

Assessment of fetal malformations in the first trimester of pregnancy by three-dimensional ultrasonography in the rendering mode. Pictorial essay.

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Abstract

We present our experience in the contribution of three-dimensional ultrasonography, using the rendering mode, to the prenatal diagnosis of congenital anomalies including neurological defects (acrania/anencephaly, encephalocele, holoprosencephaly), facial anomalies (cyclopia and facial clefts), abdominal wall defects (omphalocele and gastroschisis) and defects of extremities (fetal muscle-skeletal dysplasias). Three-dimensional ultrasonography may contribute to improve the prenatal diagnosis with further revision of the fetal images, allowing a better prenatal counsel to the parents.

Keywords: prenatal diagnosis, congenital anomaly, three-dimensional ultrasound

Introduction

With advancing knowledge and technology, the application of ultrasound during the first trimester of pregnancy has been gaining widespread interest and increasing utility. Indeed, these advances have allowed for more accurate pregnancy dating, earlier determination and assessment of multifetal gestations, and vastly improved screening and diagnosis of embryonic and fetal malformations [1].

Perhaps, one of the most exciting advancements, and one with the greatest potential, has been the advent of three-dimensional ultrasonography (3DUS). This technology, combined with traditional two-dimensional imaging, has afforded sonologists the possibility of evaluating fetal structural morphology through the render mode,

the patients the ability to better conceptualize and understand the problems facing their fetus and geneticists the ability to see the phenotype as a tool in making their assessment [2].

Consequently, the aim of this pictorial essay is to illustrate examples of several fetal anomalies, which can be detected in early pregnancy by 3DUS in the rendering mode.

Acrania/Anencephaly

The incidence of acrania/anencephaly is approximately 1:1,000 births [3]. Genetic and environmental factors have been implicated in its etiology. The single most important environmental factor is diet, namely maternal peri-conceptual folic acid intake [4]. Anencephaly involves an absent upper cranial vault accompanied by an absence of the cerebral hemispheres above the level of the orbits. Acrania includes an absence of the cranial vault with preserved brain parenchyma and normal facial structures. It is believed that first trimester cases of acrania, will ultimately progress to anencephaly by the second trimester [3,4].

In the first trimester, the defect is best appreciated in coronal imaging of the face (fig 1A), demonstrating ab-

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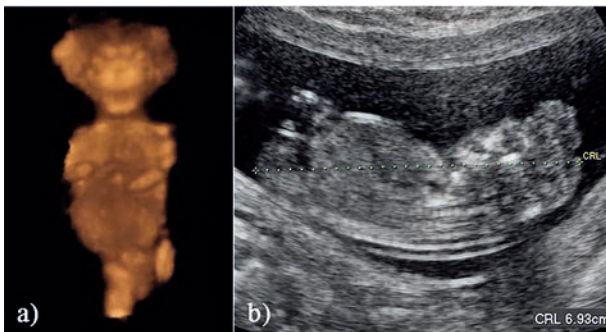


Fig 1. a) Three-dimensional rendering image of a fetus with acrania at 13 weeks of gestation; b) Two-dimensional of the same fetus with acrania at 13 weeks of gestation.

sence of the calvaria above the bony orbits, which may appear prominent. As demonstrated in fig 1B, the defect can also be evaluated in the sagittal view. Polyhydramnios, and other co-existing major congenital anomalies are best identified in second trimester [3,4].

Encephalocele

Encephalocele, whose incidence is reported to vary between 1-3:10,000 and 1:5,000 live birth [3], is a rare skull defect with resultant herniation of intracranial contents including the meninges, neural tissue, and meningoceles [4].

Depending on defect location, the encephalocele may be subdivided in occipital (defect between lambda suture and foramen magnum), or frontal (defect between bregma and anterior margin of ethmoid bone). The importance of the location of the herniation is because to different prognosis [4].

Various conditions have been associated with encephaloceles including congenital rubella, diabetes, genetic syndromes (e.g. Meckel-Gruber Syndrome), and amniotic-bands; however, a true causative factor remains unknown. The insult is hypothesized to occur from failure of closure of the rostral neural pore, versus disruption of fetal-skull formation (amnion rupture sequence), especially in the midline, which may be associated with other malformations [3,4].

As demonstrated in fig 2, sonographic findings in the first trimester include a calvarial defect with herniation of a mass, which may be cystic, solid (with giral pattern), or combined cystic and solid mass. The figures 2 and 3 illustrate an occipital encephalocele.

Holoprosencephaly

The incidence of the holoprosencephaly in the first trimester of pregnancy is unknown. However, in one se-

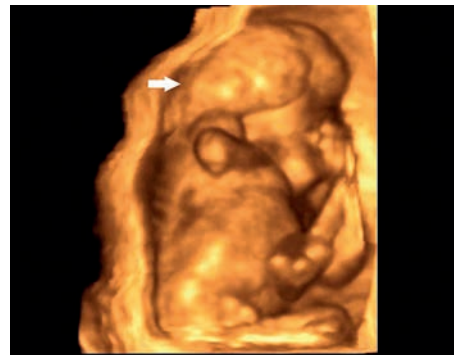


Fig 2. Three-dimensional rendering image of a fetus with encephalocele (white arrow) at 12 weeks of gestation.



Fig 3. Three-dimensional ultrasound in the rendering mode showing other fetus with encephalocele (white arrow) at 12 weeks of gestation.

ries, this defect was reported in 27% of 181 fetuses with trisomy 13 at 11–13 weeks of gestation [5].

Holoprosencephaly includes a large spectrum of cerebral and facial malformations that result from absent or incomplete division of the embryonic forebrain (prosencephalon) [4]. There are three types of holoprosencephaly: alobar, semilobar and lobar. The sonographic findings are the best illustrated in coronal imaging especially the most severe form, the alobar holoprosencephaly, where there is absent midline structures, no division of the cerebral hemispheres, single common ventricle, and fused thalami (fig 4). In semilobar holoprosencephaly there is partial separation of the hemispheres. Only in lobar holoprosencephaly is normal cortical division with the presence of two thalami, albeit accompanied by abnormalities of the corpus callosum, septum pelucidum, and/or the olfactory tract [4]. The facial anomalies accompanying holoprosencephaly include a proboscis (cylindrical protuberance), ethmocephaly (the eyes are separated but closely placed), cyclopia (most severe form of hypotelorism), and a palatine defect [4,5] (fig 5).

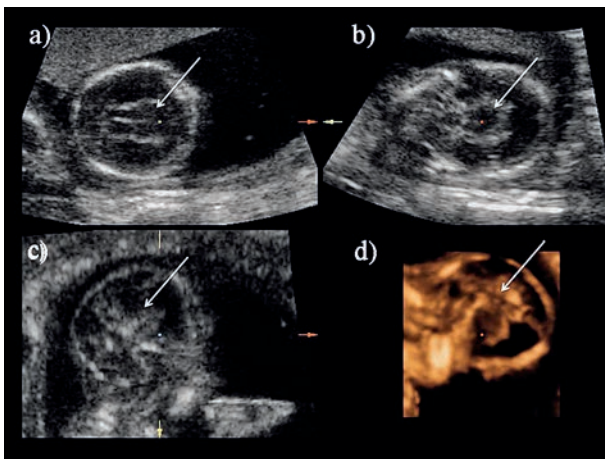


Fig 4. Three-dimensional ultrasound multiplanar imaging of the fetal head revealing holoprosencephaly (A: cross section, B: coronal section, C: sagittal section; D: 3D-ultrasound rendered imaging), with a fused thalami and lateral ventricles.

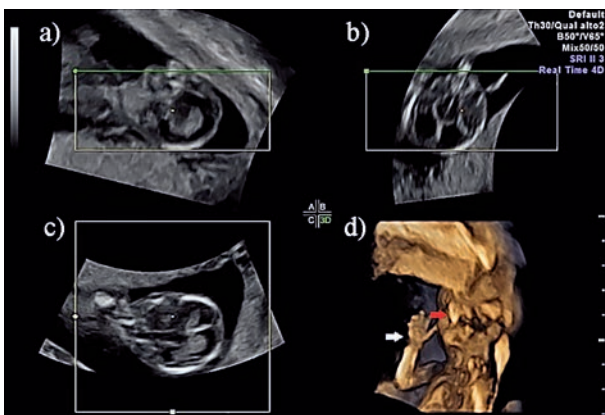


Fig 5. Three-dimensional ultrasound multiplanar imaging of the fetal trunk and head (A: cross section, B: coronal section, C: sagittal section; D: 3D-ultrasound rendered imaging) of a fetus with holoprosencephaly with polydactyly (with arrow) and proboscis (red arrow).

Omphalocele/Exomphalos

Omphalocele (otherwise known as exomphalos) is a congenital abnormality with herniation of abdominal contents through a ventral wall defect, and thought to occur during the process of body infolding. The incidence this anomaly ranges in 4,000-7,000 live births [7]. The herniation it is generally covered by a thin membrane consisting of peritoneum and amnion. The defect can vary in size from a few centimeters to as much as the entirety of the ventral abdominal wall. The umbilical cord inserts into the covering membrane at a location distant from the abdominal wall. Physiologic herniation of the fetal bowel into the base of the umbilical cord occurs normally between 8 and 12 weeks gestation. Failure of the



Fig 6. Three-dimensional ultrasound rendering image of a fetus with omphalocele (white arrows) at 14 weeks.

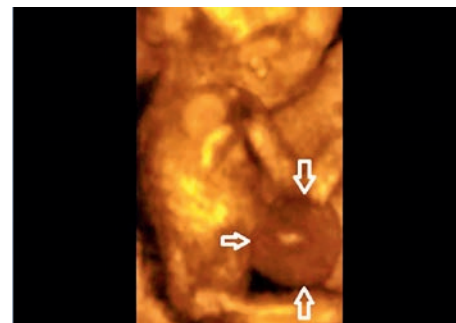


Fig 7. Three-dimensional ultrasound rendering image of a fetus with omphalocele (white arrows) at 13 weeks.

intestinal loops to return to the abdominal cavity results in the formation of an omphalocele [7]. This anomaly is characterized by a high association with others malformations and chromosome abnormalities (trisomies 18 and 13), especially with smaller lesions [6]. The diagnosis can be made as early as 10 to 12 weeks when no herniation should be visible once, especially when the crown rump length is 45 mm or more. As illustrated in figures 6 and 7, the sonographic finding this malformation is an echogenic mass anterior to the fetal abdomen with the umbilical cord insertion into the membrane covering the abdominal wall defect [6,7].

Gastroschisis

The worldwide incidence of gastroschisis has seen an increase in recent decades [8]. Gastroschisis occurs because a defect of the abdominal wall secondary to incomplete closure of the lateral folds during the initial gestation. Contrary to an omphalocele (unruptured), the eviscerated bowel characteristically does not have a covering membrane. Characteristically, the lesion is to the right of the intact umbilical cord [7]. The differentiation between gastroschisis and omphalocele is important, as gastroschisis is not associated with aneuploidy [6].

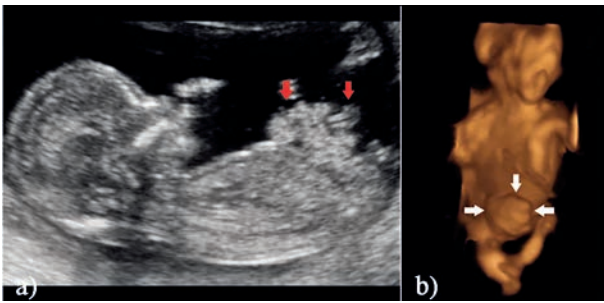


Fig 8. a) Two-dimensional ultrasonography (sagittal view) of a fetus with gastroschisis (red arrows) at 12 weeks; b) Three-dimensional ultrasonography (rendered imaging) of the same fetus showing irregular "mass" (white arrows) exteriorizing from a right-sided abdominal defect.

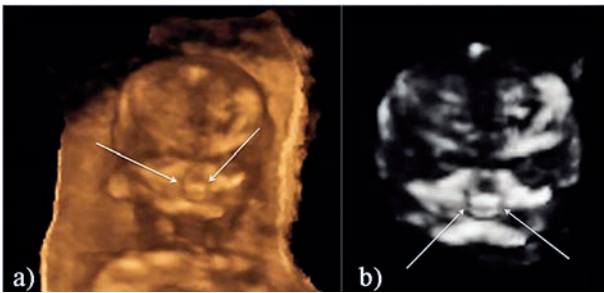


Fig 9. a) Three-dimensional ultrasound (rendering surface image) showing a bilateral cleft lip (white arrows) in a fetus at 13 weeks of gestation; b) Three-dimensional ultrasonography (rendering skeletal image) revealing bilateral cleft palate (white arrows) in the same fetus.

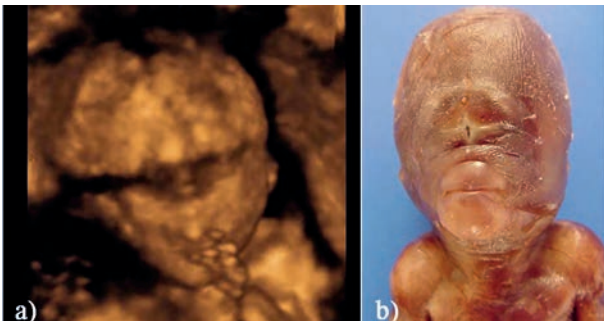


Fig 10. Three-dimensional ultrasound rendering image of fetal cyclopia at 12 weeks of gestation; a) Picture of the same fetus with fetal cyclopia at postmortem autopsy.

In first trimester vaginal ultrasound may help in distinguishing the contents of the herniation, especially as early as 12 weeks when the diagnosis of gastroschisis may be possible. The figure 8 demonstrates a fetus with gastroschisis.

Facial anomalies

Facial clefts are one of most frequent congenital anomalies, with an incidence between 1:625 and 1:1,000

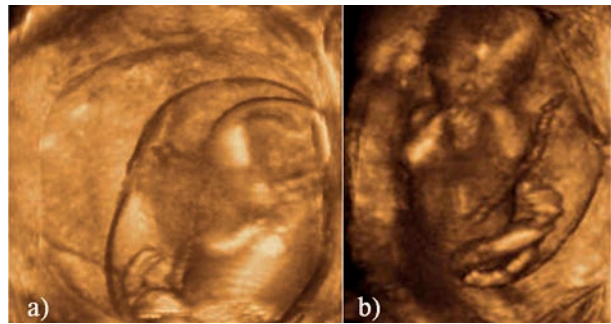


Fig 11. a). Three-dimensional ultrasound rendered imaging of an 11-week fetus with immobilism; b). Three-dimensional ultrasound rendered imaging of a 13-week fetus with immobilism.

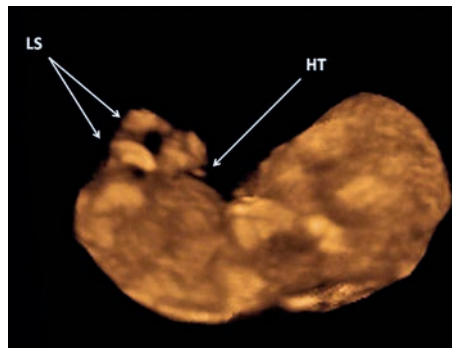


Fig 12. Three-dimensional ultrasound rendered imaging of an 11-week fetus with diastrophic dysplasia with limb shortening (LS) and hitchhiker thumbs (HT).

newborns in the USA [9]. The cleft palate stems from a failure in the fusion of maxillary lateral prominences. Most cleft palates affect the hard palate, causing interruption of anterior alveolar arch of the maxilla. The classification of clefts is determined by localization (unilateral, bilateral or median) and anatomic involvement (only the lip is engaged; lip and palate are engaged; and only the palate is engaged) [10].

3D ultrasound (rendering mode) in the first trimester of pregnancy can serve as an invaluable adjunct to 2D ultrasound in cases of cleft lip and palate. As illustrated in figure 9, the rendered visualization from 3DUS may aid parents in conceptualizing the defect and help with the counseling [11].

Cyclopia is a facial midline anomaly frequently associated with alobar holoprosencephaly (fig 10). To date, few reports have examined prenatal diagnosis of cyclopia in the first trimester [12,13]. Namely, Blass et al [12] described a case of cyclopia associated with alobar holoprosencephaly diagnosed at 9 weeks, whereas similarly Dane et al [13] described a case of semilobar holoprosencephaly with cyclopia and radial aplasia at 12 weeks.

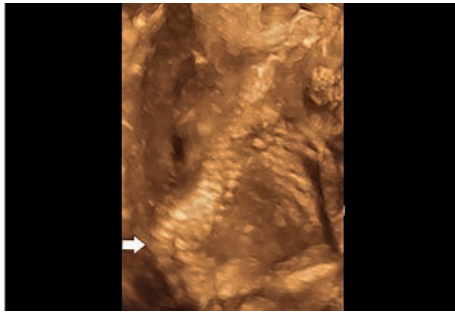


Fig 13. Three-dimensional ultrasound rendered imaging in maximum transparency of a 14-weeks fetus with neural tube defect demonstrating the bony defect in the lumbar spine (white arrow).



Fig 14. Three-dimensional ultrasound rendered imaging of a 14-weeks fetus with Femoral Hypoplasia Unusual Facies Syndrome demonstrating the large metopic suture (white arrow) and the micrognathia (red arrow).

Extremities defects – fetal muscle-skeletal dysplasias

Skeletal dysplasias are a heterogeneous group of bone disorders characterized by short long-bone length. More than 500 types of skeletal dysplasias have been described with 50% of believed to be lethal. Usually, the prenatal diagnosis may be made in the second trimester of pregnancy with an accuracy of 30 to 50% [14]. In the first trimester, lethal skeletal dysplasia has been reported to be associated with an increased nuchal translucency in 85% of cases [15]. Figures 11 show two case of fetal immobilism by 3DUS in the rendering mode with upper limbs contractures and marked skin edema. Figure 12 shows a case of tanatophoric dysplasia with markedly shortened limbs and a great disproportion between the fetal head and body.

The figure 13 shows a case of neural tube defect at 14 weeks of gestation. The 3DUS in the rendering mode with maximum transparency demonstrates the bony defect in the lumbar spine. The figure 14 shows a case of Femoral Hypoplasia Unusual Facies Syndrome at 14 weeks of gestation. The 3DUS in the rendering mode demonstrates the large metopic suture and the micrognathia.

Conclusions

The 3DUS is gaining widespread use and utility in the assessment of the growing embryo and fetus in the first trimester of pregnancy [16]. This technologic advancement and the future improvements have and will lead to increased prenatal diagnosis of fetal anomalies in the first trimester [17]. First trimester diagnosis will permit earlier counseling of parents, and in some countries interruption of the pregnancy. The 3DUS images are more similar to the reality, which seems to be a useful tool during prenatal consultations with the parents. In addition, 3DUS allows registration of the fetal images and further revision and discussion in a distant referral institute. These images can be faster acquired and stored in the hard disk for further analysis. In this pictorial essay, we attempt to show examples of the feasibility of first trimester prenatal diagnosis of some fetal anomalies using 3DUS.

Conflict of interest: none

References

1. American College of Obstetricians and Gynecologists. *Ultrasonography in Pregnancy*. Washington, DC: American College of Obstetricians and Gynecologists 2008.
2. Merz E, Bahlmann F, Weber G. Volume scanning in the evaluation of fetal malformations: a new dimension in prenatal diagnosis. *Ultrasound Obstet Gynecol* 1995; 5: 222-227.
3. Rădulescu M, Ulmeanu EC, Nedelea M, Oncescu A. Prenatal ultrasound diagnosis of neural tube defects. Pictorial essay. *Med Ultrason* 2012; 14: 147-153.
4. Bianchi DW, Crombleholme TM, D'Álton ME, Malone FD. *Fetology: Diagnosis and Management of the Fetal Patient*. 2th ed. New York: McGraw-Hill Companies 2010: 77.
5. Kagan KO, Staboulidou I, Syngelaki A, Cruz J, Nicolaidis KH. The 11-13-week scan: diagnosis and outcome of holoprosencephaly, exomphalos and megacystis. *Ultrasound Obstet Gynecol* 2010; 36: 10-14.
6. Castro-Aragon I, Levine D. Ultrasound detection of first trimester malformations: a pictorial essay. *Radiol Clin N Am* 2003; 41: 681-693.
7. Bianchi DW, Crombleholme TM, D'Álton ME, Malone FD. *Fetology: Diagnosis and Management of the Fetal Pa-*

- tient. 2th ed. New York: McGraw-Hill Companies 2010: 426.
8. Tannuri AC, Silva LM, Leal AJ, Moraes AC, Tannuri U. Does administering albumin to postoperative gastroschisis patients improve outcome? *Clinics (Sao Paulo)* 2012; 67: 107-111.
 9. Croen LA, Shaw GM, Wasserman CR, Tolarová MM. Racial and ethnic variations in the prevalence of orofacial clefts in California, 1983-1992. *Am J Med Genet* 1998; 79: 42-47.
 10. Nyberg DA, Sickler GK, Hegge FN, Kramer DJ, Kropp RJ. Fetal cleft lip with and without cleft palate: US classification and correlation with outcome. *Radiology* 1995; 195: 677-684.
 11. Ghi T, Arcangeli T, Radico D, Cavallotti D, Contro E, Pelusi G. Three-dimensional sonographic imaging of fetal bilateral cleft lip and palate in the first trimester. *Ultrasound Obstet Gynecol* 2009; 34: 119-120.
 12. Blaas HG, Eik-Nes SH, Vainio T, Isaksen CV. Alobar holoprosencephaly at 9 weeks gestational age visualization: two- and three-dimensional ultrasound. *Ultrasound Obstet Gynecol* 2000; 15: 62-65.
 13. Dane B, Dane C, Aksoy F, Yayla M. Semilobar holoprosencephaly with associated cyclopia and radial aplasia: first trimester diagnosis by means of integrating 2D-3D ultrasound. *Arch Gynecol Obstet* 2009; 280: 647-651.
 14. Doray B, Favre R, Viville B, Langer B, Dreyfus M, Stoll C. Prenatal sonographic diagnosis of skeletal dysplasias. A report of 47 cases. *Ann Genet* 2000; 43: 163-169.
 15. Ngo C, Viot G, Aubry MC, et al. First-trimester ultrasound diagnosis of skeletal dysplasia associated with increased nuchal translucency thickness. *Ultrasound Obstet Gynecol* 2007; 30: 221-226.
 16. Zanforlin Filho SM, Araujo Júnior E, Guimarães Filho HA, Pires CR, Nardoza LM, Moron AF. Sonoembryology by three-dimensional ultrasonography: pictorial essay. *Arch Gynecol Obstet* 2007; 276: 197-200.
 17. Pooh RK, Kurjak A. 3D/4D sonography moved prenatal diagnosis of fetal anomalies from the second to the first trimester of pregnancy. *J Matern Fetal Neonatal Med* 2012; 25: 433-455.