Obstetric Ultrasound for Diabetes-related Congenital Anomalies

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ABSTRACT

Major structural fetal anomalies occur in approximately 3% of births and are the main cause of infant mortality in developed countries. Pregestational diabetes is well recognized as the main cause, with up to a significant increase (ninefold) in structural defects when compared with the rates observed in nondiabetic pregnancies. In this Editorial, we will discuss the association between diabetes and the risk of congenital anomalies and the type of defects seen in diabetics. We will focus this Editorial on the Ultrasound Semiology of the Diabetes-related Congenital Anomalies.

Keywords: Congenital anomalies, Diabetic embryopathy, Gestational diabetes, Pregestational diabetes, Ultrasonography.

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INTRODUCTION

Diabetes is the most common medical complication in pregnancy. Women with diabetes in pregnancy can be divided into two groups: Pregestational diabetes that complicates less than 1% of all pregnancies, and gestational diabetes, which is observed in about 2% of pregnancies in which the glucose intolerance is first diagnosed during pregnancy. Gestational diabetes is further subdivided according to the degree of severity of the glycemic control disturbance. Women with a normal fasting plasma glucose are referred to as class I and those with abnormal fasting plasma glucose are categorized as class II. The latter type might in reality represent undiagnosed pregestational diabetes type II.

The risk of major congenital malformations is significantly higher in women with pregestational diabetes mellitus, especially when glycemia is not well controlled during the periconceptional period. Whether the risk of major congenital anomalies is also higher in gestational diabetes mellitus is still the subject of a debate. Some authors have reported that there is an increased risk of congenital anomalies in the offspring of a diabetic mother, while others have reported a risk, i.e., similar to the reference group except for women with class II gestational diabetes.

INCIDENCE AND RANGE OF DEFECTS

It is reported that in the offspring of women with pregestational diabetes, the risk of congenital anomalies is increased by five when compared with the general population. The two fetal organs that are most frequently affected are the fetal heart with the incidence of cardiovascular abnormalities ranging from 0.2 to 3% and the central nervous system with the incidence of abnormalities ranging from 0.1 to 5%. Other organ systems that are frequently affected are the musculoskeletal (abnormalities from 0.2 to 2%) and the genitourinary (abnormalities from 0.2 to 3%) systems.

Caudal regression syndrome (also frequently referred to as sacral dys- or agenesis, caudal dysplasia, or phocomelic diabetic embryopathy) is characterized by abnormal formation of the distal spine and pelvis. It is the only abnormality known to be specifically associated and typical for diabetes in pregnancy. Given the interdependency of neighboring structures on the caudal elements, an entire range of congenital malformations (Table 1) affecting the caudal region of the fetus can also be seen.

Table 1: Characteristic elements of caudal regression syndrome

| Anomalies of the lower extremities | Bilateral femoral hypoplasia |
|-----------------------------------|-----------------------------|
| Vertebral anomalies                | Sacral agenesis             |
| Gastrointestinal tract            | Anal atresia                |
| Urinary tract                     | Renal agenesis              |
| Genital anomalies                 | Cloacal anomaly             |
|                                   | Hydrometrocolpos            |
|                                   | Cryptorchidism              |
|                                   | Hypospadia                 |
as part of this condition. The incidence of this congenital anomaly in the normal population is about 1 per 25,000 live births and is about 150–200 times more common in infants of diabetic mothers.7-10

Imaging of the spine is usually easily achieved when the fetus is in a dorsoanterior position with enough amniotic fluid above it (Fig. 1). The fetal thoracolumbar spine curvature has a “c” shape with sacral “tapering,” which should be seen in all fetuses after 22 weeks of gestation. Prenatal diagnosis of caudal regression syndrome by ultrasound is possible by showing a sudden interruption of the spine with absent “tapering” due to absence of lower vertebrae (Figs 2 and 3).

The position of the conus medullaris in relation to the spine changes with advancing gestational age as the spine develops and grows faster than the spinal cord. Its position is most frequently between L2 and L3 between 19 and 24 weeks’ gestation (Fig. 4). Then, it undergoes its progressive relative ascent to be located above L2–L3 at term. The conus medullaris in caudal regression syndrome is abnormally high. Absent pelvic bones can be challenging to demonstrate.

Congenital heart defects are among the most important causes of perinatal mortality in offspring of diabetic mothers.11-18 The commonest cardiac anomalies associated with diabetes in pregnancy are transposition of the great vessels, common arterial trunk, ventricular septal defects, visceral heterotaxia, and coarctation of the aorta.19,20 Transposition of the great arteries is a conotruncal abnormality in which the right heart receiving blood from the body ejects blood directly into the aorta and the left heart receiving blood from the lungs ejects blood directly into the pulmonary artery. It is a common form of cyanotic congenital heart disease and one in which prenatal diagnosis has an important impact on neonatal outcomes. The outflow tract assessment is important for the diagnosis of transposition of the great arteries. Characteristic ultrasound images in D-transposition of
the great arteries demonstrate that the great vessels are arising from the “wrong” ventricle. The aorta runs anterior and to the right of the pulmonary artery. Additionally, the great vessels have a parallel course instead of crossing each other (Fig. 5). Another feature is an abnormal three-vessel trachea view in which only the aortic arch on the left side and the superior vena cava on the right side can be identified (Fig. 6). The pulmonary artery is positioned inferior to the aorta and, thus, not visible in the three-vessel view in transposition of the great arteries. 

Examination of the great arteries is important to diagnose the common arterial trunk. Inclining the transducer cranially will reveal a large, single great vessel that overrides a ventricular septal defect. Further anterior angulation of the transducer confirms that there is only a single great vessel with branches to the pulmonary, systemic, and coronary circulations arising from the heart (Fig. 7). A large, malaligned outlet ventricular septal defect is a common association.

In poor maternal glycemic control-related fetal hyperglycemia, glycogen can accumulate in the cardiac muscle and growth will be stimulated by the hyperinsulinism due to fetal pancreas hyperstimulation. This hypertrophy can obstruct the cardiac blood flow and even cause cardiac failure. Hypertrophic subaortic stenosis has been reported in very severe cases. One of the common explanations for the unexplained death in late pregnancy of fetuses of diabetic patients is this phenomena. However, the absolute prenatal risk of a hypertrophic myocardiopathy in pregnant women with diabetes and the adequate management and interventions are still poorly understood.

Hypertrophic myocardiopathy is characterized by hypertrophy of the interventricular septum and the ventricular walls. The interventricular septum should be measured in its midway part in the four-chamber view with the ultrasound beam perpendicular to the interventricular septum preferably in the end-diastolic phase. Hypertrophic myocardiopathy can be suspected if the interventricular septum measures more than 5 mm (Fig. 7).

The incidence of neural tube defect in the diabetic obstetric population is increased when compared with the nondiabetic one (approximately 20/1,000 vs 1–2/1,000). Myelomeningoceles account for more than 98% of open spina bifida while myeloceles are rather rare. The main difference between a myelomeningocele and myelocele is the position of the neural placode relative to the spinal canal. The neural placode is outside the spinal canal and protrudes above the skin surface with a myelomeningocele (Fig. 8) and is inside the spinal canal and flush with the skin surface with a myelocele (Fig. 9).

Accurate diagnosis of open spina bifida requires a thorough examination of spine and intactness of the overlying skin. However, the latter is difficult to demonstrate...
in myelocoele in which there is no cystic structure above the skin defect (Fig. 9). The only reliable way to diagnose open spina bifida is, thus, through a thorough examination of the posterior fossa. The typical abnormal shape of the cerebellum due to its dorsocaudal displacement into the spinal canal (so-called banana sign) with obliteration of the cisterna magna (Chiari II malformation) (Fig. 10) is pathognomonic for open spina bifida and will lead to the diagnosis.24

Recent first trimester ultrasound studies have shown that signs of caudal displacement of the posterior brainstem are present in fetuses with open spina bifida as early as 11–14 weeks gestation. This displacement causes enlargement of the fourth ventricle by compression of the cisterna magna (Figs 11 and 12). As a consequence, the so-called intracranial translucency will be absent.25

Anencephaly is with a rate of 1/200 diabetic pregnancies, a common complication of diabetic pregnancies. It is easily diagnosed as characterized by absent bony calvarium and prominent bulging eyes. Microcephaly is another central nervous system malformation associated with diabetes in pregnancy.

Imperforate anus is one of the most common gastrointestinal malformations associated with diabetes. An imperforate anus had been thought to be difficult to diagnose prenatally. However, prenatal diagnosis by direct visualization of the fetal perineum has been reported.26-29 The fetal anal structures are best visualized on tangential views of the fetal perineum. The normal fetal anus appears as a hypoechoic ring surrounding the hyperechoic anal mucosa (so-called “target sign”) (Fig. 13). Characteristic images of anal atresia are the nonvisualization of the anal sphincter muscles and anal mucosa and only a hyperechoic linear line across the perineum (Figs 14 and 15).

The association of the so-called femoral hypoplasia – unusual facies syndrome with maternal insulin-dependent diabetes – is well recognized.30,31 Patients suffering from femoral hypoplasia–unusual facies...
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Fig. 12: Normal mid-sagittal plane of the fetal brain in the first trimester showing brain stem (BS), fourth ventricle (V4) and cisterna magna (CM).

Fig. 13: Abnormal mid-sagittal plane of the fetal brain in the first trimester. The fourth ventricle (V4) appears enlarged and the cisterna magna is not visible.

Fig. 14: Normal anal sphincter muscles appears as hypoechogenic ring surrounding the hoperchogenic anal mucosa (So called “target” “sign”).

Fig. 15: Non-visualization of the anal sphincter muscles and anal mucosa and only a hyperechoic linear line across the perineum in anal atresia.

syndrome are characterized by a variable degree of unilateral or bilateral femoral hypoplasia associated with facial clefting and occasionally other minor anomalies.

CONCLUSION

While the risk for major congenital defects has been well established in women with pregestational and gestational diabetes, their detection remains a challenge. One should bear in mind that ultrasound examination of obese diabetic pregnancies showed up to suboptimal image quality in up to 37% of the cases and incomplete examinations with repeat examinations in up to 17% of the cases. The malformation detection rate was markedly reduced in diabetic women when compared with the low-risk population (30 vs 73%). Knowledge about the spectrum of anomalies and their ultrasound semiologies is important for their accurate prenatal diagnosis.

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