Fetal Face Malformations in Ultrasound

Marek Pietryga¹, Kinga Toboła-Wróbel², Rafał Iciek³, Jacek Brązert⁴

Donald School Journal of Ultrasound in Obstetrics and Gynecology (2020): 10.5005/jp-journals-10009-1660

Embryology

Branchial arches appear around 4th to 5th week of embryological development, and the fourth branchial arch with a bunch of mesenchymal tissues is separated by the palate. At the turn of 4th/5th week, the stomodeum is formed in the central part of the face and surrounded by the first pair of branchial arches. Each arch consists of an ectoderm, endoderm, and “neural crest cells” that help in the development of the facial skeleton.

The mesodermal tissue of the arches forms the muscular parts of the face and neck.² The first branchial arch gives rise to facial formation and to the growth of the jaw. Facial formation occurs at the 5th week of pregnancy (Figs 1 and 2).

The nasal plate forms the nasal cavity, and the surrounding crests form the frontal nasal eminence, at which time the mandible eminence is also formed. Between 5th and 8th week of pregnancy, the maxillary tuberosity increases, closing the sulcus between the nasal and maxillary eminences. The upper lip is formed by the fusion of maxillary tuberosity with middle nasal eminence. Mandibular protrusion forms the lower lip, cheek, and jaw.² The nose is formed from five eminences:²

- Frontal hautheight of the face (bridge of the nose).
- Two middle nasal eminences (comb, tip, central part of the lip).
- Two lateral nasal eminences (nose wings).

A very important stage of development is the time of merging the two medial nasal eminences, the combination of which forms the middle segment of the jaw and partly the upper lip, teeth, anterior palate, and primary palate (Fig. 3).¹⁻⁴⁻⁷ Joints of jaw eminences with middle nasal is a key element of forming lips and palate.

The total lack or partial combination of these eminences results in one-sided or two-sided cleft of lip and palate at 6 weeks of pregnancy. Cleft lateral appears between the lateral incisors and the canine, lengthwise upper lip in the middle position. Central (middle) lip strain is caused by the incomplete union of the two medial nasal eminences.

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¹Department of Obstetrics and Female Health, Chair of Gynecology, Obstetrics and Gynecological Oncology, Poznan University of Medical Sciences, Poznan, Poland; Prenatal Diagnostic Center, Gynecology and Obstetrics Hospital, Poznan University of Medical Sciences Poznan, Poland
²Department of Obstetrics and Female Health, Chair of Gynecology, Obstetrics and Gynecological Oncology, Poznan University of Medical Sciences, Poznan, Poland; Prenatal Diagnostic Center, Gynecology and Obstetrics Hospital, Poznan University of Medical Sciences Poznan, Poland

Corresponding Author: Marek Pietryga, Department of Obstetrics and Female Health, Chair of Gynecology, Obstetrics and Gynecological Oncology, Poznan University of Medical Sciences, Poznan, Poland; Prenatal Diagnostic Center, Gynecology and Obstetrics Hospital, Poznan University of Medical Sciences Poznan, Poland, Phone: +48(50)1098555, e-mail: marekp2003@gmail.com

How to cite this article: Pietryga M, Toboła-Wróbel K, Iciek R, et al. Fetal Face Malformations in Ultrasound. Donald School J Ultrasound Obstet Gynecol 2020;14(3):178–194.

Source of support: Nil

Conflict of interest: None

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Figure 1: Imaging of the fetal face with two-dimensional (2D) ultrasound
This disadvantage is associated with heavy multiorgan defects, especially with holoprosencephalia.

Irregularities that are primarily related to the first branchial arch as a result of failure of cell migration to this bow, we can observe as Treacher Collins syndrome (TCS) (mandibulofacial dysostosis) and Pierre Robin syndrome. These cells also take part in the formation of the aorta, pulmonary arteries, and their abnormality might cause congenital heart disease1 (Fig. 3).

Standard craniofacial ultrasound imaging in 2D projection should be performed during the second prenatal examination between 18th and 22nd weeks of pregnancy, in three basic planes (Fig. 4):1,2,5,6,8

- Coronal/frontal plane.
- Sagittal plane.
- Transverse plane.

In addition, we can use Doppler study.

In the coronal plane, we assess nostrils, nasal column, alveolus, nasal septum, hard palate, and the vomer (most important ones in the evaluation of the integrity of facial anatomy) (Fig. 4A).

In the sagittal plane, we assess forehead, profile, nasal bones and nasal column, upper lip with philtrum/medical cleft, secondary palate, tongue, lower lip, and chin (at the height of the forehead) (useful in the assessment of the normality of the profile) (Figs 4B and C).

In the transverse (axial) plane, we assess orbits — interorbital and biorbital distance, nasal septum, upper lip, jaw with compounded teeth, hard palate, tongue, and V-shaped mandible (easily reveals both orbits) (Fig. 4D).

In the craniofacial imaging, we can perform the following measurements:9
- Lip width.
- Interbuccal frenum distance (chick to chick diameter).
- Mandible.
- Tongue.
- Eye sockets (interorbital and biorbital distances).
- Nose.

We carry out these measurements in cases of malformations, diagnostic doubts, but not in routine ultrasound examination.

In assessing the continuity of the upper lip and palate, proper imaging is very important.

In order to get a clear picture of the lips, we cannot press the probe, but sometimes move it away. On the contrary, if we want to assess the alveolar arch — the “image of the seagull” — in the case of cleft palate, we will see a hypoechoic fissure in the arch behind
the incisor teeth. Then, we have to move the probe in the same position, toward the head (Fig. 5).

In extreme facial edema, we observe distortion of the facial contours in frontal and axial planes. Deformations are so intense that it is impossible to highlight the nose, lips, or eyelids (Figs 6 and 7).

In other cases, the changes are insignificant, for example, a slight degree of nasal bone hypoplasia and dilatation of the anterior tissue in trisomy 21.

Nose Imaging

Nose imaging is performed in the sagittal and coronal planes. Nasal abnormalities are mainly associated with chromosomal abnormalities (hypoplasia or lack of nasal bone in trisomy 21, triploidy, or tetrasomy). In the second trimester of pregnancy, the trisomy 21 marker is also frontal thickening — prenasal thickness. Maxilla–nasion–mandible (MNM) angle measurement is also very important (Fig. 8).

We can also observe a flat and small nose in other malformation syndromes:

- Binder syndrome.
- Aarskog syndrome.
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- Raine syndrome.
- Brachmann de Lange syndrome.
- Pierre Robin syndrome.

and after exposure to valproic acid during epilepsy treatment (Figs 9 to 14).

Imaging of the Lips and Palate

Imaging of the lips is performed in the coronary plane, showing the tip of the nose, nostrils, upper and lower lip, chin, and tongue. By moving the probe toward the head, we can see the alveolar arch, tooth buds, and palate (Figs 15 to 21).

The most common facial cranial defect that we can diagnose prenatally with ultrasound is cleft lip and palate.

Imaging of the lip and palate is performed in two-dimensional (2D) ultrasonography according to standards. However, if we have the option of additional three-dimensional (3D) imaging, it is also helpful. Sensitivity of the test 2D and 3D in the diagnosis of cleft is similar, although in some cases 3D examination is more sensitive. However, these differences are small, between 2 and 5%10 (Figs 22 and 23).

Technical Difficulties in 3D Imaging

The condition for 3D imaging is the correct position of the fetus and the right amount of amniotic fluid.

Imaging difficulties can be caused by (Fig. 24):
- Oligohydramnios/insufficient amniotic fluid over the fetus’s face.
- “Low-reaching” head or other unfavorable positioning of the fetus.
- Umbilical cord loops above the fetus’s face.
- Fetal hands covering the face.

In 3D imaging, we use the rendering function as well. To select individual elements of face, we can also use the magic-cut function.

The latest improvement in 3D technique is 3D-HD imaging. The image obtained in this projection reflects natural colors and is very similar to visualization in fetoscopy. Changing the “light” setting during the examination may turn out to be a new direction in 3D research (Fig. 25).
Eye Socket Imaging

The measurements of the distance between the eye sockets are associated with the concepts of hypotelorism and hypertelorism. To recognize them, we should measure the interocular and binocular distances (Fig. 26). After 20th week of pregnancy, we can visualize a transparent, round lens in the eye socket, muscle fibers, optic nerve, and yolk artery11 (Figs 27 to 29).

Hypertelorism:
- Aneuploidic syndrome (TR 21, 13, 45X).
- Non-aneuploidic syndrome.
  - Aarskog syndrome.
  - Apert syndrome.
  - Crouzon syndrome.
  - DiGeorge syndrome.
  - Ehlers–Danlos syndrome.
  - Frontonasal dysplasia.
  - Greig syndrome.
  - Gorlin syndrome.
  - Leopard syndrome.
  - Loey–Dietz syndrome (LDS).
  - Mucopolysaccharidoses.
  - Morquio syndrome.
  - Neu-Laxova syndrome (NLS).
  - Noonan syndrome.
  - Saethre–Chotzen syndrome.
In cases of eyeball reduction or lack thereof, we can recognize microphthalmia (small eyes) or anophthalmia (no eyeball). Microphthalmia is observed in Fraser's syndrome (associated with mental retardation — prenatal diagnosis is very difficult), and in some cases it is a “genetic beauty” that occurs in the family, without changes in the brain.

Orbital imaging and visualization of the lenses in the eyeball provide opportunities in the diagnosis of congenital cataracts from 14th week of pregnancy. Congenital cataracts are also associated with chromosomal aberrations, mainly with trisomy 13, and may also be a symptom of CMV infection, rubella, and toxoplasmosis.¹⁻³

Due to the very rare occurrence, prenatal diagnosis as an isolated defect is very difficult (Figs 30 to 32). Cataracts can be caused by:
- Idiopathic (∼50%)
- Hereditary, e.g.
  - Down syndrome.
  - Trisomy 13
  - Lowe syndrome.
  - Marfan syndrome.
  - Arthrogryposis.

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• Cerebro-oculo-facio-skeletal (COFS) syndrome.
• Roberts syndrome.
• Chondrodysplasia.
• NLS.
• Smith–Lemli–Opitz syndrome.

• Branchio-oculo-facial syndrome.
• Infection, e.g., rubella, varicella-zoster virus (VZV), cytomegalovirus (CMV), herpes simplex virus (HSV), toxoplasmosis.
• Metabolic, e.g., galactokinase deficiency, homocystinuria.
Tear Bag Cyst (Dacryocystocele)
Dacryocystocele — rare variant of a relatively common congenital nasolacrimal duct obstruction, accounting for only 0.1% of infants with congenital nasolacrimal duct obstruction\(^\text{11}\) (Fig. 33).

Imaging of the Language
The language can be represented by an axial and sagittal plane.
Macroglossia (enlargement of the tongue) may be caused by a wide variety of congenital and acquired conditions:

The most common causes are Beckwith–Wiedemann syndrome and chromosomal aberration: mainly in Down’s syndrome.

However, the ultrasound recognition of the enlarged tongue over time is not entirely true. Partially sticking out or not, the hiding tongue we see during the ultrasound is not always associated with
Figs 29A and B: Congenital cataract with hyperechogenic lens — sagittal view

Fig. 30: Congenital cataract in coronal view

Fig. 31: Congenital cataract in coronal view
its enlargement. In the case of Beckwith-Wiedemann syndrome, the enlargement of the tongue is true because the lips are too small to hide it freely. In cases of chromosomal aberrations, these magnifications are not always associated with the lip line and the exposure beyond the lip line is associated with hypotonia (Figs 34 and 35). In such cases, we can also observe a flattening and reduction of the auricle.

**Hair**

In ultrasound imaging, the deposition of mineral syntaxes in amniotic fluid on the hair of the fetus is shown as a hyperechoic layer. This layer can be imaged from the 30th week of pregnancy (best visible after the 34th week of pregnancy), and in some cases even after the 20th week of pregnancy (Fig. 36).

**Cleft Lip and Palate**

The first classifications of lip and palate clefts in ultrasonography were published in 1995 by Nyberg. This classification did not differentiate between alveolar cleft and hard palate cleft.

In recent years, prenatal detection of lip cleft and palate cleft in the low-risk population reaches 23 to 58%, and the detection of isolated cleft without lip cleft is close to zero. In high-risk
pregnancies, the detection rate for lip cleft is 80 to 90% and for cleft palate, once lip cleft is detected, the detection rate is up to 97% (Fig. 37).

In fetuses with cleft lips and palates, other developmental defects accompany about 50–60%, most often with chromosomal aberrations, heart defects, foot deformities, and additional toes. The risk of cleft occurrence in the fetus, when one of the parents has this defect, increases by about 5%, while for both parents it increases to about 60% (Figs 38 to 41).

Common forms of cleft lip and palate:
Group I.4,9,12 Upper lip clefts:
- Subcutaneous-submucosal (unilateral).
- Partial (middle).
- Total (two-sided).

Group II. Clefts of the upper lip and alveolar process:
- Subcutaneous-subcutaneous (unilateral).
- Partial (middle).
- Total — to the alveolar process opening (two-sided).

Group III. Clefts of the palate:
- Submucosal.
- Partial soft.
- Total soft.
- Total soft and partial hard.
- Total hard and soft (to the incisive foramen).

Group IV. Clefts of the upper lip, alveolar process, and the palate:
- Unilateral.
- Bilateral.

Group V. Combination clefts.

Group I. Lip Cleft: Hidden, Partial, Total (Cheiloschisis: Oculta, Partialis, Totalis)
Depending on the severity of the developmental defect, the continuity of tissues within the skin, the circular muscle of the mouth and mucous membrane is interrupted. In one-sided form, the cleft line runs laterally from the midline of the body. A cleft includes part or all of the height of the lip. There is also subcutaneous-subcutaneous-mucosal cleft, the so-called hidden cleft, which only affects the circular muscle of the mouth. Lip cleft causes disorders in its normal anatomical system. The activity of the lip is impaired. In a double-sided lip cleft, a discontinuation occurs on both sides of the gutter. As a result, the upper lip is divided into three parts. The middle part contains the labial red and the two lateral sections of the lip.

In the sagittal plane, the assimilated labial red is visible beyond the lip line (most often in connection with the nose, no possibility of imaging the correct post in case of bilateral clefts) and the nose is flattened. In the coronal plane, there is a visible loss of lip continuity. In the axial plane, there is a visible loss of lip continuity, the emphasis of the labial red and flattened nostrils with wings of normal anatomy.

Figs 36A to C: Fetal hair in two-dimensional view
In the axial plane, a visible cleavage covering the peritoneal bone (the protrusion of the peritoneal bone with red lips) or reaching it with a displacement of the jaw plane. In the coronary plane, there is no continuity of the alveolar arch.

In the sagittal and parasagittal planes, there is no continuity of the hard palate, hyperechoic vomer.

In the axial plane, the most common is the lack of continuity in the bilateral cleft and the hyperechoic vomer. In the coronary plane, a visible cleft with uneven palate surfaces and a blade supported on the damaged part — a one-sided cleft, and in the case of a two-sided cleft, there is no possibility of imaging the hard palate — a vomer without visible support.

**Group II. Lip and Alveolar Cleft: Hidden, Partialis, and Totalis (Cheiloschisis: Oculta, Partialis, Totalis)**

In this form, the lip and alveolar process are split into the incisive foramen. This group of clefts is characterized by significant
displacement of the lip and alveolar process. In one-sided forms, part of the lip from the prolabium and part of the alveolar process of a larger section containing the peritoneal bone are displaced forward and upward in a healthy direction. A defective jaw and vomer arrangement, which supports the skeleton of the nose, leads to a significant disturbance in its shape.

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In the bilateral clefts, the peritoneal bone and the prolabium are protruded forward. There is a significant functional and esthetic disturbance of the face.

Group III. Hard and Soft Palate Cleft: Hidden, Partial, and Total (Uranostaphyloschisis: Oculta, Partialis, Totalis)

In palate cleft, there is a lack of continuity of tissues within the oral cavity mucosa and nasal mucosa and a discontinuity of bone that reaches to the incisive foramen. In the hidden form of a cleft, only the continuity of the palate muscles is broken.

Group IV. Lip, Alveolar Process, and Palate Cleft (Cheilognathouranostaphyloschisis)

In the unilateral forms of clefts of the upper lip, alveolar process, and palate, the anatomical continuity of the tissues within the upper lip, nasal fundus, alveolar process, and palate is broken, dividing the lip and jaw into two unequal parts. The larger section includes the lateral side of the lip, the prolabium with a philtrum and Cupid’s bow, the alveolar process with the peritoneal bone, and the palate connected in the line of the palatal suture with the vomer. The smaller section contains the remaining lip, alveolar process, and palate.

Anatomical abnormalities in this form of cleft are characterized primarily by a cleft gap whose width varies from 0.3 to 3 cm and displacement of the lip, alveolar process, and palate in relation to three spatial planes. The larger section of the lip within the prolabium is displaced upward and forward together with the bone base. There is a significant vertical shortening of the lip, and the lip philtrum runs obliquely. The outline of Cupid’s bow is distorted.

Face and Neck Tumors

We can also diagnose lesions that occur very rarely, e.g., changes in the interorbital region — a tumor arising from the ethmoid bone (Fig. 42) and changes in the neck (thyroid goiter, lymphatic angioma) (Fig. 43) as well as changes in the lips (epulis or edema of the incisive bone — Fig. 44).

Facial tumors:

• Mouth:
  • Sarcoma, gingival granuloma, Neumann’s tumor (epulis).
  • Oropharyngeal teratoma (epignathus).
• Nasal cavity:
  • Teratoma.
• Cheek and soft tissues:
  • Hemangioma.
  • Rhabdomyosarcoma.
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- Cerebral hernia (encephalocele).
- Lymphangioma and vascular hamartoma.

Neck tumors:
- Teratoma.
- Goiter.
- Lymphangiomas.
- Hemangiomas.

Mandibular Retraction (Micrognathia)
Micrognathia, or mandibular retraction, is a result of mandibular hypoplasia occurring between 6 and 7 weeks of pregnancy. Isolated micrognathia is rare and is associated with family, constitutional factors. In most cases, it is associated with other malformations and chromosomal aberrations. Usually we recognize micrognathia between 18th and 22th week of gestation but in some cases, there is a possibility of imaging it in the first trimester (Figs 45 to 49). 5,6,13 Syndromes with micrognathia:
- Achondrogenesis.
- Amniotic band syndrome (ABS).
- Atelosteogenesis.
- Campomelic dysplasia.
- Carpenter’s syndrome.
- Cornelia de Lange syndrome (CdLS).
- Crouzon syndrome.
- Jacobsen syndrome (11q terminal deletion disorder).
- Wolf–Hirschhorn syndrome.
- Fryns syndrome.
- Goldenhar syndrome (GS).
- Joubert syndrome.
- Meckel–Gruber syndrome.
- Nager syndrome.
- NLS.
- Mohr syndrome.
- CHARGE team (Coloboma, Heart anomaly, Anal atresia, Retardation, and Genital and Ear anomalies).
- Pena–Shokeir syndrome.
- Pierre Robin syndrome.
- Roberts syndrome.
- Shiel syndrome.
- Smith–Lemli–Opitz syndrome.
- Thrombocytopenia.
- TCS.
- Triploidy.
- Trisomy 10.
- Trisomy 18.
- Trisomy 9.

Pierre Robin syndrome is characterized by the triad of symptoms:
- Palate cleft.
- Micrognathia.
- Glossoptosis.

Differential diagnosis: trisomy 13, 18, otocephalia.
Otocephalia.
- Abnormal development of the auricles, very low ears set forward.
- Always associated with micrognathia or agnathia.
- Absence of the mandible.
- Hypotelorism or hypertelorism.
- Central eye.
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Figs 44A and B: Neck hemangioma

Fig. 45: Micrognathia — three-dimensional view

Fig. 46: Micrognathia — three-dimensional view

Fig. 47: Micrognathia — three-dimensional view

Fig. 48: Micrognathia — two-dimensional view

Fig. 49: Micrognathia — two-dimensional view

• Proboscis.
• Holoprosencephalia.
• Cephalocele.
• Tracheoesophageal fistula.
• Heart defects.
• Situs inversus.
• Kidney malformations.
• Adrenal hypoplasia.
• Single umbilical artery (SUA).
• Rib defects.

Imaging the Ear

The ear grows linearly with gestational age, its length is one-third of the biparietal diameter (BPD). It has been shown that reduced size (<0.8), flattened shape, and low-set ears correlate with trisomy 21 — 75 to 98% (Figs 50 to 55).
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