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REVIEW ARTICLE

Ultrasonography and Birth Defects

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ABSTRACT

Birth defects are major global problems. Even in developed countries, the incidence of birth defects has not reduced.

The prevalence of birth defects diagnosable (65%) and preventable (2.5%). Ultrasound screening is a very reliable tool for assessing birth defects.

A well done genetic scan at 11 to 14 weeks and at 22 weeks (TIFFA) can accurately detect over 85% of birth defects.

With the advent of 3D and 4D ultrasound, the accuracy for functional defects has also increased.

Each pregnancy deserves a prenatal diagnostic test and ultrasound is a near ideal diagnostic test to be applied, to large pregnant population, specially in developing countries.

Keywords: Birth defects, Ultrasonography, Trisomy, Genetic defects, Prenatal scan, Screening.

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INTRODUCTION

'Care Is Absolute, Prevention Is Ideal'.

Ultrasound has revolutionized obstetric practice all over the world and there is no doubt about it. With good resolution machines, Color Doppler, 3D and 4D scanning it is now possible to make a prenatal diagnosis of many structural anomalies, which are lethal, life-threatening and debilitating.

All pregnancies are at risk of producing fetal malformations or birth defects. Some pregnant women are at a greater risk. The world consensus on whether all pregnancies should be screened by ultrasound for anomalies and when, is still divided.

Birth defect is a global problem. Birth defect is one of the leading causes of perinatal mortality and morbidity, accounting for 2 to 3% of all live-births.[1]

Presence of anomalies and their undesirable consequences for the affected neonate, family and medical fraternity is a very convincing argument by many experts on universal screening.

Regardless of whether a woman is in low risk (majority cases) or high risk category (genetic, diabetes, etc.) the risk of fetal malformation is always there and because there are no symptoms and these pregnancies may be uneventful.

It is estimated that every year 7.9 million children are born with a serious birth defects of genetic or partly genetic origin. A further 1 million are born with serious birth defects of postconception origin which result from environmental teratogens such as alcohol, rubella, syphilis and iodine deficiency which can either cause death or lifelong disability.[1]

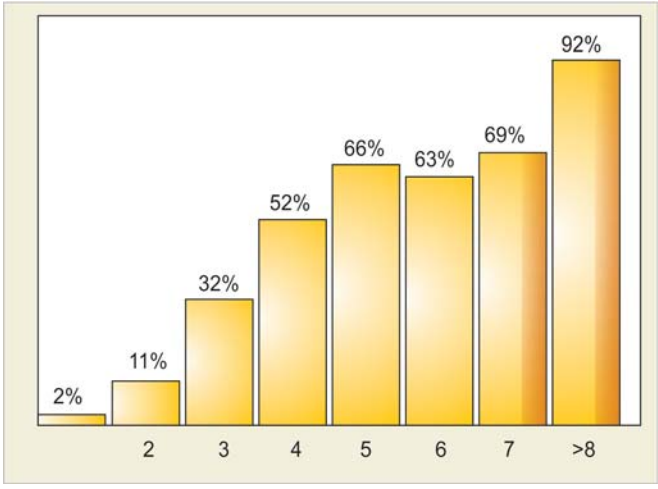


Fig. 1: Frequency of aneuploidies *vs* number of anomalies

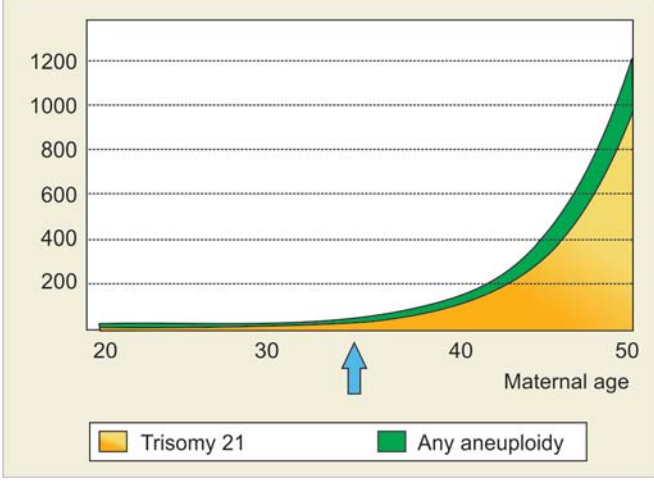


Fig. 2: Incidence of aneuploidy (trisomy 21) screen with maternal age

While this problem has been addressed in the West, it is yet to be addressed in developing countries where 94% of those born with birth defects reside and where 95% of the children who die from birth defects are born.[1]

The prevalence of fetal malformations is 65% though only 2 to 2.5% are potentially life-threatening, lethal or represent a major cosmetic defect[1] (Fig. 1). It is seen that incidence of aneuploidy (Trisomy 21) screen with maternal age (Fig. 2).

Ultrasound routine screening is a very valuable tool for detecting birth defects.[2]

In India, due to its high birth rate, population and consanguinity in certain communities, the burden of birth defects is significant. This has been reported by the Federation of Obstetric and Gynecological Societies of India (FOGSI) birth defects registry (unpublished data).

An estimated 495,000 infants with congenital malformations are born every year.[2] In addition, 21,400 with Down's syndrome, 9,000 with thalassemia, 5,200 with sickle cell anemia, 390,000 with G6PD deficiency and 9,760 with amino acid disorders are born every year.[3]

Diagnosis is generally late or ineffective and the infrastructure for management and rehabilitation of the families is not easily accessible. This makes the burden of genetic diseases and birth defects particularly severe as compared to the western countries.

Social stigma, discrimination, lost hopes and lack of opportunities add to the emotional and financial burdens. To reduce the impact of birth defects, national health policy makers need to first recognize the prevalence, disability and burden of the disease.

CAUSES

The incidence of birth defects in USA is one out of 33 and may be much more in developing countries and the countries where no formal and structured registry exists.

There are three major categories of causes as follows:

1. Genetic
2. Environmental
3. Complex genetic/unknown.

Genetic Causes

Chromosomal or single-gene disorders are known to account for about 25 to 30% of all birth defects. Chromosomal abnormalities are seen in about 0.5% of live newborns. Recently, use of 'telomeric probes' has increased this incidence further as about 5 to 7% of mentally challenged children have a cryptic translocation that cannot be detected by traditional cytogenetic methods. A 'mutation' in the genetic locus can give rise of 'single gene disorder'. Not all mutant genes manifest at birth or lead to structural problems.

Some birth defects are caused by errors in genes or chromosomes. Those caused by genes can be inherited—passed by parents to their children. Some inherited disorders are more common in certain ethnic groups, such as sickle cell disease, cystic fibrosis, and Tay-Sachs disease.

Chromosomal defects are caused by missing, damaged or extra chromosomes. These defects are often the result of an error that occurred when the egg and sperm were joining. Common chromosomal disorders are Down syndrome and trisomy 18. Generally, the risk of having a baby with Down syndrome, trisomy 18, and other chromosomal disorders increases with advancing maternal age.[3]

Environmental Causes

These causes account for 5 to 10% of birth defects. These include nutritional deficiencies, maternal illnesses, teratogenic drugs or radiation and infectious agents. However, the extent of the damage depends upon the timing of exposure and the individual's genetic susceptibility.

Other birth defects result from the fetus being exposed to harmful agents, such as medications, chemicals, and infections. Whether a woman or her baby is harmed depends on how much of the agent they have been exposed to, when during her pregnancy a woman is exposed to the agent and for how long.

Complex Genetic/Unknown Causes

These comprise of about 65 to 70% of birth defects. This may be caused by defects in more than one gene or a complex interaction of the environment and genes.

Sometimes, a mixture of factors is the cause. For many birth defects, the exact cause is not known.

Thorough screening of all pregnant patients is impossible in the current scenario, but we can and should offer ultrasound to all possible pregnant women as a prenatal diagnostic test.[4]

Most of the birth defects can be identified and diagnosed *in utero*. A careful history, proper biochemical screening and ultrasound added with invasive testing wherever required can pick up structural, chromosomal, metabolic abnormalities in the unborn. An early diagnosis leads to good counseling and informed choice to the parents with option of termination.

Table 1: Clinical markers of high-risk pregnancy

1. Advanced maternal age
2. Previous birth of a malformed fetus
3. Family history of a malformed fetus
4. Consanguinity
5. Exposure to drugs/radiation
6. Maternal diabetes mellitus
7. Bad obstetric history
8. Bleeding in early pregnancy

Table 2: Sonographic findings: first trimester

1. Oligoamniotic sac
2. Embryonic bradycardia
3. Abnormal yolk sac
4. Increased nuchal translucency
5. One identified anomaly
6. Dates size discrepancy at 9 to 12 weeks

Table 3: Sonographic findings: second and third trimesters

1. Increased nuchal translucency
2. Symmetric IUGR
3. Polyhydramnios
4. Oligohydramnios
5. Breech presentation
6. Twins
7. One identified anomaly

Table 4: Nonsonographic findings

1. Abnormal results from a CVS/amniocentesis
2. Abnormal immunoglobulin profile
3. Abnormal triple test/increased alfa fetoprotein/abnormal pregnancy associated plasma protein (PAPP)
4. Abnormal first-trimester dual marker test

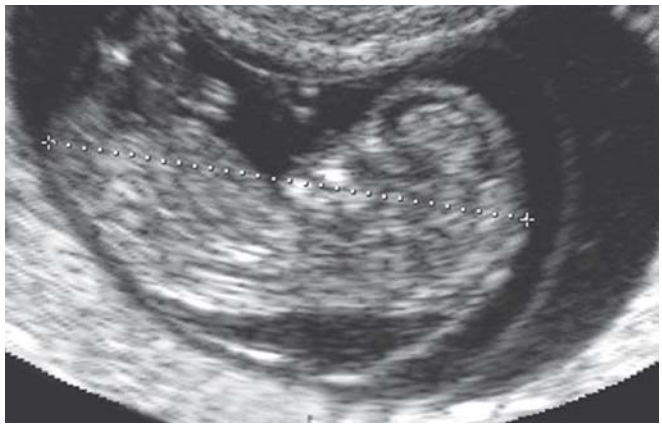


Fig. 4: Measurement of crown-rump length

Clinically, high risk groups for a detailed anomalies scan are shown in Table 1.

The sonographic findings which are indications for a detailed anomalies scan are listed in Tables 2 and 3.

Nonsonographic laboratory investigations which can warrant a detailed anomalies scan are listed in Table 4.

ULTRASOUND FOR CONGENITAL DEFECTS

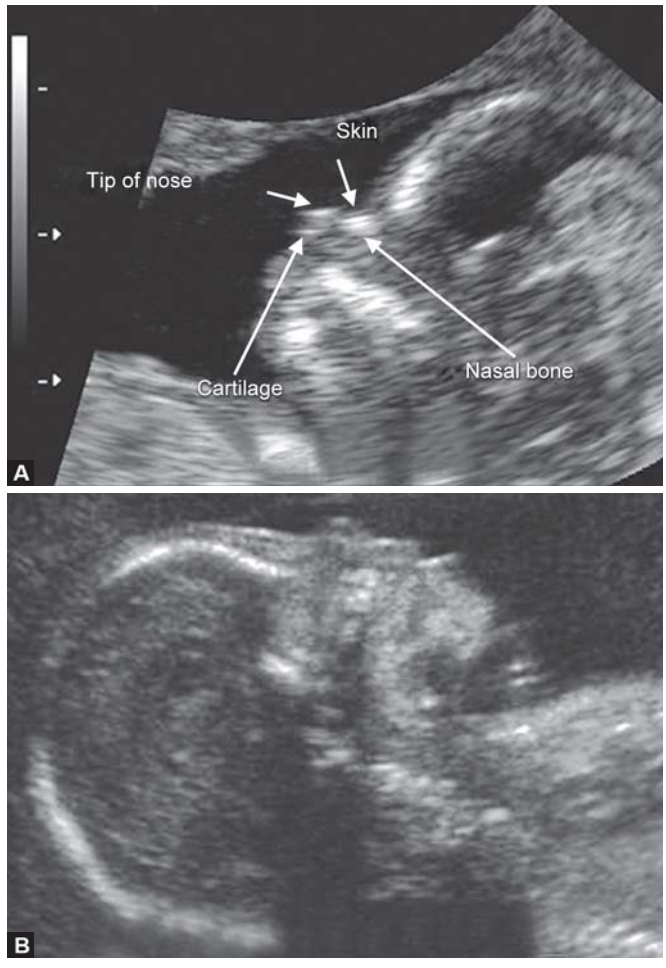
First Trimester

Nuchal Translucency

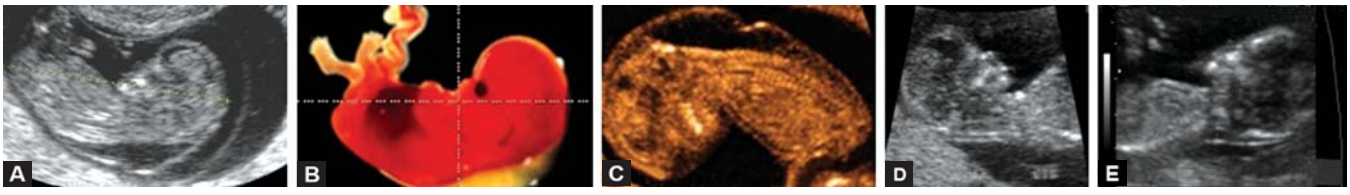
This prenatal test also called the NT or nuchal fold scan. It assesses the baby's risk of having Down's syndrome (DS) and some other chromosomal abnormalities as well as major congenital heart problems. The NT test uses ultrasound to measure the clear (translucent) space in the tissue at the back of developing baby's neck. Babies with abnormalities tend to accumulate more fluid at the back of their neck during the first trimester, causing this clear space to be larger than average. The NT scan is done between 11 and 13 weeks. It is offered along with blood test in what is known as first-trimester combined screening[5] (Figs 3A to E).

Pitfalls in measuring the nuchal translucency include the presence of an encephalocele, a nuchal cord, an amniotic band or a loose amnion that can be mistaken for the nuchal skin edge.[5] It is therefore imperative to magnify the image. It is sometimes helpful to wait for spontaneous fetal activity.

A cut off of 3 mm was used in many studies as a threshold for an abnormal nuchal translucency, although recently it has become apparent that normal nuchal translucency thickens with increasing gestational age.



Figs 5A and B: (A) Nasal bone, (B) absent nasal bone



Figs 3A to E: Measurement of nuchal translucency in the first trimester

Other First-Trimester Signs of Aneuploidy

Growth patterns of the crown-rump length have been evaluated to determine whether growth abnormalities could be utilized as signs of aneuploidy.[6] Growth rates are significantly reduced among fetuses with trisomies 13,18 and with triploidy (Fig. 4).

Other sonographic method for detecting aneuploid fetus include abnormal fetal heart rate at 10 to14 weeks, absent nasal bone, faccio maxillary angle, intracranial translucency, umbilical cord thickness and wide iliac angle.

By combining maternal age, nuchal translucency and heart rate, 83% fetuses with trisomy 21 were detected[7] (Figs 5A and B).

Second Trimester

Nuchal Fold

Excessive soft tissue in the back of the neck is known to be a feature of newborns with Down's syndrome. Callen et al[8] described the use of thickened nuchal fold as a sonographic marker for Down's syndrome in 1985. They showed that 2 out of 6 fetuses with Down's syndrome had a nuchal thickness of equal to or greater than 6 mm. This measurement is done using the transverse section of the fetal head angled posteriorly to include the cerebellum and the occipital bone. The measurement is made outside the occipital bone to the outer skin edge. This measurement has remained the most sensitive and specific single marker for the mid trimester detection of Down's syndrome.

Major Anomalies

Infants with trisomy 21 have a 50% incidence of heart defects, most commonly ventricular septal defects and common atrioventricular canal.

Other major anomalies include ventriculomegaly, cerebellar hypoplasia, duodenal atresia, hydrops, omphalocele and limb anomalies.[8]

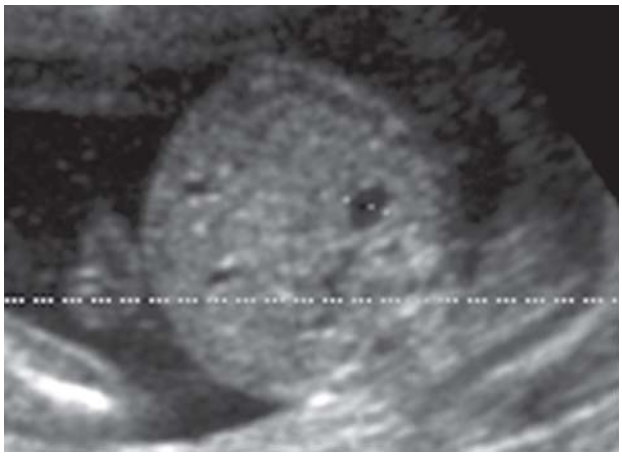


Fig. 6: Fetal pyelectasis

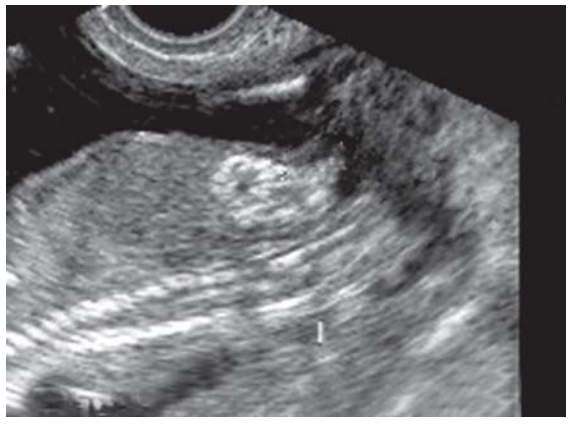


Fig. 7: Echogenic mass in the small bowel

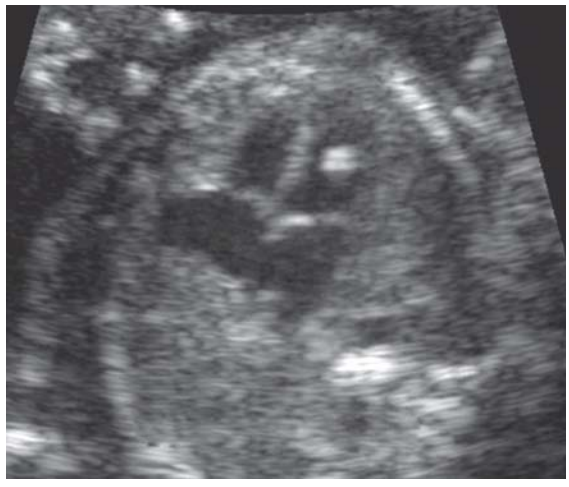


Fig. 8: Echogenic intracardiac focus

Femur length: Individuals with trisomy 21 are of short stature and have small femur and humerus.[8]

Absent nasal bone: Fetuses with absent nasal bone (Figs 5A and B) are associated with an increased risk of Down's syndrome.

Mild fetal pyelectasis (Fig. 6) was associated with an increased risk of Down's syndome. Crane and Gray defined pyelectasis as an anteroposterior diameter of the renal pelvis equal to or greater than 4 mm.[9]

Nyberg et al were the first to demonstrate that hyperechoic bowel (Fig. 7) is associated with Down's syndrome. There is also an increased risk of cystic fibrosis among fetuses with this sonographic finding, and parental allele testing for cystic fibrosis carrier status is recommended to evaluate this risk.[10]

The echogenic intracardiac focus (EIF) (Fig. 8) has been seen among normal fetuses for many years and was considered a normal variant till 1994. Brown, Roberts and Miller in a case report showed that mineralization of the papillary muscle was associated with trisomy 21 in one of three fetuses.[11]

Lehman et al were the first to report the association of EIF with trisomy 13.

Several investigators have suggested that the association between an EIF and chromosomal abnormalities is low enough that, in the absence of other findings in an otherwise low-risk patient, fetal karyotyping is unwarranted.

Minor Markers

Anomalies of the pelvic bones, particularly the iliac wings is associated with Down's syndrome. Children with Down's syndrome have a wider lateral span of the iliac wing than do normal children.

It is known among pediatricians and geneticists that infants with Down's syndrome have brachycephaly and frontal lobe shortening. An attempt is made to evaluate the use of this feature in detecting second-trimester fetuses with Down's syndrome.

The transverse cerebellar diameter was evaluated as a possible marker for Down's syndrome.

Other possible markers for the prenatal detection of Down's syndrome have been put forth, including abnormal fetal heart rate patterns, abnormally shortened ear length, flat facies, clinodactyly, sandal gap great toe and the simian crease of the palm.

Trisomy 13 (Pateau syndrome): The incidence of trisomy 13 is 1 in 5,000 births and it is the most severe of the three autosomal trisomies that can lead to live-born infants. The fetal anomalies most commonly seen with these fetuses include abnormalities of the brain, face, extremities and heart. In particular holoprosencephaly is a common finding that is invariably associated with severe midline facial defects, including hypotelorism, cyclopia, midline clefts, microophthalmia and absence of the nose. Other intracranial anomalies that can be seen with trisomy 13 include microcephaly, abnormal posterior fossa, agenesis of corpus callosum and ventriculomegaly. In addition, approximately 40% fetuses with trisomy 13 have echogenic intracardiac focus. More than 90% of these fetuses have cardiac defects. Abnormalities of the limbs include polydactyly and radial aplasia. Other major defects include neural tube defects and anterior wall abdominal defects. Thirty percent of affected fetuses have enlarged echogenic kidneys, similar to polycystic kidneys. Placental abnormalities such as partial mole also have been described with trisomy 13.[12,13]

Triploidy: Triploidy is a syndrome that results from three sets of chromosomes yielding 69 chromosomes. Most triploid conceptions end in spontaneous abortion. When the extra set of chromosome arises from the maternal side, the placenta is small and senescent, and there is severe early intrauterine growth restriction. When the extra set of chromosome arises from the paternal side, the placenta is large, full of echolucency and often associated with a partial mole.[14]

Usually the fetuses with triploidy have multiple congenital abnormalities of particularly every organ system. Characteristically, they also have first trimester onset intrauterine growth restriction. They also give rise to an unusual appearance of a very thin body with almost an normal sized head.

Fetal malformations associated with triploidy include early onset intrauterine growth retardation, facial anomalies such as hypertelorism, micrognathia and microphthalmia, brain anomalies such as ventriculomegaly, Dandy-Walker malformation, agenesis of corpus callosum, holoprosencephaly and meningomyelocele. Affected fetuses also have thickened nuchal lucency/cystic hygroma, heart defects, renal anomalies, clubbed feet, single umbilical artery and oligohydramnios. Most helpful of all in the specific diagnosis of triploidy is the syndactyly of the third and fourth digit of the hand, recognizable sonographically.

Turner's syndrome: Turner's syndrome is a chromosomal anomaly due to the loss of one sex chromosome, resulting in a 45X karyotype. The missing chromosome is usually paternal and the syndrome is not related with maternal age. In most cases conceptions with Turner's syndrome are spontaneously aborted, some fetuses may persist into the second trimester with severe lymphatic abnormalities. These fetuses have large cystic hygromas that are typically septated but clear.

Hydrops, pleural effusion, ascites and edema of all body parts is seen.

Mosaicism for Turner's syndrome is more likely to result in live births and these individuals are often not diagnosed until puberty. They suffer from sexual infantilism and short stature.

In general, half of fetuses with Turner's syndrome have cardiac anomalies and 19% have renal anomalies.[15]

Trisomy 18 (Edward's syndrome): Trisomy 18 have an incidence of 3 out of 10,000 live births and is associated with multiple severe structural abnormalities that mostly involve the heart, extremities, face and brain. Affected fetuses are often miscarried or die *in utero*.[16]

Structural abnormalities associated with trisomy 18 involve abnormal cisterna magna and Dandy-Walker syndrome. Affected fetuses can also have myelomeningoceles and ventriculomegaly. Limb abnormalities include preaxial upper limb reduction and clenched hands with overlapping index fingers. Second-trimester fetuses with trisomy 18 tend to have strawberry shaped skull,

cerebellar deviation beyond two standard deviation below the mean, rocker bottom feet, clubbed feet, single umbilical artery and renal anomalies such as hydronephrosis. Gastrointestinal tract anomalies include omphalocele and diaphragmatic hernia. The triad of polyhydramnios, growth restriction and abnormal hand posturing is highly predictive of trisomy 18 in third trimester.

Umbilical cord cysts have also been associated with an increased incidence of trisomy 18.

Choroid plexus cysts are present in approximately one-third of fetuses with trisomy 18.

USG EXTRA FETAL EVALUATION

Liquor Amnii

Quantity

- The measurement of the amniotic fluid can be done either by a single pocket measurement or the four quadrant approach amniotic fluid index (AFI). The AFI is easily reproducible and more accurate (Table 3).
- Fetal swallowing and urinary flow are the primary regulators of amniotic fluid. So abnormalities of these systems cause oligohydramnios (decreased liquor amnii) (Table 4) or polyhydramnios (increased liquor amnii), which can be indirect signs for detecting anomalies.

Amniotic Bands

- Whenever, it is seen that the amniotic bands in the uterine cavity are traversing the gestational sac, one should be careful of evaluating whether any fetal part is impinged upon by these bands causing limb reduction defects or any other external anomaly of the cranium, face, anterior abdominal wall or spine (Fig. 8).

Umbilical Cord

Number of Vessels

- There should be two arteries and one vein in the umbilical cord.
- Whenever a single umbilical artery is diagnosed, a careful search for anomalies should be done especially of chromosomal abnormalities, major cardiac defects, holoprosencephaly, anterior abdominal wall defects and skeletal deformities. With no other anomaly detected, continuation of pregnancy can be thought of.
- In a 2D ultrasound look for the rail-track appearance (Fig. 9) to assess for number of vessels.
- On color flow mapping it is easy to see for two arteries and one vein but whenever in doubt always look for the hypogastric arteries adjacent to the urinary bladder to evaluate whether there are two arteries or not.

Origin and Insertion

- Origin in respect to anomalies is important to differentiate between omphalocele and gastroschisis.

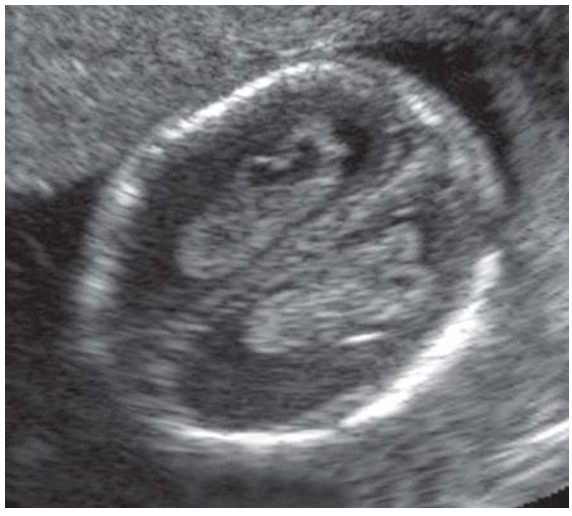


Fig. 9: Choroid plexus cyst

ULTRASONOGRAPHY FOR FETAL MORPHOLOGY EVALUATION

Choroid Plexus

This is evaluated for the following abnormalities (Fig. 9):

- Cysts
- Hydrocephalus
- Isolated ventricular dilatation
- Tumors.

Cerebellum

This is evaluated for following parameters:

- Cerebellar transverse diameter
- Superior and inferior cerebellar vermis
- Communication between fourth ventricle and cisterna magna.

Cisterna Magna

This is evaluated for following parameters:

- Posterior fossa cyst
- Depth.

Nuchal Skin

This is observed for following parameters:

- Thickness
- Septation
- Generalized hydrops.

Fetal Orbits and Face

The following parameters are observed:

- Hypo or hypertelorism
- Lens
- Lips
- Nostrils
- Ears.

Fetal Spine

This is observed for following parameters:
- Soft tissues
- Longitudinal
- Coronal
- Axial
- Ossification centers.

Fetal Thorax

In this following parameters are observed:
- Ribs
- Diaphragm
- Echotexture of lung
- Lung length
- Masses
- Cardiothoracic ratio.

Fetal Heart

The parameters observed for are as under:
- Situs
- Size
- Rate
- Rhythm
- Configuration
- Connections
- Tumors.

Fetal Abdomen

Gastrointestinal

- Stomach
- Duodenum
- Small bowel
- Large bowel
- Omentum
- Mesentery.

Pancreas

Spleen

Hepatobiliary

- Liver
- Gall bladder.

Genitourinary

- Kidneys
- Urinary bladder
- Genitalia.

Fetal Skeleton

The skeleton is observed for following parameters:
- Cranium
- Mandible
- Clavicle
- Spine
- Extremities.

Fetal Biometry

Following parameters are observed in fetal biometry:
- Biparietal diameter
- Occipitofrontal distance
- Head perimeter
- Abdominal perimeter
- Femoral length
- Humeral length
- Nuchal skin
- Cerebellar transverse diameter
- Cisterna magna depth
- Width of body of lateral ventricle
- Ocular diameter
- Interocular distance
- Binocular distance
- Foot length.

ULTRASOUND TECHNOLOGY AND ADVANCEMENT IN SCREENING

Is Routine Screening Justified?

Screening to be justified should fulfill many criteria; the procedure should be safe, reliable, reproducible, easily available and cost-effective. For a population which is at risk an ultrasound scan is justified but in developing countries like India where still almost half of our pregnant women have no access to a proper antenatal care, a routine ultrasound currently may not be practically feasible test for screening even though its utility and efficacy are beyond doubt.[2]

Is Incidence of Fetal Malformation High Enough to Merit Screening?

According to Heinonen (1977) approximately 150,000 children are born with malformations annually in USA where almost 100% pregnant women have antenatal care and institutional deliveries.[1] In developing countries the incidence is higher due to inability for detection, screening and more exposure to teratogens.

Is Outcome of Undetected Congenital Malformations Detrimental Enough to Warrant a Routine Screening?

Out of an incidence of around 6% congenital malformations almost half (2.5%) are lethal, life-threatening and have a major cosmetic defect.[17]

Major congenital defect mostly manifest in fetal intrauterine life (ultrasound detectable), sometimes in fetal life (ultrasound suspicion) and occasionally in childhood (ultrasound undetectable). Some experts question the need of routine prenatal ultrasound screening for this reason.[18]

Fetal medicine is still not advanced to treat potential life-threatening conditions like open neural tube defects and cardiac defects where death is the expected outcome after delivery. Occasionally, these defective babies survive and are severely handicapped. Diagnosis of such conditions during pregnancy can give the couple an option of termination. Current technology enables detection of over 60% fetal malformations.[19,20]

Can a Prenatal Diagnosis of Anomalies Ease Emotional Pain?

An antenatal diagnosis of congenital anomaly whether lethal, life-threatening or even less serious can still help couples and doctors to prepare themselves for the challenge to come.[21] There is a definite benefit of screening for both patients and physicians. Usually a normal ultrasound scan is good news for the expecting parents because of the relative low prevalence of anomalies in general population and also relative low incidence of false-positive results by ultrasound.[22]

If the ultrasound screening is positive for anomaly then the counseling and discussion of all options can be done and choice left open to the expecting parents.[23]

Is Prenatal Ultrasound Screening Cost Effective?

It is difficult to assess cost-effectiveness of screening and there are only a few studies on this. Certain costs like purchase, maintenance of equipments, salary of well trained technicians and doctors can be assessed and is expensive.[24] Emotional costs of family disorganization and suffering cannot be calculated. Because of the many options for handling anomalies available from termination to major plastic surgery it is again difficult to assess whether it is cost-effective to detect an anomaly. Helsinki ultrasound trial (1996)[25] has shown that second-trimester screening for anomalies by ultrasound is cost-effective.

How does Prenatal Anomaly Scan for Screening Influence Infant Health?

Ultrasound screening is not primary prevention because it cannot prevent the anomaly. It can only detect the problem and if the anomaly is lethal, it gives the expecting parents an option to terminate pregnancy— secondary prevention. Also in many cases, severe but curable defects (cardiac) can be managed by treating newborn without delay, if the pediatric surgery unit is prepared. Expertly performed prenatal ultrasound screening and autopsy reports correlate and provide accurate information.[26]

What are the Options after Diagnosis of Congenital Malformations?

The options for managing congenital malformation pregnancy have to be discussed with the expecting parents and the final choice lies with the parents. A team of specialists should provide all information and counseling. This team should consist of obstetrician, sonologist, geneticist, neonatologist, pediatric surgeon and a psychologist.

Options selected depend on severity of the anomaly and can be as mentioned below:

- Termination of pregnancy
- Intrauterine treatment
- Maternal transport to tertiary care center
- Premature delivery
- Immediate specialized neonatal care
- Additional diagnostic tests
- Extensive monitoring.

Alternatives or Adjuncts to Ultrasound?

There are various blood tests like maternal serum alpha fetoprotein (MSAFP), triple test, quadruple tests and many interventional procedures like chorionic villus sampling (CVS) and amniocentesis, cordocentesis and fetal biopsy which can help in direct karyotyping and chromosomal analysis of the fetus. These procedures and techniques are expensive, not easily available and also carry a procedure related risk of miscarriage.

Noninvasive magnetic resonance imaging (MRI) is definitely not a cost-effective method for screening.

Ultrasound advances have made this technology for screening an ideal test because it is:

- Relatively low cost
- Ease to perform
- Real-time display
- Acceptable to all
- Widely available
- Accurate
- Safe
- Reproducible
- Available as office investigation
- Can now be applied from late first trimester also.[27]

How Long does It take?

A primary screening ultrasound examination is a systemic analysis of fetal growth and fetal morphology system and will take 10 to 20 minutes to scan. The screening will stop if everything appears normal in all significant organs and structures.

Depending on image quality, maternal obesity, gestational age, type of anomaly, color Doppler or 3D scan still the total scan duration rarely exceeds 30 minutes. For subtle defects or solitary markers or inexperienced sonologists a second opinion scan might be required by an expert which will take another 30 minutes.

What does a Prenatal Ultrasound Scan show?

Depending on the gestational age the defects can be seen and identified, e.g. nuchal translucency in first trimester, duodenal atresia, gastrointestinal defects, neural tube defects and some cardiac defects in second trimester.[28]

When we do not see the expected image of the fetus we suspect a defect. Sometimes, we have to look for soft markers and signs of chromosomal anomalies, e.g. banana sign, lemon sign, etc.

Ultrasound can also pick up functional abnormalities and abnormal fetal biophysical profile and abnormal fetal behaviors.

Abnormal Fetal Activity

- Rapid uncoordinated fetal movements
- Fetal arrhythmia
- Fetal vomiting
- Fetal GI stenosis.

When should a Screening Prenatal Scan be done?

Nicolaides has suggested a 11 to 14 weeks scan for screening for chromosomal anomalies, trisomy 21 by looking at the nuchal translucency and nasal bone ossification.[28] Other workers have suggested addition of biochemical markers.[29] The detection rate for trisomies varies from 80 to 89% with a false-positive rate of 5% by using multiple markers study in first trimester scan (11-14 weeks).

A second-trimester anomaly scan should be done between 18 and 22 weeks and a detailed fetal echocardiography and color Doppler uterine artery and ductus venosus should be done.

Third-trimester screening should not be delayed more than 32 weeks gestation and is mainly done for growth and color Doppler studies for hypoxia detection. Late anomaly screening for GI and urinary tract anomaly is usually done at 32 weeks.

Ideal time for ultrasound screening for each and every gravida should be a monthly ultrasound but as this is not practical and feasible, at least each pregnancy should have two scans one 11 to 14 weeks scan and one second-trimester scan.[30,31]

Ultrasound: How Sensitive it is for Malformation Detection?

In a major study on 500,000 cases about 11,000 (2.2%) were found to be malformed fetus with a range of sensitivity from 14 to 80% (mean 45.5%).

In another study on 170,000 pregnant women, 4,000 malformed fetus were detected with a sensitivity of 61%.[31]

What Counts as Success in Genetic Counseling?

Whenever, anomaly is detected for some people, the abortion and termination of pregnancy is a matter of course response and no ethical dilemma arises. However, among certain religions groups objections to termination pose an ethical dilemma.

Advances in Fetal Surgery

This option is still a research tool and there is an ethical aspect that many of these fetal surgical procedures are still experimental and of uncertain value and to give or not to give this option to couples carrying a malformed pregnancy is a dilemma.

Are 3D and 4D Scans for Screening Useful or Gimmicks?

There is now an increasing availability of 3D ultrasound. The benefits of 3D and 4D ultrasound techniques are now a matter of debate. The 3D and 4D screening help in maternal fetal bondage and also help in recognition and better confirmation of certain anomalies like cleft lips, polydactyly, micrognathia, malformed ears, club foot, vertebral malformations and other exterior surface anomalies. Development of transvaginal scanning (TVS) 3D probes have further enhanced its value in early diagnosis of malformations.

Reassurance Scans: How Reassuring?

It was proposed by Prof Stuart Campbell that a 3D routine scan is to reassure the parents and to rule out anomalies, but also criticized these as entertainment scans used and marketed for unprecedented profit particularly after 4D ultrasound.

SCREENING METHODS AND TESTS

Maternal and Fetal Screening Tests

Noninvasive and Invasive

Introduction: There are many screening tests conducted on the mother or directly on the fetus/pregnancy products, which may be invasive or noninvasive. These tests vary in their effectiveness, i.e. the detection rate or the sensitivity and specificity of the test. The best way to assess which is the best screening test would be to fix the false-positive rate and compare the detection rate of various tests.

Noninvasive tests: These tests are performed on maternal blood (serum screening) and by an ultrasound scan. Detection of any abnormal level of hormones in maternal blood or abnormal measurement of fetal parameters increases the relative risk for the fetus to have a chromosomal defect. The 'detection rate' of any test depends upon following the highest standards of practice in both, scanning and as well as in the laboratories. Hence, the 'efficacy' of the test largely depends upon the laboratory performing the blood tests and the operator performing the fetal scan.

Invasive tests: These tests are largely done to confirm a suspected diagnosis of genetic disease and in a few cases for fetal infections. Test samples are taken from the placenta (chorionic villous sampling, CVS), amniotic fluid (amniocentesis) or fetal blood (cordocentesis). These tests involve inserting a needle into the pregnancy sac to retrieve the sample. This requires a high level of expertise as it carries a risk of miscarriage of the entire pregnancy, which largely depends upon the operator skills.

Screening Tests *vs* Diagnostic Tests

It is important to know and understand the difference between screening test and a diagnostic test.

- Screening tests help to evaluate the risk for certain birth defects, but they cannot diagnose a birth defect. Screening tests are noninvasive and pose no risk to mother or baby.

Diagnostic tests, such as aminocentesis, cordocentesis and chorionic villus sampling (CVS), are highly accurate at diagnosing or ruling out birth defect. However, these tests are invasive and may pose a very small risk of miscarriage.

Application of Various Maternal and Fetal Screening Tests to Pregnant Women

Screening test such as an ultrasound can be performed at any stage of the pregnancy. However, most screening tests, particularly blood tests are not performed after 22 weeks; firstly because the efficacy of the tests declines steeply after that period and secondly in most countries late termination of pregnancy is restricted. The best detection rate for the tests can be obtained when performed in the particular window period of gestations. The following tests are the most widely performed.

CONCLUSION

With improved technology, in particular the development of high frequency transvaginal ultrasound probes and its increased acceptance with the patients, it has become possible to examine the detailed fetal anatomy even in the late first trimester and early second trimester.

The new panorama of normal embryological development is possible with 3D ultrasound and with computers handling the pre- and postprocessing of the ultrasound images gives us a future insight into the future of technology being applied to achieve a better understanding of early human developments and its defects.

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