean ± 2 SD interval defined the normal population. Sensitivity, specificity and positive and negative predictive values (PPV and PPN) for the diagnosis of abnormal mandibles were computed using the cut-off values obtained in the normal fetuses. When the dependent variable varied with gestational age, the regression line and the 95% prediction limits were computed.

Reproducibility was assessed by one observer making repeated independent measurements. Ten fetuses were tested. For each fetus, the 3D volume was reanalyzed five different times. The three parameters of interest were measured (IFA, MD, MX) and the MD/MX ratio was calculated. The coefficient of variation (CV) was computed for each variable and each fetus, then a mean CV was calculated for each parameter. The fetuses were chosen in order to study values in the high, medium and low range of the different parameters. The mean coefficients of variation were 1.63 (SD, 0.77) for the IFA, 0.85 (SD, 0.83) for MD, 2.31 (SD, 0.95) for MX, and 3.56 (SD, 1.22) for the MD/MX ratio.
RESULTS

The IFA was measured in 371 normal fetuses. The MD and MX were obtained in 245 normal fetuses. An example of a normal mandible, with the tracing of the IFA angle, and the measurement of MD and MX, is shown in Figure 1.

Representative examples of retrognathic mandibles are shown in Figures 2–4. Figure 2 shows a normal-sized
retrognathic mandible, while in Figures 3 and 4, retrognathia is associated with micrognathia or mandible agenesis.

**Inferior facial angle (IFA)**

The distribution of IFA values obtained in normal fetuses ($n = 371$) is shown in Figure 5. The IFA did not change over the 18–28-gestational-week time period (regression line, $P = 0.48$). The mean value of IFA in the 18–28-gestational-week interval was 65.5 (SD, 8.13)$°$. Consequently, an IFA value $< 49.2°$ defined retrognathism.

The IFA was $< 49.2°$ (range, 39–47)$°$ in four cases of this normal population. Rounding the cut-off value up to 50$°$ made no difference to the number of cases. In four fetuses of the normal population, the sonographic report indicated a visual

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**Figure 3** Retrognathic mandible, associated with micrognathia. Ultrasound images were obtained at 20 gestational weeks. (a) Sagittal view showing the inferior facial angle (*, 34°). (b) Axial view showing mandible width (>…<, 20 mm). (c) Axial view showing maxilla width (>…<, 28 mm). (d) Three-dimensional surface rendered image. (e) Photograph taken after birth.
impression of retrognathism. In one, the IFA (39°) was less than the mean –2 SD. The newborn had clinical retrognathia. In the three other cases, the IFA was above this limit. The newborns had a normal morphological appearance. Retrospective examination of the sonograms showed that a large or a protruding upper lip caused a false impression of retrognathism.

The IFA values measured in different pathological states are shown in Figure 6. The values measured in all the fetuses with Pierre Robin sequence (range, 35–46°), Treacher–Collins syndrome (range, 28–40°), or PAAFD (35°) were below the inferior limit of the normal distribution. The IFA values were below this limit in two of the eight fetuses with trisomy 21. The values in the 18 fetuses with cleft lip and palate without Pierre Robin sequence or complex were evenly distributed, with two being below the inferior limit of the normal population.

The IFA values measured in all of the pathological fetuses and in four fetuses of the normal population were below the mean – 2 SD cut-off value of 49.2°. Thus, the IFA had a sensitivity of 1.0, a specificity of 0.989, a PPV of 0.750, and a NPV of 1.0 to predict retrognathia. A similar performance was observed using the rounded-up cut-off value of 50°.

**Mandible width/maxilla width (MD/MX) ratio**

The MD and MX measured in normal fetuses (n = 245) are shown in Figure 7a and b. Mandible width increased over the 18–28-gestational-week period (regression line, MD = 0.74 × GW + 7.76; r² = 0.206; P = 0.0001), where GW = gestational weeks. The same pattern was observed with MX (MX = 0.75 × GW + 7.41; r² = 0.106; P = 0.0001).

The MD/MX ratio (Figure 7c) was constant between 18 and 28 gestational weeks (regression line, P = 0.8). The mean value of the MD/MX ratio in the 18–28-gestational-week interval was 1.017 (SD, 0.116). Consequently, a MD/MX ratio < 0.785 defined micrognathism.

The values measured in the eight fetuses with Pierre Robin sequence were evenly distributed between those with normal-sized mandibles (n = 4) and those with micrognathia (n = 4). The values measured in the four fetuses with Treacher–Collins syndrome or PAAFD, were less than the mean – 2 SD, indicating the presence of micrognathia (Figure 7).
Inferior facial angle (IFA) and mandible width/maxilla width (MD/MX) ratio

In the fetuses with mandible anomalies, IFA values and MD were correlated \( (P = 0.008 \text{ for the regression}) \). There was no correlation between IFA values and either MX or MD/MX ratio values \( (P = 0.10 \text{ and } 0.12, \text{ respectively}) \). Figure 8 shows the respective distribution of pathological cases (Pierre Robin sequence, Treacher–Collins syndrome or PAAFD) between retrognathia and micrognathia.

DISCUSSION

Mandible anomalies are a common feature of many karyotypic and genetic syndromes. Specific syndromes are associated with pathognomonic mandible shape and/or proportion\(^5,14\). For instance, most Pierre Robin conditions are either micrognathic or retrognathic, but not both together\(^5\). Micrognathia refers to size, and retrognathia to position\(^5\). In spite of these known differences, most published studies addressing...
the antenatal sonographic recognition of mandible anomalies use the term micrognathia to include both receding chins and small mandibles.

To specifically characterize mandible recession, we adapted to sonography the X-ray cephalometric method used to analyze facial anatomy in later life. The IFA was derived from the Z-angle established by Merrifield to study facial harmony. The Z-angle was defined as the inferior angle formed by the crossing of two lines. The reference line was the Frankfort line that joins the cephalic porion to the inferior border of the orbit. It is easily visualized, both in the patient’s external appearance and in the lateral radiograph. The profile line was the line tangential to the soft-tissue chin and to the most anterior point of either the lower or upper lip, whichever protruded most.

Adaptation of the Z-angle to sonography necessitated only minor modifications of the reference line. We used the line orthogonal to the vertical part of the forehead, drawn at the level of the synostosis of the nasal bones. It is almost parallel to the Frankfort line, and ensures easy and highly reproducible tracing on sonograms. No modification was necessary for the profile line.

The mean Z-angle was found to be 78.0° (SD, 5) degrees in normal adolescents (11–15 years) and 81.4° (SD, 5) degrees in normal adults. These values are higher than the mean IFA of 65.5° measured in the present study. This is explained by the forward development of the chin after birth.

Our study shows the relevance of the IFA in fetal life. The IFA values obtained in all fetuses affected with Pierre Robin sequence, Treacher–Collins syndrome or PAAFD were below the mean – 2 SD for the normal population (Figure 6).

To check the specificity of the parameters analyzed in the present study, two populations with known abnormalities of the face were also analyzed. The IFA values in fetuses with Down syndrome were usually normal (Figure 6). Of particular interest were the results obtained in cases of facial cleft lip and palate without Pierre Robin sequence. A minor degree of mandibular retrognathia in newborns with cleft lip and palate has been found to be a frequent feature of the condition. The IFA values were essentially in the normal range (Figure 6). These results indicate that the former observation was due to a visual impression, linked to a protruding cutaneous profile, rather than to a mandible anomaly. A similar situation was observed in three fetuses with apparent retrognathia at sonographic examination, but with an IFA within the normal range. The newborns were confirmed to be normal at birth.

In the present study, four fetuses of the normal population had IFA values ≤ 50°. The sonographer made a subjective diagnosis of retrognathia on one occasion. The neonate had simple retrognathia at birth. For the other cases, the design of the present study does not allow the differentiation between positional retrognathia, measurement error, difficulty in subjective diagnosis, or minimization of symptom value at the time of the sonographic examination. Variations in soft tissue overlay over the osteous chin, which varies greatly among adolescents and adults, may perhaps represent another source of variability, although this does not appear to be the case in fetuses as the prechin soft-tissue thickness is fairly constant during the 18–28-gestational age interval (3.9 mm; SD, 0.63; n = 28; unpublished observations). However, for the time being, the existence of overlapping values may represent a limitation to utilization of the IFA.

Mandible size has been assessed by various investigators. Fetal mandible length (FML) measurements have been reported by Otto and Platt and Chitty et al. The FML measurements were obtained in a plane that imaged the main portion of one ramus of the jaw, between the temporomandibular joint and the symphysis mentis.

Both groups found similar results. The increase in FML was almost linear with increasing gestational age, and varied from a mean value of approximately 2.0 cm at 18 gestational weeks to 3.7 cm at 28 weeks. Only one pathological case, a fetus with trisomy 18, was available for analysis during the course of the first study. In spite of a visually normal profile, mandible length was below the 95% prediction limit for gestational age (late second trimester).

Other authors assessed the size of the mandible body through the measurement of its transverse diameter (TD) and anteroposterior diameter (APD). The measurements were obtained on an axial plane at the base of the cranium, just caudal to the lower dental arch, where the full extent of the horseshoe-shaped mandible is imaged. The TD was the distance between the bases of the two rami. The APD was the distance between the symphysis mentis and the middle of the TD.

Watson and Katz studied 204 normal fetuses. Both the TD and APD increased with increasing gestational age. The TD varied from a mean of 1.9 (SD, 0.23) cm at 18 gestational weeks to a mean of 3.5 (SD, 0.28) cm at 28 weeks. The APD varied from a mean of 1.3 (SD, 0.12) cm at 18 gestational weeks to a mean of 2.7 (SD, 0.23) cm at 28 weeks.

Watson and Katz emphasized that mandible diameter measurements lack reliability, as it is difficult to be certain that the full length of the horizontal part of the mandible is imaged. They insisted that the line between the base of the mandible...

Figure 8 Inferior facial angle and mandible width/maxilla width ratio in pathological fetuses. ●, Pierre Robin sequence or complex (n = 8); △, Treacher–Collins syndrome (n = 3); ▲, postaxial acrofacial dysostosis (n = 1). Solid lines, mean; dotted lines, ±2 standard deviations of the normal population.

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Our study shows the relevance of the IFA in fetal life. The IFA values obtained in all fetuses affected with Pierre Robin sequence, Treacher–Collins syndrome or PAAFD were below the mean – 2 SD for the normal population (Figure 6). Of particular interest were the results obtained in cases of facial cleft lip and palate without Pierre Robin sequence. A minor degree of mandibular retrognathia in newborns with cleft lip and palate has been found to be a frequent feature of the condition. The IFA values were essentially in the normal range (Figure 6). These results indicate that the former observation was due to a visual impression, linked to a protruding cutaneous profile, rather than to a mandible anomaly. A similar situation was observed in three fetuses with apparent retrognathia at sonographic examination, but with an IFA within the normal range. The newborns were confirmed to be normal at birth.

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two rami should touch the anterior aspect of the fetal hypopharynx to be valid. To control for the difficulty of measuring reliably the full length of the horizontal part of the mandible, we elected to measure the transverse diameter 10 mm caudal to the symphysis mentis. The measurements were normalized to MX (MD/MX ratio).

Paladini et al.\textsuperscript{12} studied 262 normal fetuses. The data obtained were tested prospectively on 11 fetuses with micrognathia confirmed at necropsy or after birth. Micrognathia affected the growth in the sagittal plane more than that in the coronal plane. The values obtained in the 11 affected fetuses were all below the 95\% confidence interval of the normal population. To increase the diagnostic value of the APD, the authors normalized the data by the biparietal diameter (BPD), thus deriving the jaw index (APD/BPD \times 100). Using a cut-off value of < 23 (corresponding to: mean – 2 SD), the jaw index had a sensitivity of 1.0 in the prediction of retrognathia and its specificity was 0.981. The PPV and NPV were indicative of micrognathia (Figure 8).

The values measured in four fetuses with Pierre Robin sequence, Treacher–Collins syndrome or PAAFD had IFA values that were less than the mean – 2 SD cut-off value of the normal distribution, i.e. they were retrognathic (Figures 6 and 8). Only four had values above the micrognathic range (Figure 8). The values measured in four fetuses with Pierre Robin sequence and all fetuses with Treacher–Collins syndrome or PAAFD had a MD/MX of a mean – 2 SD of the normal distribution, indicating the presence of micrognathia (Figure 8).

Independence of the position parameter from the size parameter is further emphasized by the absence of correlation between IFA and MD/MX values. These data confirm the observations made by Cohen\textsuperscript{5} and Laitinen and Ranta\textsuperscript{14}.

Finally, our results confirm that three scans only are necessary to characterize the fetal mandible. The views are usually obtained with 2D sonography. However, 3D scanning can be more convenient. Once the volume of interest is stored, the time necessary to visualize the relevant views is almost zero as compared to the time necessary to obtain the adequate section planes with 2D sonography. Furthermore, it is easy to obtain perfectly symmetrical views as they are computer-generated. In the present study, only 3D reconstructed views were used.

In summary, the data presented here confirm that retrognathia and micrognathia are different conditions that can readily be assessed separately \textit{in utero} using sonography. The IFA assesses mandible position. This parameter is measured using a mid-sagittal view, and the landmarks to define the angle are simple to delineate. The MD/MX ratio assesses mandible size. Two axial scans of the palate area are necessary to calculate this parameter. Both the IFA and MD/MX ratio can be obtained using standard 2D sonography, although 3D ultrasound can provide the necessary views more easily. The use of the IFA and MD/MX ratio should help in the recognition and characterization of fetal mandible anomalies \textit{in utero} using sonography, leading to more precise antenatal diagnosis and providing the potential for improved neonatal management.

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