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Review Article

Diagnosis of Fetal Anomalies by Sonography

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The last 2 decades have seen considerable advances in obstetric ultrasonography, which now forms part of routine prenatal care in most countries. Congenital anomalies often occur sporadically and unpredictably. The prenatal identification of an abnormal fetus allows the opportunity for prenatal counseling with a multidisciplinary team of experts, and a thorough discussion of pregnancy options. Furthermore, prenatal diagnosis can influence antepartum and intrapartum management, and permit the planning of the mode and site of delivery, thus ensuring optimal care of the fetus and the newborn. Prenatal surgical therapy can also be offered to fetuses with simple anatomic defects that have predictably devastating developmental consequences. This review discusses controversies regarding the accuracy, limitations and the roles of ultrasound in pregnancy.

Key Words: Ultrasonography, congenital anomalies

INTRODUCTION

Ultrasonography has become commonplace in obstetric practice since it was first introduced as a diagnostic tool in the late 1950s. The first description of obstetric ultrasound was made in an investigation of abdominal masses by Donald et al in 1958.[1] They suggested that the gravid uterus, a fluid-filled cavity with a "solid fetus", was an ideal target for ultrasound imaging. At that time, the main advantage of ultrasonography was its safety to the fetus, i.e., it employed sound waves instead of ionizing radiation. Recent advances in the technology have focused on enhanced image quality, which has made ultrasound the modality of choice for fetal imaging. During the last 2 decades, sonography has been used increasingly for prenatal diagnosis and treatment. The prenatal identification of an abnormal fetus allows an opportunity for prenatal counseling with multidisciplinary experts, and a thorough discussion of pregnancy options. Furthermore, prenatal diagnosis may influence antepartum and intrapartum management, and permit the planning of the mode and site of delivery, thus ensuring optimal care of the fetus and the newborn.

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ACCURACY IN DIAGNOSING MALFORMATIONS

Congenital anomalies are responsible for 20% to 25% of perinatal deaths, and an even higher percentage of perinatal morbidity.[2] Most occur sporadically, in fetuses without known risk factors. For these reason, routine ultrasound is an attractive concept as a screening tool.

Table 1 lists fetal malformations that have been prenatally diagnosed by ultrasound. The accuracy of obstetric ultrasonography in detecting these lesions is difficult to assess, due to differences in the extents of the malformations, the quality of the equipment, and the expertise of the sonographer. Some anomalies are more difficult to diagnose than others, for example, cardiac defects, and technical limitations, including different fetal positions, amniotic fluid volume, and maternal habitus make interpretation even more challenging.[3] Fig. 1 shows the distribution of congenital anomalies detected at our center between 1990 and 1995 (unpublished data).

Detection rates differ and are dependent on the population under investigation. Table 2 demonstrates the sensitivity and specificity of ultrasound

Table 1. Fetal Malformations that Have Been Diagnosed Prenatally by Ultrasonography

Cranial and intracranial	Meconium ileus
Agenesis of the corpus callosum	Meconium peritonitis
Anencephaly	Mesenteric cyst
Aqueductal stenosis	Persistent cloaca
Arachnoid cyst	Situs inversus
Choroid plexus cyst	Tracheoesophageal fistula
Hydrocephalus	Volvulus
Dandy-Walker malformation	**Genitourinary system**
Encephalocele	Ambiguous genitalia
Holoprosencephaly	Bladder outlet obstruction
Iniencephaly	Duplicated kidney with ectopic ureterocele
Microcephaly	Multicystic kidney
Porencephalic cyst	Infantile polysystic kidney
Schizencephaly	Ovarian cyst
Vein of Gallen aneurysm	Renal agenesis
Craniofacial	Tumors
Anophthalmia	Ureteropelvic junction obstruction
Cyclopia	Ureterovesical obstruction
Cystic hygroma	**Cardiovascular system**
Facial clefts	Atrioventricular septal defect
Hypertelorism	Cardiomyopathy
Hypotelorism	Coarctation of aorta
Micrognathia	Double outlet right ventricle
Microphthalmia	Ebstein's anomaly
Teratoma	Heterotaxy syndrome
Spine	Hypoplastic left ventricle
Hemivertebrae	Tumors
Sacral agenesis	Tetralogy of Fallot
Sacrococcygeal teratoma	Total anomalous pulmonary venous return
Spina bifida	Transposition of the great vessels
Thoracic	Valvular stenosis
Bronchogenic cysts	Ventricular septal defect
Cystic adenomatoid malformation	**Abdominal wall and trunk**
Diaphragmatic hernia	Bladder exstrophy
Hydrothorax	Cloacal exstrophy
Pulmonary hypoplasia	Gastroschisis
Pulmonary sequestration	Body-stalk anomaly
Gastrointestinal	Omphalocele
Anorectal atresia	Tumors
Choledochal cyst	Urachal cysts
Cholelithiasis	**Extrimities**
Duodenal atresia	Arthrogryposis
Hepatic cyst	Limb dysplasias and shortening
Hepatic neoplasm	Clinodactyly
Jejunoileal atresia	Cubfoot
Enteric duplication cyst	Polydactyly
Hirschsprung's disease	Radial aplasia

in low-risk populations. The sensitivities range from 14% to 85%, whereas the specificities range from 93% to more than 99%. This range of sensitivities with high specificities suggests that in low-risk populations, ultrasonography may be helpful at ruling out anomalies, but it is not particularly

reliable in terms of detection.[12] This type of information may prove useful when counseling patients about the accuracy of ultrasound. Ideally, each center should know its own sensitivity for anomaly detection in the low-risk population.

Targeted studies, performed on high-risk patients at referral centers, appear to be more accurate at anomaly detection. Overall sensitivities range from 27% to 99%, with specificities of from 91% to 100%. Tables 2 and 3 compare the detection of malformations in general versus selected populations. If these data are further analyzed using the organ system, 96% to 100% of the central nervous system lesions were detected,[13,15,16,18] 8% to 94% of the gastrointestinal abnormalities,[13,15,16] 6% to 92% of the genitourinary abnormalities, and[13,15,16] and 5% to 100% of the skeletal defects.[13,15,16]

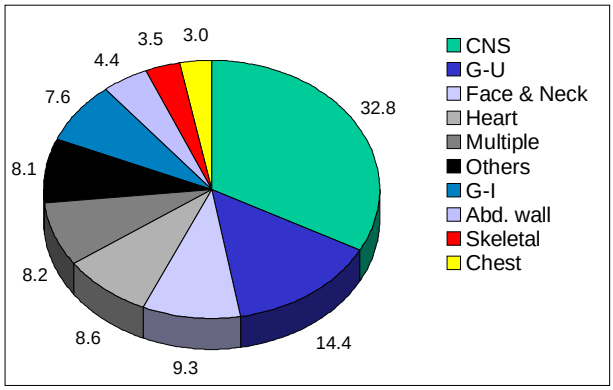

Fig. 1. Distribution of congenital anomalies between 1990 and 1995 in YUMC Values are presented as percentage (total 707 cases).

It is important to counsel patients that prenatal sonography is not the equivalent of a physical examination of a newborn, and for example, that ultrasound may miss minor malformations. Reported false-negative diagnoses involve all organ systems, but the majority concern the craniospinal, cardiac, and genitourinary structures.[13,15,16] False-positive diagnoses are infrequent but worrisome, as they may heighten patients' anxiety and lead to unnecessary invasive testing and obstetric intervention.

DETECTION OF ABNORMALITIES IN DIFFERENT SYSTEMS

Routine ultrasound examinations vary considerable in terms of abnormality detection in different systems. There are many reasons why an abnormality may not be detected. These include technical difficulties, the absence of a sonographic sign associated with the abnormality, the late appearance of the ultrasound abnormality, as well as failure to scan the fetus. It is therefore unlikely

Table 2. Accuracy of Ultrasound in Detection of Congenital Anomalies in Low-Risk Populations

Author	No. of Patients	Study Period	Sensitivity	Specificity
Lys et al[4]	8,316	1986	14%	98%
Li et al[5]	678	1980 - 1981	38%	98%
Levi et al[6]	13,309	1986 - 1987	34-55%	>99%
Rosendahl et al[7]	9,012	1980 - 1988	58%	>99%
Shirley et al[8]	6,183	1989 - 1990	67%	>99%
Chitty et al[9]	8,432	1988 - 1989	74%	>99%
Luck[10]	8,523	1988 - 1991	85%	>99%
RADIUS Trial[11]	15,151	1987 - 1991	35%	-

Table 3. Accuracy of Ultrasound in Detection of Congenital Anomalies in Selected Populations

Author	No. of Patients	Study Period	Sensitivity	Specificity
Hill et al[13]	5,420	1979 - 1983	27%	-
Sollie et al[14]	481	1980 - 1985	86%	100%
Sabbagha et al[15]	596	1980 - 1983	95%	99%
Campbell et al[16]	2,372	1978 - 1983	95%	>99%
Manchester et al[17]	257	1983 - 1985	99%	91%

that routine screening will ever achieve detect 100% of fetal abnormalities.

Craniospinal abnormalities

All recent studies, involving routine screening in the second trimester, report 100% detection of anencephaly, and many achieve rates approaching 100% for open neural tube defects. In the early days of obstetric scanning, the sensitivity of ultrasound for the detection of neural tube defects was poor (about 50%)[19,20] compared with the measurement of maternal serum alpha-fetoprotein (MSAFP) levels, which would identify about 80% of fetuses with open spina bifida,[21] but 3-5% of normal fetuses are also identified as being at increased risk. The main reason for the recent improvement is the recognition of cranial signs associated with spina bifida and the Arnold-Chiari malformation. Specifically, these are the 'lemon' sign, resulting from a scalloping of the frontal bones, and the 'banana' sign, which concerns the abnormal shape of the cerebellum.[22,23] Both appearances are thought to be a result of traction on the brain stem. Nevertheless, when these cranial signs are used in high-risk populations nearly all fetuses with open spina bifida can be successfully identified before 20 weeks.[23-25]

Other intracranial abnormalities are detectable in the second trimester, but unfortunately most studies in the literature do not differentiate between the types of abnormality. It is clear, however, that the sonographic signs associated with some intracranial abnormalities, in particular, microcephaly and hydrocephaly, may develop later in pregnancy and may, therefore, only be detected if a scan is initiated because of a clinical indication or if a third trimester scan is routinely offered. This is illustrated well in a study conducted in Belgium where only 4 of 20 cases of hydrocephalus were identified by scanning before 22 weeks gestation, with the remainder being identified later in pregnancy.[26] Similarly, only a half of the cases of microcephaly (2 of 4) were identified in the second trimester.

Cardiovascular abnormalities

Cardiac anomalies are the most common congenital anomaly, with a prevalence of 8 per 1000 live births,[27] and 10.3 per 1000 at the time of the second trimester by sonographic examination.[28] About 50% of these defects were major because they are either lethal or require surgery and have a significant effect on perinatal and long-term morbidity, and on mortality rates. Early prenatal diagnosis of these defects is important to allow patients to be accurately counseled on the long-term implications of these anomalies, pregnancy options, and their impact on neonatal care. Early detection will allow patients to consider their options and make informed decisions.

A general examination of the heart, four-chamber view, rate, and rhythm, should be included in the basic ultrasound examination. A more detailed targeted examination should be performed if any of the risk factors are present, namely, suspected cardiac abnormality seen on the four-chamber view, arrhythmia, the presence of extracardiac anomalies, a parent or sibling with heart defect, maternal diabetes, teratogen exposure, and non-immune hydrops. A detailed cardiac evaluation is usually not possible until at least the 18th gestational week. Even at this time, adequate anatomical assessment is dependent on the fetal position and activity, maternal size, amniotic fluid volume, and the availability of proper equipment and expertise. However, the study is often time-consuming and may require collaboration with a pediatric cardiologist.

The four-chamber view is central to fetal cardiac assessment. Much of the work that evaluated the sensitivity of this view was performed in the 1980s. Because equipment and experience are known to affect the ability to obtain a four-chamber view, a review of series published over the last 10 years, rather than earlier, would theoretically give a better idea of the true capabilities of the four-chamber view in terms of abnormality detection. Earlier studies are summarized by Kirk et al.[29] Table 4 lists the sensitivities of studies that were undertaken in 1990 or later. It is clear that, although the sensitivity of the four-chamber view depends on many factors, that it approximates to 50% or less when performed during the initial screening process on low-risk patients.

A complete cardiac evaluation should include an examination of the ventricular outflow tracts.

Table 4. Sensitivity of the Four-chamber View

Author	Study Period	No. of Patients	Type	Gestational age (weeks)	Sensitivity(%)
Kirk et al[29]	1990 - 1992	5,967	Low risk	14 - 40	47
Anderson et al[30]	1991 - 1993	7,880	Unselected	16 - 20	31
Levi et al[31]	1990 - 1992	9,392	Unselected	12 - 40	52
Buskens et al[32]	1991 - 1993	5,319	Low risk	16 - 24	43
Cho et al[33]	1991 - 1996	5,598	Unselected	16 - 40	52

Table 5. Accuracy of Extended Fetal Echocardiography

	Sensitivity	Positive predictive value
4-CV only	51.9%	100.0%
4-CV + SAV	57.4%	100.0%
4-CV + LAV	64.8%	94.6%
4-CV + SAV + LAV	64.8%	94.6%

4-CV, four-chamber view; SAV, short-axis view; LAV, long-axis view.

Starting with the four chamber view, slight rotation of the transducer toward the right fetal shoulder shows the aortic outflow tract. Once the aortic outflow tract has been identified, rotating the transducer in the opposite direction allows the pulmonary outflow tract to be visualized. The aortic arch is best viewed longitudinally where these two arteries appear to cross. Pulse Doppler and real-time Doppler color-flow mapping can then be used to evaluate the blood flow.[34,35] In addition, M-mode echocardiography is essential for arrhythmia evaluation, and to measure the chamber size, wall thickness, and wall and valve motion. If examination of the fetal heart is extended to include views of the great vessels, the numbers of cardiac defects detected are reported to increase from 48 to 78%.[36] Table 5 lists the sensitivities of extended examinations performed in our center between 1991 and 1995.[33]

Congenital heart abnormalities are good illustrations of how difficult it can be to define what in considered abnormal or clinically significant. Many small ventricular or atrial septal defects do not require treatment and will close spontaneously.[37] It may well be that the delay in closure in some cases is part of the spectrum of normality, and therefore, it is difficult to know whether or not to define them as congenital heart defects.[38]

Pulmonary abnormalities

Probably the most common abnormality of the respiratory system is a congenital diaphragmatic hernia, which occurs in about 1 in 2000 to 1 in 5000 births. This is an abnormality which can be diagnosed at a routine second trimester scan, but in fact many are diagnosed later in pregnancy because of associated hydramnios. Other pulmonary abnormalities include cystic lung lesions, such as cystic adenomatoid malformation (CCAM) and pleural effusions. The majority of cases of CCAM are diagnosed at the time of the routine scan, but in many instances there is no confirmation of prenatal diagnosis, as the natural history of this condition involves the apparent resolution of the lesion in utero, which often results in the neonatal chest radiograph appearing normal.

Gastrointestinal abnormalities

Anterior abdominal wall defects are regularly detected by routine ultrasound and most studies report a 100% detection rate for omphalocele and gastroschisis. However, the diagnosis of intestinal obstruction or atresia is less amenable to diagnosis in the second trimester, because the classical signs of a dilated stomach or proximal loops of small bowel do not appear until later in pregnancy. Moreover, these abnormalities are often detected

because of hydramnios in later pregnancy. Isolated esophageal atresia may be diagnosed if there is a failure to visualize the stomach bubble on several occasions. In 95% of these cases, there is a coexistent fistula to the trachea so that the stomach can fill via the trachea and thus a bubble will be visualized, although hydramnios may occur later in pregnancy. In three studies, which listed the types of intestinal atresia separately, none of the six fetuses with tracheoesophageal atresia were identified during the second trimester.[9,10,39]

Urinary tract abnormalities

Abnormalities of the renal tract are commonly diagnosed prenatally. Virtually, all cases of hydronephrosis, and the vast majority of bilateral renal agenesis or dysplasia, as well as many unilateral lesions are diagnosed at the time of routine scanning. However, in 5 of the studies, cases of mild hydronephrosis or mild pyelectasis were not reported,[8,9,26,31,39] though it is unlikely that all such cases are pathological after birth. A prospective screening program in Staffordshire reported that a total of 92 fetuses, examined at around 28 weeks gestation, were thought to have a renal abnormality, but that postnatal examination could only confirm abnormality in 46% of these cases.[40] Furthermore, complete confirmation of urinary tract abnormality is impossible unless neonates are scanned at birth and then subsequently followed up into infancy. In addition, the incidence of hydronephrosis at birth in the ultrasound screened group (26/7685) in the RADIUS study was four times greater than in the control group (7/7596).[11] This difference reflects the impact of ultrasound screening, and is indicative of the clinically silent nature of most renal problems. Other studies have described improved detection rates for urinary tract abnormalities by scanning later in pregnancy.[41,42] However, the true clinical significance of many of the prenatal findings, even when confirmed in the neonatal period, are unclear as the majority of neonates are clinically asymptomatic.

Skeletal abnormalities

Visualization of the fetal long bones at the time of a routine scan is usually achieved, and femur measurement is often incorporated as a routine part of the examination. Many lethal skeletal dysplasias are associated with severe limb shortening, which is evident at 18 weeks, making many amenable to detection by routine ultrasonography, as demonstrated by the relatively good detection rates of skeletal dysplasias by routine ultrasound screening. However, examination of the hands and feet may be more difficult, and often there are time constraints which prevent detailed examination of the extremities. This results in relatively poor detection rates for abnormalities, such as talipes and limb reduction defects.

Nuchal translucency and fetal structural abnormalities

Nuchal translucency is defined as the translucency of the normal subcutaneous tissue to ultrasound, and is observed on the first trimester ultrasound examination, between the skin and the cervical spine of the fetus. It is well recognized that nuchal translucency normally increases with gestational age.[43,44] The use of a single cutoff to define increased nuchal translucency is therefore inappropriate. The 95th percentile nuchal translucency values used by the Fetal Medicine Foundation are 2.2 mm at 10 weeks gestation and 2.8mm at 14 weeks gestation.[45] Increased nuchal translucency is known to be associated with an increased risk of aneuploidy, particularly Down syndrome.[46] In addition to this association with aneuploidy, multiple studies have now identified increased nuchal translucency as a nonspecific marker of a wide range of fetal structural abnormalities, which include congenital diaphragmatic hernia, cardiac defects, and various genetic syndromes.[47-50] The degree of nuchal translucency is directly related to the prevalence of fetal anomalies and may have prognostic significance, especially when found in association with other anomalies.[50-52] The pathophysiology of increased nuchal translucency is uncertain, but it may be the result of cardiac failure or an alteration of lymphatic drainage. Increased nuchal translucency may identify pregnancies that require further assessment, including additional sonographic evaluation and possible

fetal echocardiography. Further evaluation is required to assess the role of nuchal translucency screening in the general population.

CONCLUSION

Ultrasound is the main diagnostic tool used in the prenatal detection of congenital abnormalities. It allows examination of the external and internal anatomy of fetuses, and the detection of not only major defects, but also of subtle markers of chromosomal abnormalities and genetic syndromes. The appeal of the ultrasound examination is that it is a noninvasive, safe procedure with a high degree of patient acceptance. Moreover, the prenatal detection of abnormalities often influences obstetrical management and allows the optimization of fetal and newborn care. In addition, prenatal surgical therapy can be offered to fetuses with simple anatomic defects that have predictably devastating developmental consequences. Finally, it is important for obstetricians and sonologists to appreciate the limits of their expertise. If a malformation is suspected, and the examiner has had little experience with the abnormality in question, the case should be referred to a more experienced examiner. Only in this way will patients be best served.

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