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The essential principles of evaluation and management pathways in prenatally detected fetal anomalies

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ABSTRACT

The evaluation and management of prenatally detected fetal anomalies constitute a challenging problem. The optimal outcome for the fetus and the mother depends on the accurate diagnosis, appropriate evaluation, and informed, scientific decision-making regarding prenatal, perinatal and postnatal management. The article aims to analyze the complexities in evaluation and management of prenatally detected fetal anomalies and highlight the challenges in therapy. The current literature was reviewed to understand the issues with regard to treatment of prenatally detected fetal anomalies in the light of clinical experience and practical considerations with regard to management of these variegated group of disorders. The observations were summarized to present a broad outline of the common and challenging set of conditions. The recent advances in prenatal diagnosis and widespread adoption of fetal imaging have increased the detection of fetal anomalies. The availability of maternal screening investigations and newer methods of genetic testing have further added to the diagnostic spectrum. The abnormalities can range from minor alterations of uncertain significance to major defects with grave prognosis. The establishment of definite clinical practice guidelines for screening, diagnosis and therapy are mandatory to bring clarity to management. A deep understanding of the natural history of these disorders, their evolution during gestation and the effect on the mother, fetus and the pregnancy are critical to the optimal management of these conditions.

Keywords: Fetal diagnosis, prenatal diagnosis, maternal screening, fetal genetic testing, fetal diagnostic testing, fetal therapy, perinatal management, termination of pregnancy for fetal anomaly

INTRODUCTION

The evaluation and management of prenatally detected fetal anomalies constitute a challenging problem. The optimal outcome for the fetus and the mother depends on the accurate diagnosis, appropriate evaluation, and informed, scientific decision-making regarding prenatal, perinatal and postnatal management. The recent advances in prenatal diagnosis and widespread adoption of fetal imaging have increased the detection of fetal anomalies.

The availability of maternal screening investigations and newer methods of genetic testing have further added to the diagnostic spectrum. The abnormalities can range from minor alterations of uncertain significance to major defects with grave prognosis. The inputs of multiple specialists are required to ascertain the severity and prognosis of an anomaly, and the need for fetal diagnostic and therapeutic modalities. The decision regarding termination of pregnancy for fetal anomaly and need for advanced perinatal therapy or changes in obstetric management are also vital in this regard.

AIM

The article is designed as a narrative review on the broad topic of prenatally detected fetal anomalies, with the aim of summarizing and synthesizing clinically relevant information from literature. The aim is to review the common prenatally detected fetal anomalies with regard to their diagnosis, evaluation and management principles. The article aims to analyze the complexities in evaluation and management of prenatally detected fetal anomalies and highlight the challenges in therapy, while formulating and elaborating the scientific approach to treatment.

MAIN TEXT

The evaluation and management of prenatally detected fetal anomalies constitute a challenging problem. The optimal outcome for the fetus and the mother depends on the accurate diagnosis, appropriate evaluation, and informed, scientific decision-making regarding prenatal, perinatal and postnatal management. The effect of the fetal anomaly on the physiological interaction between the fetus and mother

is complex and variable, with a significant bearing on the outcome of pregnancy. These factors should also be accounted for in the management of such cases.[1-3]

Prenatally detected fetal anomalies constitute a challenging problem because of the following reasons[4-6]:

- The wide spectrum of the disorders (hydronephrosis, heart disorders, hydrocephalus etc.)
- Differentiation of transient physiological changes from structural anomalies (renal pelvic dilatation, ventricular dilatation, bowel dilatation etc.)
- Variable significance and severity of the defect that require detailed evaluation like grading/ detailed organ measurements (renal anomalies, lung anomalies, cardiac anomalies)
- Possibility of evolution of the problem during the gestation (hydronephrosis, lung lesions, teratoma etc.)
- Occurrence as a part of a syndrome/ genetic disorder/ association (Trisomy 21; Potter's syndrome, VACTERL association of vertebral, anorectal, cardiac, tracheoesophageal, renal and limb anomalies etc.) where multiple anomalies can co-exist
- Findings like oligihydramnios, polyhydramnios, fetal hydrops etc. could be secondary manifestations of an underlying anomaly (fetal obstructive uropathy, fetal intestinal obstruction and fetal teratoma/ major lung lesion, respectively)
- Decision on the need for further evaluation/fetal imaging (fetal MRI)/invasive fetal diagnosis (amniocentesis/ chorionic villus sampling-CVS)
- Decision on the need for antenatal intervention/ex-utero intrapartum treatment (EXIT) procedure
- Decision on the need for termination of pregnancy, in cases incompatible with life
- Determination of the prognosis and parental counselling

METHODS

This narrative review analyses current literature with emphasis on relevant guidelines and recommendations, with reference to the evaluation and management of prenatally detected fetal anomalies. The literature was reviewed, in the light of the clinical experience and observations made with regard to the management of these cases. The databases searched for literature this narrative review included EMBASE, PubMed, Cochrane, and Web of Science. The studies analysed were English-language, peer-reviewed journal articles, particularly consensus statements and commonly followed guidelines.[1-5] Institutional review board, as well as the ethical committee approval were not required. An effort has been made to break down the problem into its various aspects including clinical challenges, investigative modalities, therapeutic options and their appropriate use. The generally accepted principles in the treatment of usually encountered anomalies were reviewed thoroughly to simplify and tabulate management principles. An overview of the various clinical scenarios and a broad outline of the management strategies are presented here.

RESULTS

Prenatal Genetic Testing

The availability and widespread application of maternal screening and prenatal genetic testing modalities have revolutionized the diagnosis of genetic, metabolic and syndromic disorders. But the clinical application of these new techniques has presented challenges regarding patient selection, communication with patents, factual interpretation of results, analysis of benefit as well as moral and ethical concerns. The methods employed for prenatal genetic testing, maternal screening and fetal imaging are to be performed, interpreted and communicated with diligence and caution.[2-6] A brief summary of the applications of the modalities of fetal genetic testing, maternal screening, fetal diagnostic tests and fetal imaging techniques is presented here (**Table 1**).

Prenatal Sonological Diagnosis

Ultrasound scan (USG) in the first trimester is helpful in accurate dating, diagnosis of twin chorionicity, and early diagnosis of major structural anomalies like Anencephaly. Measurement of nuchal translucency (NT) on USG is a marker for fetal genetic and chromosomal disorders, neural tube defects (NTD), and cardiac anomalies.[1,2,4] Second trimester USG is helpful to assess major defects of the heart, brain and spine, kidneys, abdomen, craniofacial region, limbs etc. It is to be done between 18 weeks and 22 weeks of pregnancy. Detailed fetal imaging using 3D/4D USG, fetal echocardiogram, fetal MRI and serial USG are indicated in complex anomalies. Fetal structural defects can occur with or without fetal aneuploidy. Therefore, all patients should be offered a second-trimester USG between 18 and 22 weeks of gestation (+/- second-trimester maternal serum alfa fetoprotein-AFP).[3,5,6]

"Soft Markers" on Antenatal Sonology-What are They, and When Should They be Considered Significant?

With regard to the prenatally detected structural anomalies in the fetus on USG, it is imperative to recognize some of the abnormalities, that are generally referred to as sonological "soft markers". These findings should be reassessed diligently and interpreted carefully as they can be markers or features of very significant pathology, in spite of some of them being benign findings on many occasions. These findings generally mandate a detailed anatomical assessment and systemic survey to confirm findings and evaluate other organs.[7-9]

Many of these findings require systematic follow up based on the initial assessment of grade/ severity, possibility of associated pathologies and likelihood of complications. Some of these mandates additional testing like TORCH (Toxoplasma, Rubella, Cytomegalovirus, Herpes simplex) screening and fetal imaging like fetal ECHO/fetal MRI, while others mandate invasive fetal diagnostic modalities. Many of these could serve as markers of genetic disorders like Trisomy 21 or other causes of aneuploidy. They can also help to predict the occurrence of prenatal/postnatal complications like Intrauterine growth retardation (IUGR), Uteroplacental insufficiency (UPI), Oligohydramnios, preterm birth, preeclampsia, need for caesarean and still birth.[10-12]

Table 1. Fetal diagnostic modalities and their applications

Fetal screening and diagnostic modalities	Details	Timing	Advantages	Comments
Prenatal genetic screening tests				
Carrier screening	Couples undergoing IVF with increased risk of genetic/ chromosomal disorder; Blood or buccal smear.	On those planning pregnancy/ during pregnancy.	Can detect gene for inherited disorders like spinal muscular atrophy, cystic fibrosis, hemoglobinopathies, fragile X syndrome, and Tay-Sachs disease.	Can only assess the chance of aneuploidy/ other disorders.
Preimplantation genetic diagnosis		Before pregnancy. Only embryos that do not test positive for the disorders are transferred.		
Cell-free fetal DNA	Isolation of fetal cells in the maternal circulation by advanced sorting techniques permit genetic testing from a maternal blood sample. Accurate test for the common fetal aneuploidies.	Can be done from 10 weeks of pregnancy and beyond.	Can be used for the screening of Trisomy 21, 18, 13 and sex-chromosome aneuploidy. A positive cell-free DNA test result should be followed by a diagnostic test with amniocentesis or CVS.	It is not recommended for the screening of microdeletion. There is a low positive predictive value of this test in low-risk group and the possibility of 'no call' from inadequate sample.
Maternal screening				
First trimester screening (maternal serum biomarkers and US screening)	Pregnancy-associated plasma protein A (PAPP-A) and free beta-human chorionic gonadotropin (HCG); Nuchal Translucency (NT) on US.	At 10-13 weeks of pregnancy; the testing for NT should be done at 11-13 weeks, not earlier or later.	USG aids in precise dating, detection of twin chorionicity, and early detection of major structural abnormalities. A high NT measurement (> 3.5 mm) is a marker for fetal chromosomal disorders, structural anomalies (cardiac) and genetic disorders such as RASopathies.	The combined first trimester screening test can identify a pregnancy with increased chance of Down syndrome (trisomy 21) and Edward syndrome (trisomy 18).
Fetal diagnostic test: Chorionic Villus Sampling (CVS)	Transvaginal/trans abdominal; USG guided procedure. Sample taken from the placenta for the diagnosis of genetic and chromosomal disorders.	Between 10 to 13 weeks of pregnancy.	Detect conditions such as Down syndrome, Edwards' syndrome, or Patau's syndrome	Complications are pregnancy loss, bleeding, infection, rupture of membranes, and indeterminate results. Limb reduction defects and oromandibular hypogenesis are reported with early CVS.
Second trimester screening	The quad screen test is a maternal blood screening test for four markers: alfa fetoprotein (AFP), hCG, estriol, and inhibin-A.	Between the 16th-18th week of pregnancy	It screens for Down syndrome, Edwards syndrome (trisomy 18), and NTDs; The penta screen also measures hyperglycosylated hCG; MSAFP can be performed between 16 and 18 weeks for NTD screening.	An elevated AFP level in maternal serum/ amniotic fluid is seen in NTD, Abdominal wall defects and tumors like Sacrococcygeal Teratoma. Other markers like Estriol and HCG are useful in Aneuploidy screening
Second trimester USG	Assess major defects in the CVS, CNS, kidneys, abdomen, craniofacial region, Limbs etc.	Between 18 weeks and 22 weeks of pregnancy.	The second-trimester uterine arteries' pulsatility index (PI) can detect the presence of issues with the placenta that could lead to stillbirth.	Detailed USG for structural defects and feta ECHO are to be done in the second trimester for follow-up.
Fetal diagnostic test: amniocentesis	For diagnostic evaluation in the form of chromosomal, biochemical, histopathological, and microbial assessments.	Second trimester; can be performed from 15 weeks of gestation.	Common indications: advanced maternal age, known carrier state and history of genetic disorder in previous child.	When performed as a therapeutic procedure, it is done to reduce the volume of amniotic fluid in patients with polyhydramnios (Amniodrainage). Complications are fetal loss, bleeding, infection, rupture of membranes, amniotic fluid leak and indeterminate results.
Fetal blood sampling or cordocentesis	For haematological, immunological, and biochemical analysis. Used in diagnosis of fetal anemia, genetic disorders, fetal infections etc.	Considered safer to perform at 20 to 28 weeks of gestation	Can be used with therapeutic intent in fetal anemia, for drug administration and Rh disease.	The benefits include conversion to fetal transfusion.
Fetal urine sampling	Used to assess status of renal function in bilateral renal disease associated with oligohydramnios. Assessment of urine electrolytes, beta 2 microglobulin etc.	Second trimester.	Commonly indicated in complicated posterior urethral valves.	Abnormal urine biochemistry indicates poor prognosis for renal outcome and less benefit of fetal therapy.
Fetal imaging modalities				
3D/4D USG	Detailed assessment of fetal anomalies. Serial USG can help to define the natural history and progression of fetal disease like hydronephrosis, ventriculomegaly, lung anomalies etc.	After 10 weeks.	Can facilitate the performance of USG-guided intervention procedures; USG measurement of organ volume/ volume ratio/ size measurements that imply severity and prognostic significance (lung-to-head ratio, left ventricular wall thickness etc.)	Real-time USG gives information about fetal well-being like fetal movement and fetal vital functions like fetal heart rate variability and fetal breathing movements.
Fetal MRI	Defects detected on US that require detailed analysis can undergo ultrafast fetal MRI.MRI can image the fetus in any plane, providing a large field of view of the fetus and placenta with excellent soft tissue resolution of the brain, airway, lungs, and abdomen.	After 20 weeks.	Enable detailed study of fetal CNS malformations, lung malformations, cystic hygroma, teratoma etc.	MRI is not limited by fetal lie, oligohydramnios, overlying bone, or obesity. Advanced techniques provide volumetric data, spectroscopy, and functional images.

The most commonly observed soft markers on prenatal sonology and their details are listed below:[13-18]

1. **Fetal pyelectasis/ renal pelvic dilatation:**

- Definition**:** Renal pelvic anteroposterior diameter in transverse plane (APD) of 4 mm or more in second trimester and/or 7 mm or more in the third trimester.
- Pelvic APD of 10 mm or more is the criteria for definition of hydronephrosis.
- Fetal renal pelvic dilatation can be a transient physiological finding, but it can also be the sign of a major urinary tract disorder/marker of aneuploidy.
- A follow-up USG at 32 weeks of gestation should be performed. If the APD measures >7 mm at 30-week USG, postnatal follow-up is suggested.

- A significant proportion of prenatally detected pelvic dilatation, especially in the second trimester, will resolve either prenatally or during postnatal life.
- A significant progression of dilatation during prenatal follow up is indicative of a pathological cause.

2. **Single umbilical artery (SUA):**

- Definition: The absence of one of the umbilical arteries, which occurs in 0.5 to 5% of pregnancies. This is an isolated finding in 60–80% of cases.
- Isolated SUA is associated with small for gestational age (SGA) babies, higher rate of placenta or umbilical cord abnormalities and a higher rate of caesarean due fetal heart rate abnormalities.
- It is associated with a higher risk of SGA, preterm delivery, pregnancy-induced hypertension, requirement of intensive care and perinatal mortality.
- The finding should prompt targeted anatomical survey and growth assessment.

3. **Thickened nuchal fold (NF):**

- Definition: The thickening of the skin and the subcutaneous tissues on the posterior aspect of the fetal neck measuring 6 mm or greater before 20+6 weeks' gestation.
- In fetuses with normal USG screening for aneuploidy in the first trimester, thickened nuchal fold in second trimester is the most important soft marker in the detection of Down syndrome.
- Karyotyping should hence be offered when thickened nuchal fold is detected.
- Even with normal karyotyping, targeted USG and fetal ECHO are indicated when a thickened nuchal fold is identified, due to the association with structural defects, like congenital heart defects.

4. **Intra-cardiac echogenic focus (IEF):**

- Definition; A small echogenic spot inside the heart, most commonly seen in the left ventricle, having brightness equivalent to that of the bone.
- In about 90% of cases, it resolves by the third trimester.
- Isolated IEF are associated with an increased risk of Down syndrome.
- The presence of an IEF is not an indication for invasive procedures in low-risk populations for aneuploidy. In the presence of negative first trimester screening (FTS)/non-invasive prenatal testing (NIPT), IEF can be described as a normal variant.

5. **Isolated ventriculomegaly (VM):**

- Fetal cerebral ventricular dilatation: It is a dilatation of the lateral ventricle atrium to a width of 10 mm or more.
- Mild VM: 10–12 mm; Moderate VM: 12–15 mm; Severe VM: >15 mm. Isolated mild and moderate VM is more likely to regress or become stable, unlike severe VM.
- It can be a normal variant or be associated with aneuploidy, genetic syndromes, primary brain abnormalities, congenital infection and intracranial haemorrhage.
- MRI can be used for detailed evaluation of cases of VM and TORCH screening is also indicated.
- The prognosis of VM depends on the severity, the presence of other abnormalities and also an asymmetric pattern of VM.

6. **Choroid plexus cysts (CPC):**

- Definition**:** CPC is a small fluid-filled space ≥5 mm within the choroid plexus, which is sonologically discrete, usually seen at 16 to 24 weeks of gestation.
- Isolated CPC is usually an isolated finding in an otherwise normal low-risk pregnancy and not considered as a structural or functional abnormality.
- CPC typically regresses by 23 weeks regardless of the underlying karyotype.
- Amniocentesis is indicated only if other anomalies, like those of Trisomy 18 are present.

7. **Echogenic bowel:**

- Definition: Fetal bowel of similar or greater echogenicity than the surrounding bone or fetal liver. Two-third are detected during the first and the second trimesters.
- Echogenic bowel resolves spontaneously in ~20% of cases.
- Echogenic bowel can be a normal variant, and may also be associated with congenital viral infections like cytomegalovirus, aneuploidy (Down syndrome), intra-amniotic bleeding, severe UPI, meconium peritonitis, cystic fibrosis, anemia, and fetal growth restriction.
- It mandates detailed evaluation including evaluation for cystic fibrosis, TORCH screening and USG at 32 weeks to assess bowel obstruction.
- The likelihood of postnatal surgical intervention for intestinal anomalies is significantly increased if the finding is seen during the third trimester.

8. **Shortened humerus and femur:**

- Definition: Bone length below the 5th percentile for gestational age.
- Shortening of the fetal long bones is seen associated with aneuploidy, skeletal dysplasia, fetal structural anomalies, preeclampsia, stillbirth and IUGR.
- Shortened humerus and femur length may be an early sign of placental dysfunction. It mandates prenatal surveillance with serial USG for growth assessment and blood pressure monitoring.
- USG at 32 weeks is done to rule out skeletal dysplasia and to assess growth.

9. **Absent or hypoplastic nasal bone:**

- Definition: A nasal bone that is not visible in first trimester/ nasal bone with a length of <2.5 mm in the second trimester.
- It is described as one of the phenotypic features of Down syndrome, but also has racial differences.
- The finding mandates a detailed evaluation of fetal anatomy. Microarray studies should be done in addition to fetal karyotype when the finding occurs with other anomalies on USG.
- The prognosis is good if there are no other anomalies and karyotype is normal.

Soft marker screening is a tool in screening for non-aneuploidy-related conditions such as, structural anomalies and adverse pregnancy outcomes that requires follow-up during marker in the setting of a negative non-invasive prenatal testing (NIPT) result.[16-18]

DISCUSSION

The Common Management Pathways of Prenatally Detected Fetal Abnormalities

The broad, general pathways in management only apply for the specific abnormality, in isolation. The decision-making in complicated, multisystemic and genetic disorders are to be taken in consideration of the major, life-threatening anomaly as the key parameter, on an individualized basis.[19-24]

1. **Fetal abnormalities that usually need prenatal follow up and postnatal therapy:**

- Renal anomalies like hydronephrosis (unilateral/bilateral-without complications like oligohydramnios and Potter's syndrome), unilateral multicystic dysplastic kidney/ unilateral renal agenesis
- Isolated congenital diaphragmatic hernia and oesophageal atresia.
- Gastrointestinal anomalies like intestinal atresias, anorectal malformation, meconium ileus, enteric cysts and duplications, small and intact exomphalos/gastroschisis
- Tumors/cystic lesions like small sacrococcygeal teratoma, small lymphovascular malformations/cystic hygroma, benign cysts such as adnexal (ovarian) cysts and choledochal cyst
- Uncomplicated craniofacial/limb/chest wall abnormalities

2. **Fetal abnormalities that may require induction of preterm delivery:**

- Ruptured exomphalos/gastroschisis
- Progressive hydrops fetalis
- Progressive hydrocephalus
- Progressive hydrothorax
- Arrhythmias like supraventricular tachycardia
- Severe IUGR

3. **Fetal abnormalities that need planned caesarian section:**

- Large sacrococcygeal teratoma
- Severe hydrocephalus
- Large myelomeningocele
- Conjoined twins
- Large omphalocele/gastroschisis
- Large cervical lympho-vascular malformation/cystic hygroma
- Malformations that require preterm delivery in the presence of inadequate labor/fetal distress

4. **Fetal abnormalities that may require an ex-utero intrapartum treatment (EXIT) procedure:**

- Conditions that require emergency upper airway access like congenital high airway obstruction syndrome (CHAOS), large cervical tumor like teratoma and mass lesions causing obstruction to the oral cavity/trachea (lymphatic or vascular malformations)
- Conditions requiring immediate Extracorporeal membrane oxygenation (ECMO) cannulation
- Thoracic/mediastinal mass lesion that prevents lung expansion

5. **Fetal abnormalities that are usually managed by termination of pregnancy for fetal anomaly (TOPFA):**

- Severe neurological defects like anencephaly
- Severe chromosomal anomalies like Trisomy 13
- Bilateral renal agenesis and infantile polycystic kidney disease
- Severe metabolic disorders like Tay-Sach's disease
- Severe and lethal bone dysplasias like recessive osteogenesis imperfecta

The essential principles regarding the evaluation and management of some of the common prenatally detected fetal anomalies is summarized here (**Table 2**).

Major congenital malformations are abnormalities that are severe enough to reduce life expectancy or compromise normal function. They cause neonatal death in more than 20% of cases. They are considered to be lethal if they cause stillbirth or infant death in 50% of cases. If newborn infant with major malformation cannot survive without medical intervention, then they are considered severe.[22-27]

The Antenatal Diagnosis of A Fetal Anomaly can Lead to One of the Following Outcomes

- Continuation of pregnancy, without the need for any further evaluation other than the routine follow up scans (applies when the anomaly detected is deemed to be physiological/ mild with no perceived risk to the fetus or mother/no risk of worsening or complications)
- Continuation of pregnancy, with targeted serial follow up scans/detailed USG assessment or grading (to assess the evolution of the problem/ involvement of other organ systems/complications like organ damage)*
- Continuation of pregnancy with the need for further imaging like CT/MRI or fetal sampling (when major congenital disorders are suspected, with the findings of evaluation having a significant bearing on the outcome)*
- Continuation of pregnancy with the need for maternal/fetal intervention (in occasional cases of treatable major disorders where the intervention is expected to reduce morbidity and mortality of the fetus)*
- Continuation of pregnancy with changes in the timing and mode of delivery to improve the outcome of the fetus (option of early induction of delivery/caesarian section) *
- Termination of pregnancy for fetal anomaly (TOPFA) after counselling when a serious disorder that is incompatible with life is diagnosed sufficiently early in gestation

*Delivery should be conducted only at an appropriate center, with maternal transport if required

The apt use of the techniques of maternal screening, genetic testing, first trimester USG screening and diagnostic fetal testing would help in timely diagnosis and early detection of major fetal disorders and major structural anomalies, thus offering an opportunity for early termination of pregnancy. Similarly, the use of advanced fetal imaging and fetal sampling studies can help to assess the severity of the disorder in doubtful situations, and in also assist their follow up. Though fetal therapy is not yet widely practiced, the

Table 2. Common fetal anomalies and the general principles of evaluation and management in specific situations

Fetal anomaly	Associated issues	Prognostic factors	Complications (Prenatal and Postnatal)	Fetal diagnosis/ fetal therapy (In select cases)	Perinatal management: general guidelines
Fetal cardiac defects	20-40% incidence of extracardiac anomalies; high incidence of chromosomal anomalies; occur in association with syndromes, CDH, OA, genetic disorders etc.	Single/multiple defects; associated conditions; type of lesion (duct dependent)	Fetal Arrhythmias; IUGR; Cardiac failure; Hydrops fetalis; Preterm labour; Chorioamnionitis	Fetal ECHO (18-22 weeks); Fetal genetic testing; Fetal therapy includes medical therapy for arrhythmias, FETENDO	Delivery at specialised center with access to cardiology services; Term gestation ~39 weeks; Vaginal delivery; Caesarian for obstetric indications.
Neural tube defects (usually associated with Hydrocephalus/ myelomeningocele-MMC)	Associated with other CNS anomalies, non-CNS anomalies and genetic disorders.	Severity of defect; type of defect (Chiari type II); associated conditions.	Progressive hydrocephalus; neurological damage; complications due to large MMC	Fetal Neurosonogram; Fetal MRI; Fetal genetic testing; Seral USG; Fetal surgery for MMC and FETENDO for Hydrocephalus.	Delivery at center with access to Paediatric Neurosurgery services; Term gestation; Vaginal delivery; Caesarian delivery for possible dystocia due to MMC/ large Hydrocephalus.
Congenital diaphragmatic hernia	Associated anomalies (cardiac, NTD, genetic disorders); syndromic association.	Side of the defect; fetal lung-to-head ratio (LHR); Liver herniation; associated anomalies; left ventricular wall thickness	Polyhydramnios; Lung immaturity; Pulmonary arterial hypertension; pulmonary hypoplasia; Persistent fetal circulation.	Fetal MRI; Fetal ECHO; Fetal genetic testing; Serial USG; Fetal therapy includes Antenatal steroids and FETO. EXIT for reversal of FETO.	Delivery at center advanced neonatal ventilation, ECMO and Paediatric Surgical services; Term gestation (38-39 weeks)-planned induction; Vaginal delivery; Caesarian for obstetric indications.
Oesophageal atresia-tracheoesophageal fistula	Associated anomalies (cardiac, ARM, renal, skeletal); Chromosomal disorders like Trisomy 18; syndromic association (CHARGE).	Type of the anomaly; associated conditions/ syndromes (VACTERL); growth retardation	Polyhydramnios; Growth retardation; Cardiac anomaly related issues; Respiratory distress; Aspiration pneumonia.	Fetal MRI; Fetal ECHO; Fetal genetic testing. Amniodrainage in severe polyhydramnios.	Delivery at center with advanced neonatal ventilation and paediatric surgical services; Term gestation-38 weeks; planned induction; Vaginal delivery; Caesarian for obstetric indications.
Obstructive airway lesions of the fetus, congenital high airway obstruction syndrome (CHAOS)	Lymphovascular lesions like cystic hygroma are associated with genetic syndromes/ chromosomal disorders in 40-50% cases; cervical teratomas are usually isolated lesions.	Type of lesion; size of the lesion; hydrothorax; associated conditions.	Fetal anemia, thrombocytopenia; Fetal hyperdynamic circulation with placentomegaly, hydrops fetalis and heart failure; Polyhydramnios; Maternal Mirror syndrome (preeclampsia); Dystocia	Fetal MRI; Fetal ECHO; Fetal genetic testing in Cystic Hygroma; EXIT Procedure in case of airway compromise.	Delivery at center with advanced neonatal ventilation and paediatric surgical services; Term gestation-38 weeks; planned induction for Vaginal delivery; Caesarian for dystocia/ obstetric indications.
Abdominal wall defects: exomphalos, gastroschisis	Associated genetic disorders, syndromes (BWS, OEIS), cardiac defects in exomphalos; associated gastrointestinal anomalies in gastroschisis-other disorders are rare.	Type of defect; size of defect; presence or absence of cover; herniated viscera; associated conditions/ syndromes	Oligohydramnios in Gastroschisis; Rupture of sac in Exomphalos; Bowel related complications in Gastroschisis; IUGR; Fetal death; Preterm delivery; Term stillbirth	Fetal ECHO, Fetal genetic testing in Exomphalos; Serial USG in Gastroschisis.	Delivery at center with advanced neonatal and paediatric surgical services Term gestation (37-38 weeks); planned induction for Vaginal delivery; Caesarian if large Exomphalos/ Gastroschisis with extracorporeal Liver.
Sacrococcygeal teratoma	Genetic disorders are not associated; commonest type is external; benign lesion with potential for malignant change; highly vascular.	Type of lesion; size of lesion; vascularity.	High output cardiac failure; Fetal anemia, thrombocytopenia; Hydrops fetalis; Polyhydramnios; Maternal Mirror syndrome (preeclampsia); Preterm delivery; Dystocia; Malignant transformation in infancy	Fetal ECHO; Serial USG; Fetal therapy includes fetal blood transfusion, Amniodrainage, FETENDO for LASER vascular occlusion, and fetal surgery.	Delivery at center with neonatal and paediatric surgical services; Term gestation~ 38 weeks; Vaginal delivery; Preterm Caesarian for large lesions and high-risk cases.
Congenital lung malformations (CPAM, BPS, CLE)	CPAM can be microcystic/ macrocystic; BPS can be intralobar/extralobar and has systemic blood supply. No genetic disorders.	Size of the lesion; extent of involvement of lung; vascular supply	High output cardiac failure; Polyhydramnios; Hydrops fetalis; Chance of spontaneous involution; may become apparent again postnatally; Respiratory distress in newborn (CLE)	Fetal ECHO; Serial USG; Fetal therapy includes Thoracoamniotic shunt, maternal steroids and fetal surgery.	Delivery at center with advanced neonatal ventilation and paediatric surgical services; Term gestation ~38 weeks; Planned induction for Vaginal delivery; Caesarian for high-risk cases.
Adnexal cysts (Ovarian cysts)	Commonly sporadic, association with maternal DM and Rh isoimmunization.	Size of the lesion; associated syndromes (Mc Kusick -Kaufman); associated gastrointestinal and genitourinary defects.	Torion; Hemorrhage; Rupture and ascites in large cysts (>6cm) Polyhydramnios in large cyst;	Serial USG (Monitor size and to be differentiated from other intraabdominal cysts- mesenteric/ omental/ duplication); USG aspiration of large cysts.	Delivery at center with paediatric surgical services; Term gestation ~38 weeks; Vaginal delivery.

Continues

Table 2. Common fetal anomalies and the general principles of evaluation and management in specific situations (Continues)

Congenital urinary tract obstruction (CAKUT)	Especially significant for severe bilateral hydronephrosis with renal damage, as in PUV, bilateral PUJO etc. Genetic disorders are seen in multicystic kidneys, renal agenesis etc.	Inherent renal dysplasia; Bladder outlet obstruction.	Progressive renal damage due to pressure changes/ reflux; Oligohydramnios; Pulmonary hypoplasia;	Serial USG and grading of HN; Fetal Urine sampling for electrolytes and beta 2 microglobulin; Fetal genetic testing in select cases.	Delivery at center with paediatric surgical services; Term gestation ~38 weeks; Vaginal delivery.
Intestinal atresias	Commonly duodenal and jejunoileal atresias. High incidence of chromosomal anomalies and other defects in duodenal atresia and other intestinal issues in jejunoileal atresias.	Type of atresia; associated anomalies.	Polyhydramnios; Growth retardation; Complications due to associated anomalies; bowel related issues like perforation, meconium peritonitis and meconium pseudocysts.	Serial USG; Fetal ECHO; Fetal genetic study in select cases with suspicion of genetic disorders. Amniodrainage in severe polyhydramnios.	Delivery at center with paediatric surgical services; Term gestation ~38 weeks; Vaginal delivery.
Anorectal malformations	Commonly rectourethral fistula in male and rectovestibular fistula in female; Association with syndromes (VACTERL) and genetic disorders.	Type of anomaly; Associated anomalies (OA/ cardiac, renal)	Complications due to associated malformations.	Serial USG; Fetal ECHO; Fetal genetic study.	(Dictated also by major associated anomalies-OA, cardiac). Delivery at center with paediatric surgical services; Term gestation ~38 weeks; Vaginal delivery.

detailed diagnosis and prognostication can aid in instituting the appropriate perinatal management.[28-30]

CONCLUSION

The evaluation and management of fetal anomalies poses unique challenges, due to the variegated nature of the disorders and the wide spectrum of presentation. The distinction of minor, physiological alterations from actual structural defects is crucial in this regard. The establishment of definite clinical practice management pathways for screening, diagnosis and therapy are mandatory to bring clarity to management. Greater understanding of the natural history of these disorders, their evolution during gestation and the effect on the mother, fetus and the pregnancy are critical to the optimal management of these conditions.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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