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REVIEW ARTICLE

Surgically Correctable Fetal Anomalies: Ultrasound Diagnosis and Management

Sanja Zaputovic, Milan Stanojevic, Ulrich Honemeyer, Tanja Turudic, Asim Kurjak

ABSTRACT

A significant proportion of fetal anomalies are surgically correctable. Their accurate and reliable prenatal diagnosis is of great importance, and will have significant influence on both postnatal and postsurgical outcome. The influence of prenatal diagnosis of simple structural defects will interfere with organ development. In the light of recent achievements, traditional teratology has to be reexamined more critically.

Keywords: Fetal anomalies, Prenatal diagnosis, Ultrasound, Surgical correction.

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INTRODUCTION

Fetal congenital malformations, whose cause is unknown in almost 70% of cases, continue to represent a significant and growing problem of perinatal morbidity and mortality.[1] The proportion of postnatal morbidity attributable to congenital malformations has also increased. Unfortunately, prevention of congenital malformations is mostly unavailable, and the only realistic approach is early antenatal diagnosis of gross congenital malformations and termination of pregnancy when dealing with malformations incompatible with life. However, during the recent 5 decades, advances in diagnostic and surgical techniques have provided a new opportunity for prenatal prevention of certain congenital malformations and fetal therapy in some rare conditions, enabling the fetus to become a patient. For more than 30 years it is possible to identify fetal conditions and sometimes to treat the fetus actively and successfully even when dealing with severe congenital malformations.[2-5]

Many fetal abnormalities can now be detected. Most defects are best treated after birth, and prenatal diagnosis improves outcome enabling optimal postnatal care. Only a few disorders are potentially amenable to treatment before birth.[2-5] New, very sophisticated, surgical techniques enable the possibility for such correction. The malformations that warrant consideration for treatment *in utero* are simple structural defects that interfere with organ development and whose alleviation might allow fetal development to proceed normally. At present, congenital diaphragmatic hernia, hydronephrosis and hydrocephalus are the candidates. In the light of these achievements, traditional teratology has to be reexamined meaning that simple description or morphology of malformations is no longer sufficient. The pathogenesis of malformations has to be evaluated with reference to the organogenesis for better planning secondary and tertiary prevention of the congenital malformations. Although, the emphasis of treatment of congenital anomalies has been on surgery, we believe that it is important to diagnose these abnormalities already *in utero*. Since, there is no existing specialty which has all the knowledge and technical expertize to handle the potential myriad of intrauterine pathology, it is important that these fetuses are evaluated and treated in a medical setting with a team providing knowledge and expertize in areas of genetics, neurosurgery, gastroenterology, urology, neonatology, pediatric surgery and perinatology.[6] Postnatal diagnosis of these conditions comes largely from recognition of certain clinical findings in the neonatal period often followed by imaging techniques to make correct and timely diagnosis.

The aim of the paper is to present the data on surgically correctable congenital malformations in the 6 years period in the tertiary medical institution of perinatal care, their management and outcome.

MATERIALS AND METHODS

In the 6 years period (from 2005 to 2010), there were 19,876 live-born neonates of whom 198 (1%) have been prenatally diagnosed with surgically correctable congenital malformation. The case records of these children and of other children with the same condition diagnosed postnatally—have been studied in order to assess the accuracy of the prenatal diagnosis and its potential influence on the neonatal management and outcome. The prevalence rate of congenital malformations in the 6 years period is presented in the Figure 1.

Total number of live-borns was 19,876, 198 (prevalence rate 1%) with surgically correctable gross congenital malformations.

RESULTS

Urinary Tract

There were 58 out of 198 infants with urinary tract congenital malformations detected prenatally which was

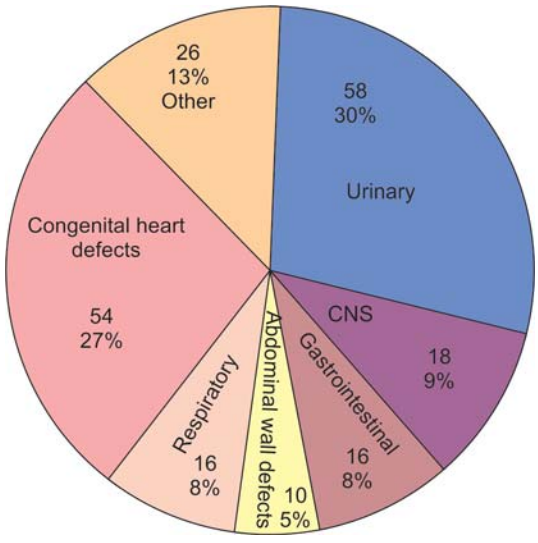


Fig. 1: Prevalence of surgically correctable anomalies in the 6 years period

30% of all malformed fetuses or 0.3% of live-born neonates (Fig. 1). Successful and accurate antenatal diagnosis of urinary tract malformations could influence their management. Some cannot be corrected and most of the correctable lesions are best treated after normal term delivery. However, a few are amenable to treatment before term. Prenatal ultrasonography may be helpful for making postnatal treatment more efficient and clinicians and parents more aware of the nature of the malformation.[7] From the practical point of view fundamental distinction should be made between unilateral and bilateral malformations of urinary tract. If one is dealing with unilateral conditions like multicystic kidney or unilateral hydronephrosis meaning that the other kidney is healthy, then prenatal intervention is mostly not indicated. Only weekly ultrasonographic check ups till delivery will be sufficient. At birth, the newborn will undergo all necessary check ups including clinical examination, laboratory work-up and imaging.[8,9] As soon as a certain diagnosis is available, surgical correction will be performed at the most appropriate time. If there is massive enlargement of the fetal abdomen, elective cesarean delivery should be considered to prevent the dystocia that might occur with vaginal delivery and to prevent further damage to these vital organs.

In bilateral renal agenesis, bilateral multicystic kidneys, or bilateral infantile polycystic kidneys are demonstrated early in gestation, the obstetrician and parents may choose to terminate the pregnancy because these conditions are not compatible with extrauterine life.[10]

Ultrasound examination in pregnancies at increased risk with family history of Bardet-Biedl syndrome (BBS) should seek prenatal diagnosis using second-trimester ultrasound examination to detect anomalies, such as postaxial polydactyly and renal cysts, found in BBS as reported by Dar et al 2001.[11,12] BBS is an autosomal recessive disorder characterized by postaxial hexadactyly, obesity, mental retardation, pigmented retinopathy, hypogonadism and renal disease.[13]

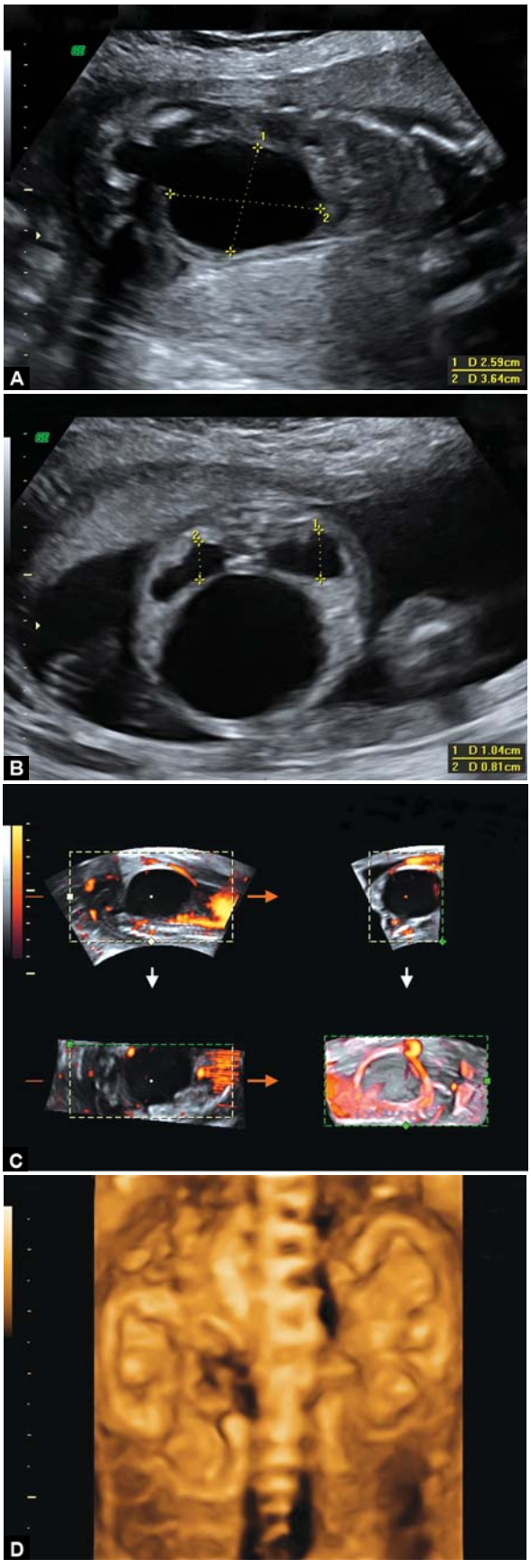
Morphological changes are present in all areas of the kidney, the renal medulla being the most frequently affected site. Cystic and dysplastic changes are prevalent. Cassart et al studied 11 pregnancies by ultrasound examination and concluded that in families in which BBS had occurred previously, the prenatal appearance of enlarged hyperechoic kidneys without corticomedullary differentiation should be considered recurrence of BBS.[14]

Obstructive Uropathies

Prenatal diagnosis of obstructive uropathies (Figs 2A to D) opens new possibilities in the pediatric urologic management of these lesions, and the benefits of fetal ultrasonography are now increasingly evident. This is particularly significant since, data suggest that relief of obstruction in the young infant (under the age of 12-18 months) is associated with improvement in renal function, while in the older child, renal function stabilizes only after surgical repair. Male infants with posterior urethral valves often demonstrate renal failure, dehydration and sepsis at the age of 2 to 4 weeks.

If this diagnosis is anticipated at birth, initial transurethral catheterization and subsequent endoscopic destruction of the valves would minimize the risk of further damage from prolonged obstruction and infection. Likewise, the infant with bilateral ureteropelvic or ureterovesical obstruction, or obstruction of a solitary renoureteral unit could be operated on early and electively.[9,14] Several problems remain, however, which must be resolved to obtain maximum benefit from early detection *in utero*. Since, not all obstructions are severe, despite marked dilatation of collecting system, the criteria like renal parenchymal growth, changes in renal pelvic size, fetal urine flow should be taken into account to establish the follow-up of renal damage, which, if progressive would justify early delivery for urgent surgical management of obstructive uropathy. While definitive surgical repair may be difficult or impossible in a tiny, premature infant, temporary cutaneous diversions (pyelostomy, ureterostomy, vesicostomy) could be accomplished at any age or size, if necessary.[9]

Fetal diagnosis of congenital paraureteral urinary bladder or so called Hutch diverticula associated with vesicoureteral reflux (VUR) influences postnatal management significantly. VUR is the most common urologic diagnosis in children, occurring in approximately 1% of newborns



Figs 2A to D: Obstructive uropathy: (A) Enlarged urinary bladder, (B) megacyst and bilateral hydronephrosis transverse view, (C) multiplanar power Doppler view with encircling umbilical arteries around the enlarged bladder, (D) 3D surface rendered view of bilateral hydronephrosis

and as high as 30 to 45% in children with urinary tract infection (UTI). Current management is based upon the long-held belief that VUR is a risk factor for renal scarring because it predisposes patients to recurrent acute pyelonephritis by transporting bacteria from the bladder to the kidney. The development of renal scarring increases the risk of hypertension and chronic kidney disease (CKD).[15]

Where obstructive lesion are evidently leading to progressive renal damage at a time when premature delivery cannot be reasonably undertaken, early intervention is necessary, because if unrelieved, the obstruction interferes with the fetal development and the severity of damage depends on the degree and duration of obstruction.

Prune belly syndrome (PBS) incidence is estimated to be 1 in 30,000 to 50,000 newborn babies. At an early stage during the first trimester screening, key hole sign of dilated proximal urethra, and oligohydramnios are not yet visible.

There are several alternatives for decompressing an obstructed fetal urinary tract. The fetal bladder or renal pelvis can be aspirated percutaneously under ultrasonographic guidance. Another possibility is early delivery and decompression of the urinary tract *ex utero*, This will maximize the opportunity for further renal development and minimize the adverse effects of oligohydramnios. The ideal management is early decompression of the urinary tract and continued gestation. The first successful urinary tract bypass *in utero* was performed by Golbus and others in 1982 who developed techniques for the ultrasonographically guided percutaneous placement of fetal shunt catheters and for the surgical exteriorization of the fetal urinary tract.[16]

When the performance of urinary tract diversion is being considered, we are very much of the opinion that the risks of shunt placement are too high in the case of unilateral lesion or those causing mild bilateral hydronephrosis associated with normal amniotic fluid index. If serial scans show progressive bilateral renal calicle dilatation, in association with increasing oligohydramnios in a fetus too premature for delivery, surgical intervention may be plausible. However, at present we do not know whether such intervention would be justified in terms of the optimal additional time to be gained *in utero*. Once a shunting procedure is to be attempted when obstruction seems complete in the second trimester, the parents should be warned that irreversible changes may already have occurred and that operation which could appear to be technically successful, may nevertheless be of no benefit.[17]

If upon initial scanning, a patient with pulmonary immature fetus, in the third trimester, appears to have a bilaterally obstructed fetal genitourinary system with accompanying oligohydramnios, a shunt would probably be advisable. Decompression of the obstructed system in a

situation where the kidneys are not dysplastic may prevent further renal damage, and correction of the oligohydramnios could save the life of the fetus. Irreversible renal or pulmonary damage may already have occurred, but it cannot be determined prior to delivery. In cases of significant oligohydramnios, the insertion of a bladder—amniotic fluid shunt is a considerable technical problem as the placement of the distal end of the catheter within the amniotic sac is hindered by low volume of amniotic fluid. As further experience in the treatment of genitourinary lesion *in utero* reported, it will be possible to develop guidelines for the selection of appropriate patients. In the meantime, the management of these cases should be undertaken by a team of experts including the obstetrician, neonatologist and pediatric urologist, meeting regularly to discuss progress after each ultrasonic examination.[18] The neonatal surgeon will also observe number of cases simply suspected or diagnosed *in utero* as being at the 'limit of indication for intervention,' showing a light obstructive uni-or bilateral pathology.

Future serial tests and experience over the next years will indicate how such cases should be managed: Whether to operate in the 1st weeks, or after 6 or 12 months, or not operate at all.

Thus, fetal hydronephrosis is the consequence of the obstruction at the level of the urethra, the vesicoureteric orifice, the pelviureteric junction or associated with vesico-uretheric reflux. It is the most common urinary tract abnormality. The ureteropelvic junction is the most common site of congenital urinary obstruction above the level of the bladder.[19,20] The resulting hydronephrosis may be unilateral or bilateral.

In adults, pulsed Doppler sonography was used for the diagnosis of lower pole arteries, which cross the uretero-pelvic junction and are possibly the reason for hydronephrosis.[21] Prenatal diagnosis has become possible through combined use of three-dimensional (3D) sonography and power Doppler allowing topographic evaluation of renal arterial blood flow and surface rendered renal pelvis anatomy.

To evaluate efficacy of laparoscopic management of ureteropelvic junction obstruction, 329 patients underwent laparoscopic transperitoneal ureteropelvic junction obstruction management from June 2001 to March 2009. Intraoperatively, lower pole crossing vessels were identified in 117 patients (35.5%). Laparoscopic cephalad relocation of the lower pole crossing artery after division of the crossing vein in selected cases was found to be an ideal alternative for dismembered pyeloplasty with noticeable outcomes in long-term follow-up.[22]

Multicystic Kidney

Multicystic kidney is the most common of all neonatal abdominal masses and this condition represent 20% of all masses. As it is no threat to life in the immediate neonatal period, accurate diagnosis by noninvasive means distinguishes it from other neonatal abdominal masses. The diagnosis of a multicystic kidney is suggested by the presence of multiple cysts. The cysts are commonly of the order 1 to 2 mm in diameter but they can be up to 6 mm large. A similar cystic appearance may sometimes be produced by hydronephrosis, but multicystic kidney disease is nearly always bilateral; Dilatation of the ureters and kidneys may be either unilateral or bilateral depending on the site of the obstruction.[23]

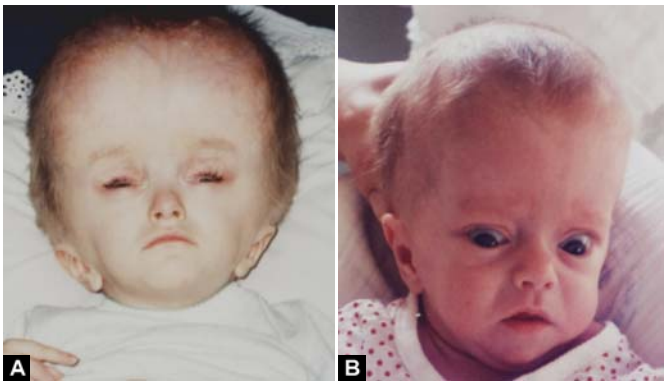
Congenital Renal Tumors

Congenital renal tumors are rare with 2.5 to 7% of all perinatal tumors. In decreasing order of frequency they could appear as congenital mesoblastic nephroma, Wilms tumor, rhabdoid tumor, clear cell sarcoma, hamartomas (e.g. angiomyolipoma), and ossifying tumor of infancy. Congenital mesoblastic nephroma (CMN) is generally benign. It develops from renal mesenchyma. Less than 5% of all pediatric renal tumors turn out as CMN. Around 90% are diagnosed during the first year of life, 50 to 75% are found in infants before they reach 3 years of age.[24] Prenatal diagnosis of mesoblastic nephroma (Bolande's tumor) by ultrasound is increasing. Findings of a 'ring' sign, an anechoic ring surrounding the tumor, were described as typical for mesoblastic nephroma. Doppler signals registered in the ring indicated intense peripheral vascularity, and histopathological evaluation confirmed the vascular origin of the ring sign.[25] The most common presentation is as a unilateral solid mass with homogeneous echogenicity near the renal hilus. There is no discernable capsule, but the mass is well-demarcated from the renal tissue. Because polyhydramnios is seen in about 70% of all cases, 25% of cases develop uterine contractions and deliver preterm. The prognosis is excellent after unilateral nephrectomy.[26]

Central Nervous System

Hydrocephalus

Hydrocephalus (Figs 3A and B appearance of the infant head; Fig. 4 postnatal 3D ultrasound) does not indicate a single clinical entity, but includes a variety of clinicopathological conditions caused by excessive cerebrospinal fluid (CSF) based on the disturbed circulation.[27] New standards for clinicopathological evaluation of hydrocephalus as well as the classification of



Figs 3A and B: (A) Excessive hydrocephaly, (B) setting-sun sign

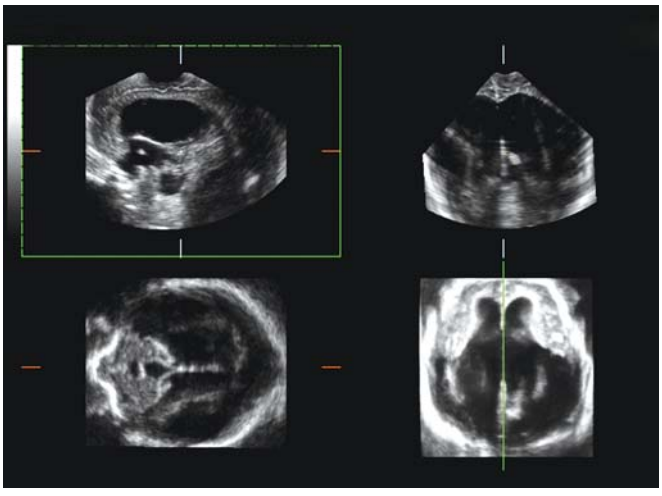


Fig. 4: Postnatal 3D ultrasound: Multiplanar view of prenatally developed posthemorrhagic hypertensive hydrocephalus

hydrocephalus have been developed in Japan.[27] The most important clinical conditions associated with hydrocephalus are: Aqueductal stenosis, myelomeningocele, postintraventricular hemorrhage due to prematurity, congenital hydrocephalus, cyst, tumor, post-head-injury, postinfectious and other.[28] Hydrocephalus with high intracranial pressure is one of the causes of severe brain damage in fetuses and in newborns if not treated. The prevalence rate in Europe is 5.84 per 10,000 births after 20 weeks of gestation.[29] It is essential to make assessment of the intracranial pressure and condition of the brain and perform the derivation of CSF at the earliest opportunity in order to avoid brain damage.[27,30,31] The ultimate goal of hydrocephalus treatment remains achieving arrested hydrocephalus by shunt surgeries. In the future, to achieve arrested hydrocephalus, minimum quantity of CSF to be drained should be elucidated.[27] High intracranial pressure can cause marked separation of cranial sutures and the setting-sun sign (Figs 3A and B).

Clinical neurological and ophthalmological assessment together with head ultrasound have been performed in all babies postnatally, while magnetic resonance imaging (MRI) or multislice-computed tomography (MSCT) were done when needed. Based on all the findings, neurosurgical treatment has been indicated whenever appropriate. A favorable outcome was reported for 66.8% of patients, 31.5% showed no change, while overall inpatient mortality was 1.7%.[32] Concerning the long-term outcome in one study 132 patients underwent 179 shunt surgeries. Forty-four (33%), 79 (60%) and 99 (75%) patients demonstrated objective improvement at 3, 6 and 24 months after shunt surgery respectively. Gait improved first in 88 (93%) patients.[32] Dementia and urinary incontinence were two-fold less likely to improve. Radiological evidence of corpus callosum distension, gait impairment as the primary symptom predicted improvement.[33]

Posthemorrhagic hydrocephalus and hydrocephalus connected with craniospinal dysraphism had significantly earlier revisions than congenital and other etiologies.[34]

Neural Tube Defects

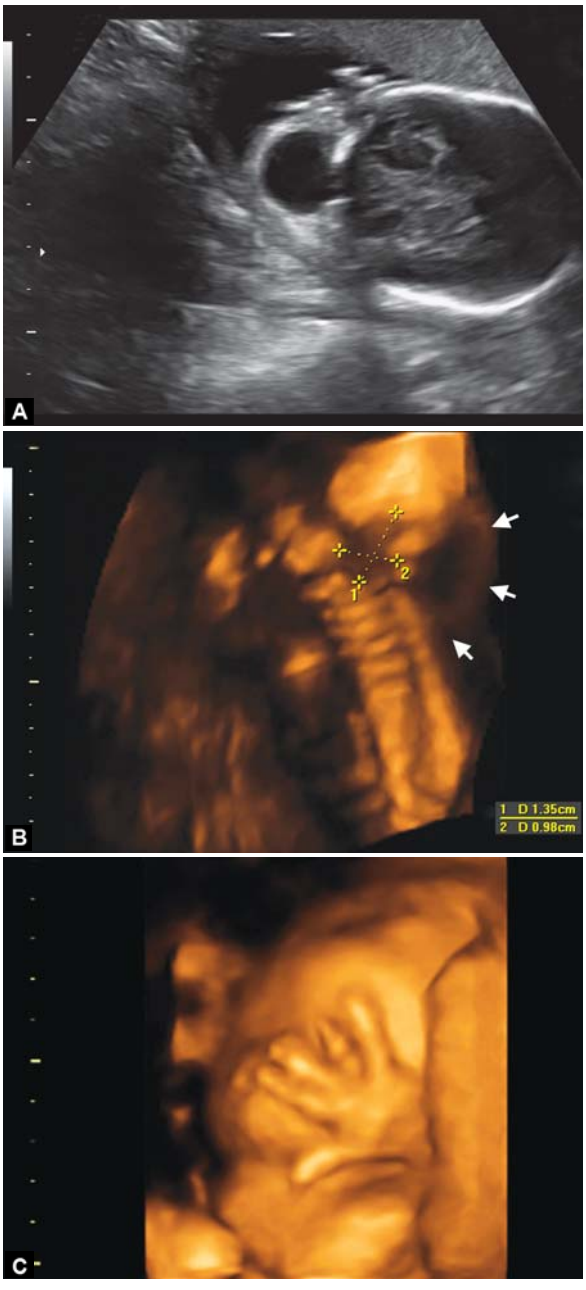
According to EUROCAT prevalence rate of all neural tube defectes in Europe from 2005 to 2009 was 9,74 per 10,000 births.[29] Prevalence rate of specific malformations per 10,000 births after 20 weeks of gestation were: Encephalocele, 1.17; spina bifida, 4.98.[29]

Encephalocele

Encephalocele is a neural tube defect characterized by protrusion of the brain and meninges through opening in the cranium. The most common localization is occipital region (67%) of the skull (prenatal US diagnosis depicted at Figs 5A to C), often associated with hydrocephalus (45.8%). Surgery should be performed as early as possible and only after careful preoperative planning especially for the anterior encephalocele.[35,36]

Spina Bifida and Meningomyelocele

Spina bifida, often prenatally detected during the second and the third trimester, is one of the CNS anomalies with the indication for immediate surgical correction after birth (Figs 6 to 7D). Spina bifida malformations fall into three categories: Spina bifida occulta, spina bifida cystica with meningocele and spina bifida cystica with myelomeningocele.[37] The most common location of the malformations is the lumbar and sacral areas (Fig. 7A). Meningomyelocele is the most significant form causing disability in most affected individuals. The incidence of spina bifida can be decreased by up to 70% when daily folic acid supplements are taken prior to conception.[38] Significant ethnic differences in prevalence are recognized; people of Celtic



Figs 5A to C: Occipital encephalocele: (A) B-mode, (B) surface-rendered 3D, (C) capture of 4D sequence with variable finger movements

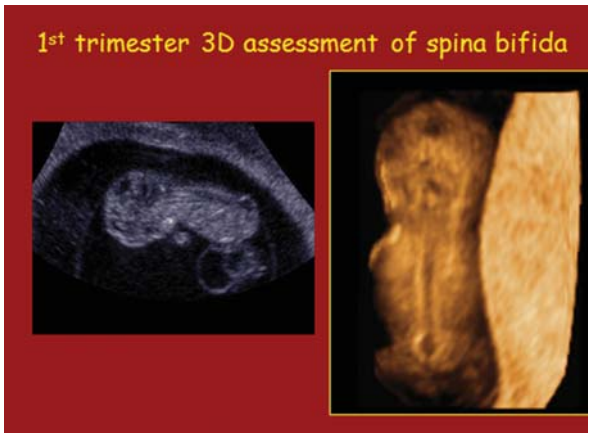
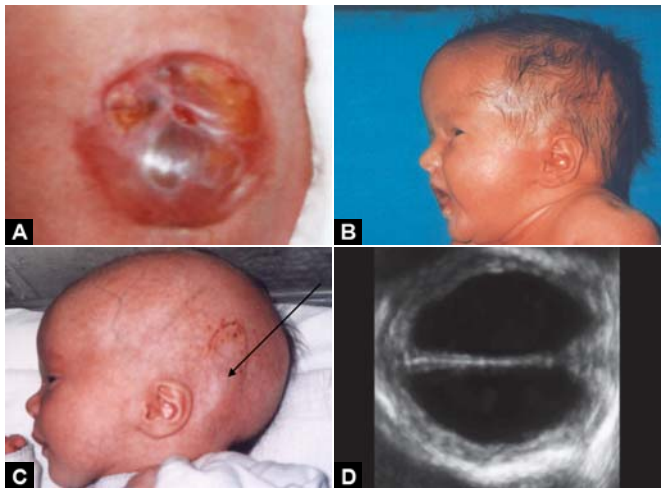


Fig. 6: Spina bifida diagnosed in the first-trimester (*Courtesy:* Dr R Pooh)

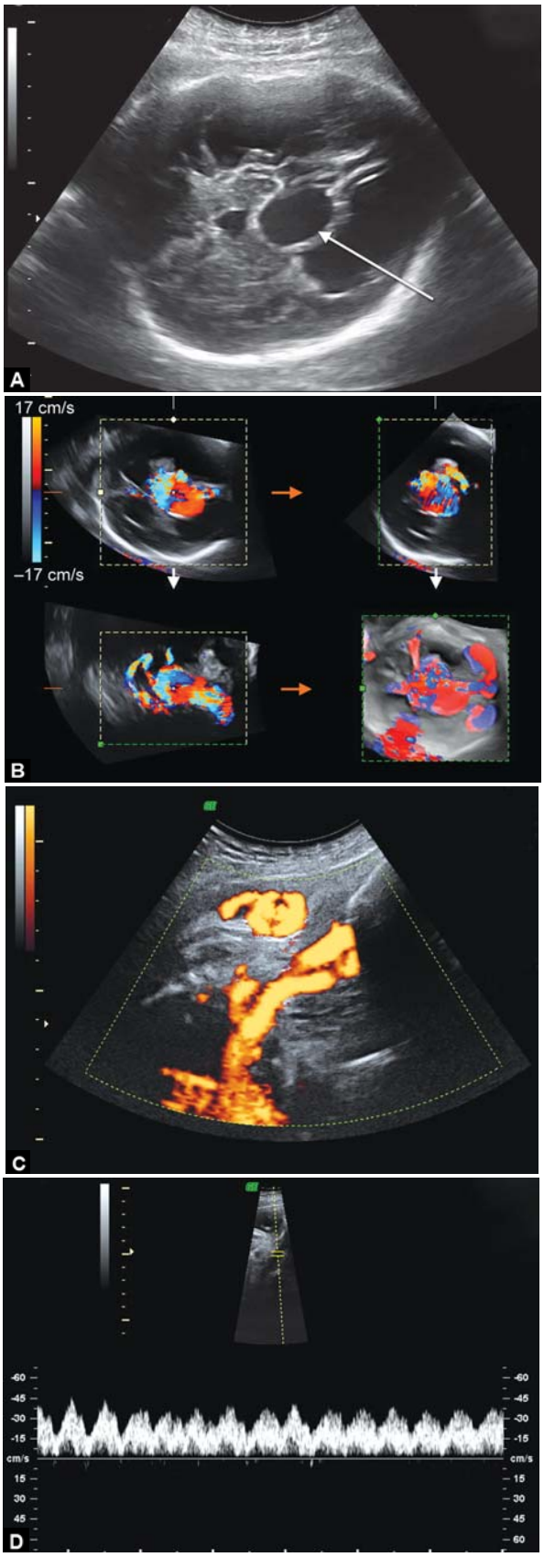


Figs 7A to D: Postnatal photo of lumbosacral meningomyelocele: (A) With consecutive hydrocephally (type II Arnold-Chiari malformation) (B), (C) shunt operation (outer part of the shunt placed behind the left ear-arrow), (D) ultrasound image of enlarged brain ventricles

origin have the highest rate of spina bifida. A female predominance is observed, with females accounting for 60 to 70% of affected children.

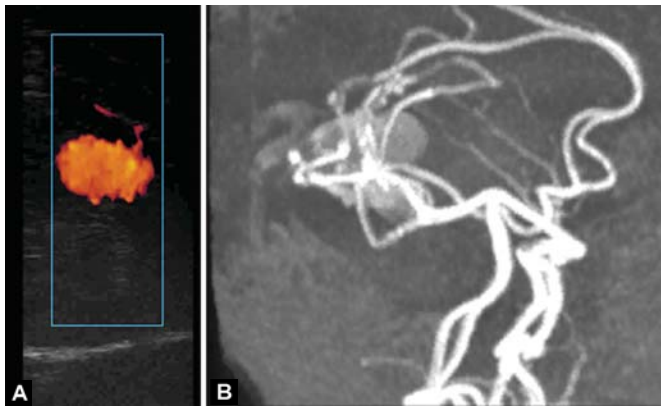
Vein of Galen Aneurysm Malformation

The vein of Galen aneurysm is a rare vascular malformation consisting of one or more arteriovenous shunts from arterial feeders from the carotid and vertebrobasilar systems in the midbrain, to the vein of Galen.[39] The malformation is due to an arteriovenous fistula of the median prosencephalic vein, a precursor of the vein of Galen, which fails to regress. High flow of blood into the vein causes it to dilate, it is however, not a true aneurysm.[39] The high rate of blood flow may result in cardiac failure due to increasingly pronounced venous return via jugular veins and vena cava superior. As much as 80% of the cardiac output may shunt through the fistula. The sonographic appearance of the dilated vein of Galen in the mid-sagittal plane is a large, well-defined, irregular, supratentorial, and sometimes pulsatile structure, along the corpus callosum above the cerebellum to the calvaria.[39] In the coronal plane, the dilated vein appears as a round, cystic, centrally located structure.[39] In color Doppler imaging, the focal lesion fills with blue-orange (aliasing) color signals due to turbulences of venous flow (Figs 8A to D).[39] Other sonographic findings include dilated jugular veins and vena cava superior, signs of high output heart failure, such as cardiac dilatation, fetal hydrops, and polyhydramnios. The enlarged vein of Galen may cause obstruction of the ventricular system through compression of the Sylvian aqueduct, eventually with resulting hydrocephaly. Neonatal vein of Galen aneurysm



Figs 8A to D: VGAM (prenatal diagnosis): (A) 2D image (B) color Doppler, (C) power Doppler, (D) pulsed Doppler wave

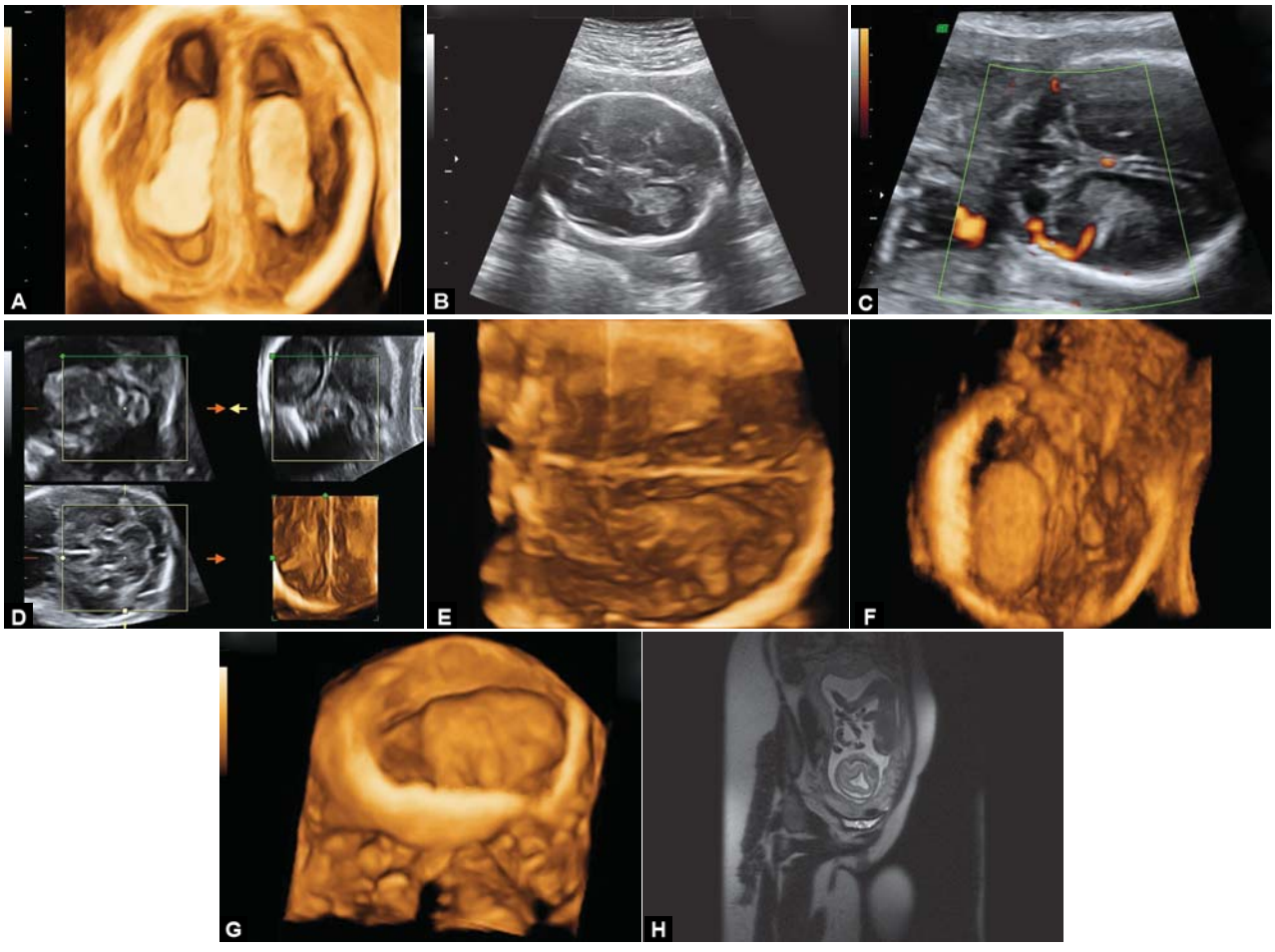
malformation (VGAM) can be treated successfully with a strategic approach integrating antenatal diagnosis, endovascular surgery, treatment at intensive care facilities, and the cooperative efforts of different specialties. Both venous and arterial embolization is possible, either with coils or acrylic glue. Patients in whom VGAM was diagnosed (postnatal diagnosis of VGAM; Figs 9A and B) and managed in infancy or childhood had more than 90% long-term survival. The better prognosis is largely determined by absence of cardiac failure.[40,41]



Figs 9A and B: Postnatal images of vein of Galen aneurysm: (A) postnatal power Doppler and (B) magnetic resonance angiography

Fetal Intracranial Hemorrhage

Hemorrhages may occur either within the cerebral ventricles, subdural space or infratentorial fossa. It has been estimated that the incidence of intracranial hemorrhage (ICH) in premature infants is high, occurring in approximately 40% of infants of less than 32 weeks gestation. Antenatal fetal ICH may occur spontaneously, or occur in association with various maternal or fetal conditions (Figs 10A to H). Predisposing maternal conditions at risk for this occurrence include alloimmune and idiopathic thrombocytopenia, von Willebrand's disease, specific medications (warfarin) or illicit drug (cocaine) abuse, seizures, severe abdominal trauma inflicting subsequent fetal injury, amniocentesis, cholestasis of pregnancy and febrile disease. Predisposing fetal conditions include congenital factor-X and factor-V deficiencies, hemorrhage into various congenital tumors, twin-twin transfusion, demise of a cotwin or fetomaternal hemorrhage.[42-45] The classification of ICH includes five major types: Intraventricular hemorrhage (IVH), cerebellar, subdural, primary subarachnoid hemorrhages and miscellaneous intraparenchymal hemorrhages.[45] IVHs are the most common variety of neonatal ICH and are characteristic of the immature brain. IVHs are subdivided according to their severity into four grades; The first three grades are limited to the ventricles, while the fourth grade includes parenchymal involvement occurring in the most severe cases.[45]



Figs 10A to H: (A) Normal 3D image of the fetal head—lateral ventricles and choroid plexus at 16 weeks, (B) 2D-IVH at 22 weeks and 1 day of gestation, (C) power Doppler of IVH, (D) 3D multiplanar view and 3D reconstruction of the IVH, (E) 3D reconstruction of the IVH in the posterior horn of left lateral ventricle, (F) 3D reconstruction of the IVH in the posterior horn of left lateral ventricle—ventriculomegaly at 23 weeks and 4 days, (G) 3D reconstruction of the IVH in the posterior horn of left lateral ventricle—ventriculomegaly, (H) MR of IVH in the posterior horn of left lateral ventricle

Transabdominal or transvaginal ultrasound can present with different sonographic features, such as hyperechoic lesions in the lateral ventricle and ventriculomegaly, irregular echogenic brain mass, intraventricular echogenic foci or periventricular echodensities and posthemorrhagic hydrocephalus (PHH) (Fig. 4). The outcome is usually poor, especially for those fetuses affected by higher grade IVH. Ventriculoperitoneal shunting postpartum in case of PHH constitutes an option to enable best as possible neurological development.[43,45]

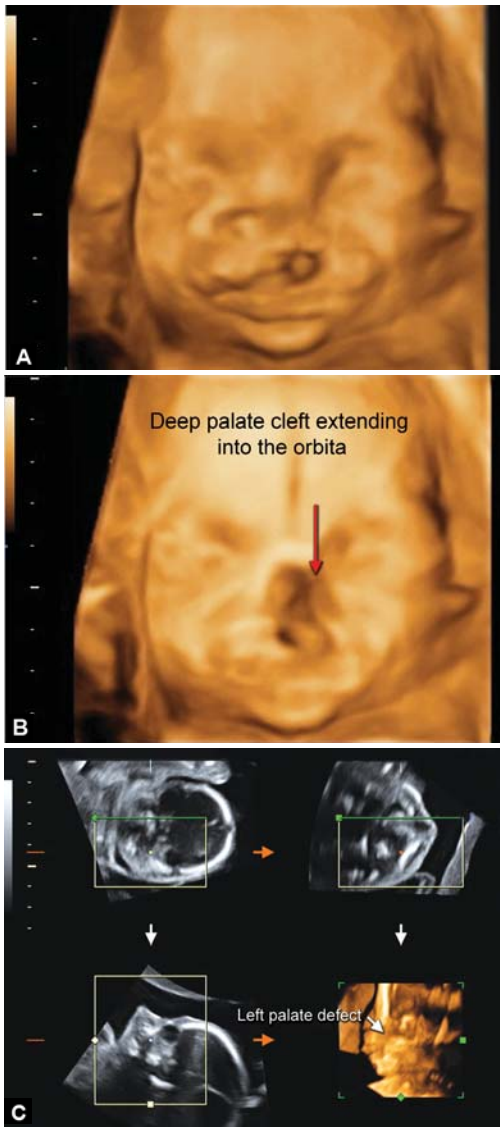
Due to the significant associated neonatal neurological impairment and potential medicolegal implications of antepartum fetal intracranial hemorrhage, it follows that obstetricians and sonographers should be familiar with predisposing factors and typical diagnostic imaging findings of these events. In addition to this, intrauterine fetal behavior visualized with 4D ultrasound can be successfully evaluated with the new Kurjak antenatal neurodevelopmental test (KANET), providing possibilities of prenatal diagnosis of fetal neurological impairment.[46]

Fetal Face

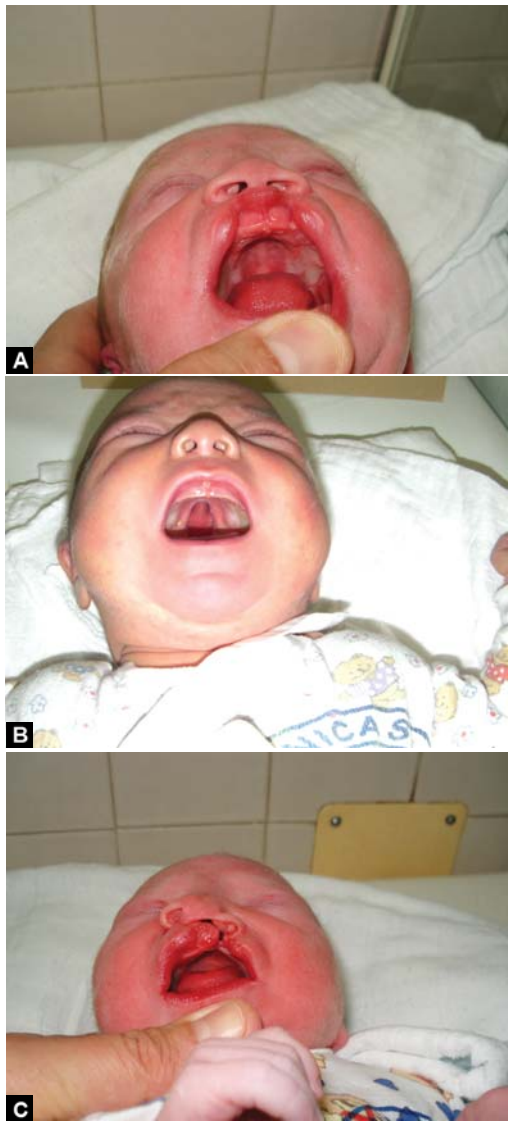
Cleft Lip and Palate

Prevalence of orofacial clefts is 15.96 per 10,000 births (cleft lip with or without cleft palate 9.41 and cleft palate 5.45 per 10,000).[29] Cleft lip occurs unilaterally or bilaterally, and in less than 10% of babies it can be associated with abnormal karyotype. Recent 3D tomographic ultrasound can demonstrate the anterior maxillary structure, showing evidence of alveolar cleft (Figs 11A to C). Prenatal diagnosis is helpful in psychological preparation of parents for the cosmetic implications of the neonate (postnatal appearance—Figs 12A to C), and in organizing immediate postnatal provision of a palatal plate to enable sucking and better growth of malformed maxilla enabling more successful surgical repair in the future.[47] Functional and cosmetic repair of even deep clefts involving the orbita is usually completed before 10 years of age.[48]

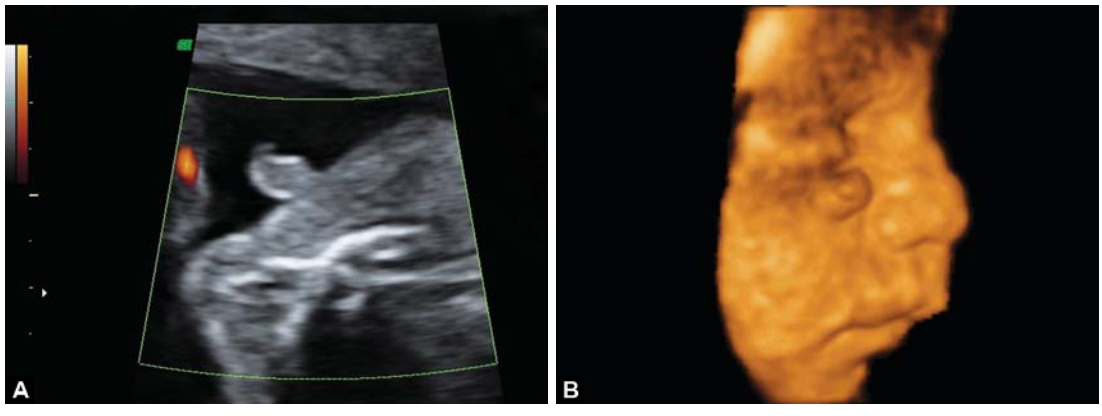
Antenatal sonographic diagnose of skin tags (prenatal diagnosis—Figs 13A and B) of the fetal face may possess



Figs 11A to C: Cleft lip and palate: (A) 3D surface rendering of cleft lip, (B) cleft palate 3D surface rendering, (C) 3D multiplanar view



Figs 12A to C: Postnatal images of: (A) Isolated bilateral cleft lip, (B) isolated cleft of the hard palate, (C) left sided cleft of the lip and palate



Figs 13A and B: Skin tags: (A) 2D image of the skin tag under the right orbita, (B) 3D surface image of the same skin tag

little clinical significance, constitutes however, an important proof of the sonographers professional competence in the eyes of the child's parents.

Gastrointestinal Tract

Recently rapid progress has been made in the antenatal recognition and diagnosis of gastrointestinal malformations.

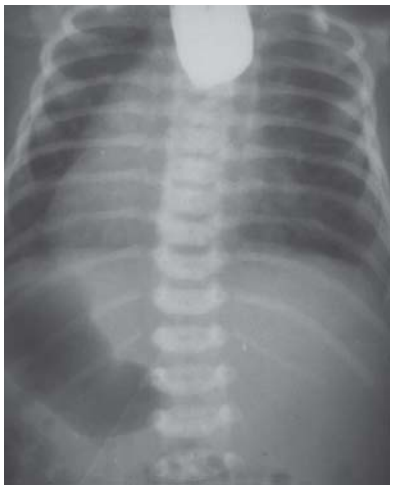


Fig. 14: X-ray of the esophageal atresia with tracheoesophageal fistula in newborn with situs viscerum inversus (dextrocardia, stomach on the right side, esophagus ending in a blind-ended pouch)

Their prevalence is rather high being 17.27 per 10,000 births in Europe.[29] Antenatal detection of potentially correctable major gastrointestinal anomalies may be life-saving since, appropriate prenatal preparation may be made for medical and surgical care of the newborn.[49]

The fetal gastrointestinal tract is the most common site of surgically correctable fetal malformations detected by ultrasound. Early detection of esophageal atresia (Fig. 14 postnatal X-ray finding of esophageal atresia associated with situs viscerum inversus) (prevalence rate 2.38 per 10,000), duodenal atresia and/or jejunal atresia (prevalence rate of 1.29 per 10,000),[29] allows planning of delivery and subsequent postnatal corrective surgery in the best equipped available center and in the most suitable conditions. This is certainly the most important advantage.[49]

Esophageal Atresia with or without Fistula

Polyhydramnios accompanied with very small stomach, valid ultrasound diagnosis with clinical features, successfully suggests the set up of the mentioned diagnosis.[50,51]

Duodenal Atresia and Jejunoileal Atresia

Doudenal atresia is not a life-threatening condition in the first few hours of life.[52,53] Immediately after birth it is usually asymptomatic, but later on the important clinical sign is persistent vomiting.[54] A typical X-ray image is presented by 'double-bubble' sign of total duodenal obstruction.[55]

Antenatal diagnosis of jejunoileal atresia in all fetuses was made on the basis of typical findings of polyhydramnios and several dilated loops of fluid-filled intestine in the fetal abdomen.[56] In the case of jejunal atresia, the parents should be informed of the possibility of an associated apple peel with the short bowel syndrome, which could be often followed by intestinal failure-associated liver disease.[57,58]

Some intestinal obstructions could possibly be caused by meconium ileus with presence of cystic fibrosis as possible causal condition.[59,60] Anorectal malformations are usually diagnosed late in pregnancy or in the early neonatal period, which is not influencing typical treatment of these malformations.[61] Early *in utero* antenatal detection of gastrointestinal malformations is very important because in antenatally unrecognized cases, surgical management of neonatal intestine obstruction may be compromised by delayed diagnosis and, consequently complicated by vomiting, electrolyte imbalance, aspiration, sepsis, peritonitis due to intestinal perforation, or bowel gangrene in cases of intestinal volvulus.[62] If corrective surgery is not performed, gastrointestinal obstruction will ultimately lead to death of the neonate.

Abdominal Wall Defects (Omphalocele and Gastroschisis)

The most frequent congenital abdominal wall defects are omphalocele (Figs 16A and B, 17A to D) and gastroschisis (Figs 15, 18A and B, and 19). In both malformations, the abdominal content is placed outside the abdomen through abdominal wall defect with membrane in omphalocele and without membrane in gastroschisis.[63-71] Both are frequently detected prenatally due to routine maternal serum screening and fetal ultrasound. Prenatal diagnosis may influence timing, mode and location of delivery. Prognosis for gastroschisis is primarily determined by the degree of bowel injury, whereas prognosis for omphalocele is related to the number and severity of associated anomalies and the karyotype. The surgical management of both conditions consists of closure of the abdominal wall defect, while minimizing the risk of injury to the abdominal viscera either through direct trauma or due to increased intra-abdominal pressure.[63-71] Options include primary closure or a variety of staged approaches. Long-term outcome is favorable in most cases; however, significant associated anomalies (in the case of omphalocele) or intestinal dysfunction (in the case of gastroschisis) may result in severe morbidity and mortality.[64]

Gastroschisis shows a normal insertion of the umbilical cord, with the abdominal wall defect and herniation of bowel occurring most often on the right side of the umbilicus.[69]

Consequently, there is no covering membrane. Differentiation of these two abdominal entities can be successful using 3D-color Doppler ultrasound but it is not critical, as management decisions for delivery of the fetus

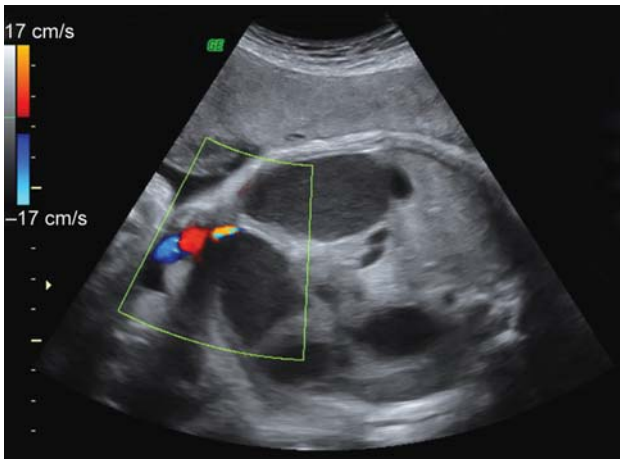
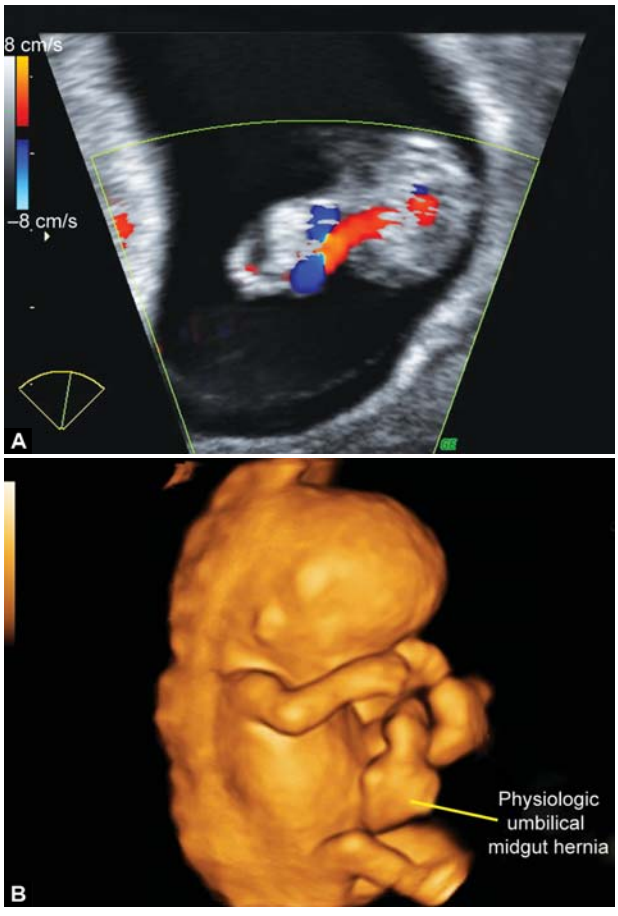
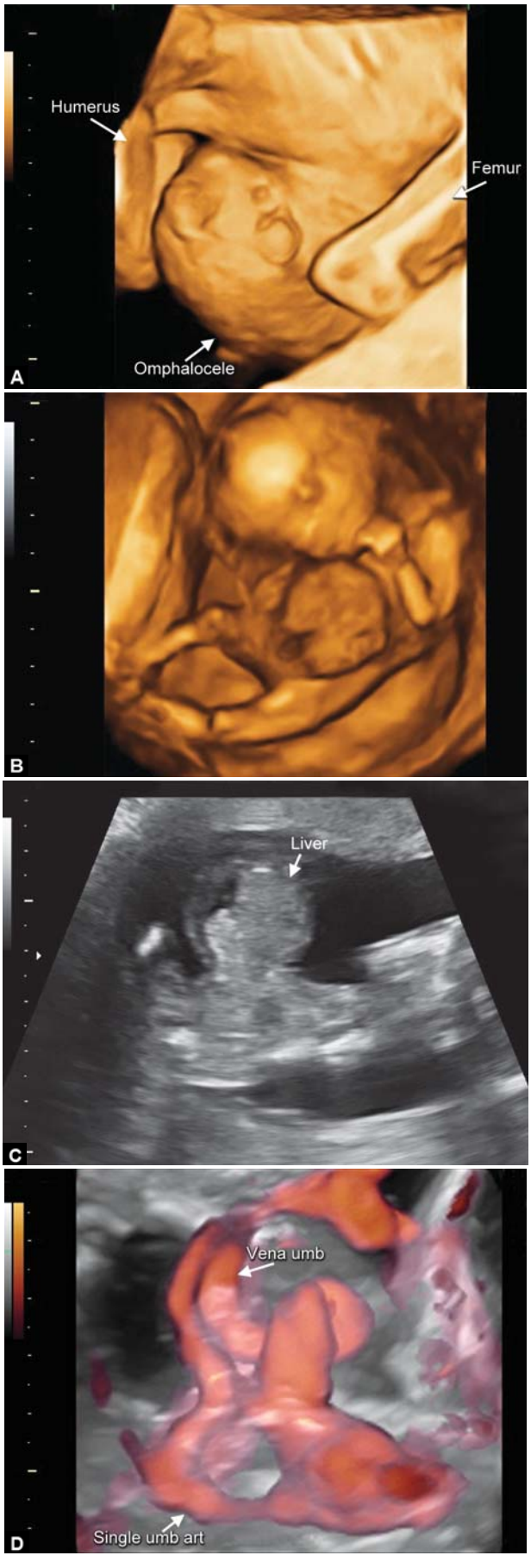


Fig. 15: Gastroschisis dilated small intestine loops due to intestinal inflammatory stenosis and necrosis

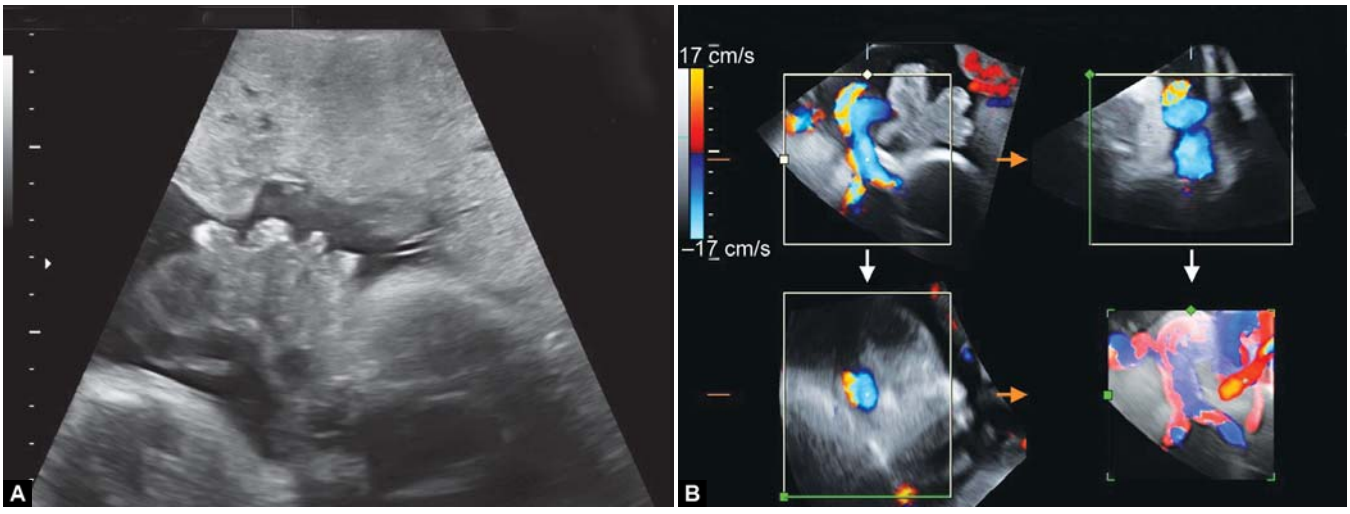


Figs 16A and B: 'Physiological' umbilical herniation in the early fetal period: (A) B-mode with color Doppler, (B) 3D surface rendered image

are the same for both. Management of gastroschisis has shifted from early primary closure to preformed silo placement and delayed closure. The change in management strategy has resulted in prolonged intensive care unit stay and time to full feeds but reduced postoperative hernias and wound infections. Most newborns need only one operation for definitive surgical treatment.[67,68]



Figs 17A to D: Omphalocele work up with 2D, 3D, and 3D glass body plus power Doppler



Figs 18A and B: Gastroschisis: (A) B-mode and (B) multiplanar rendering plus color Doppler for demonstration of free bowel loops and assessment of topography of abdominal wall defect and umbilicus

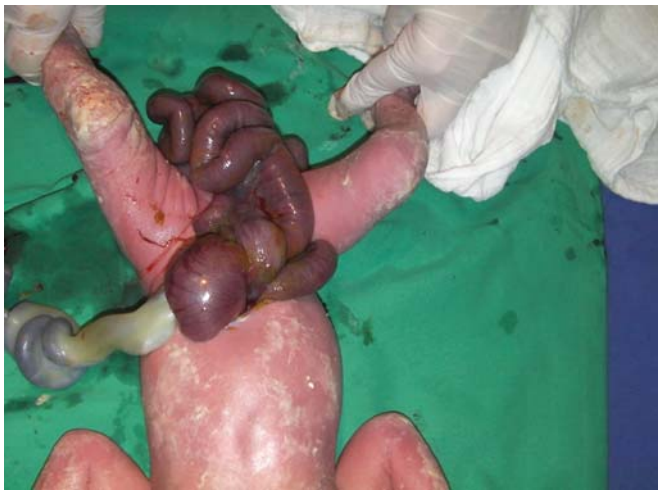
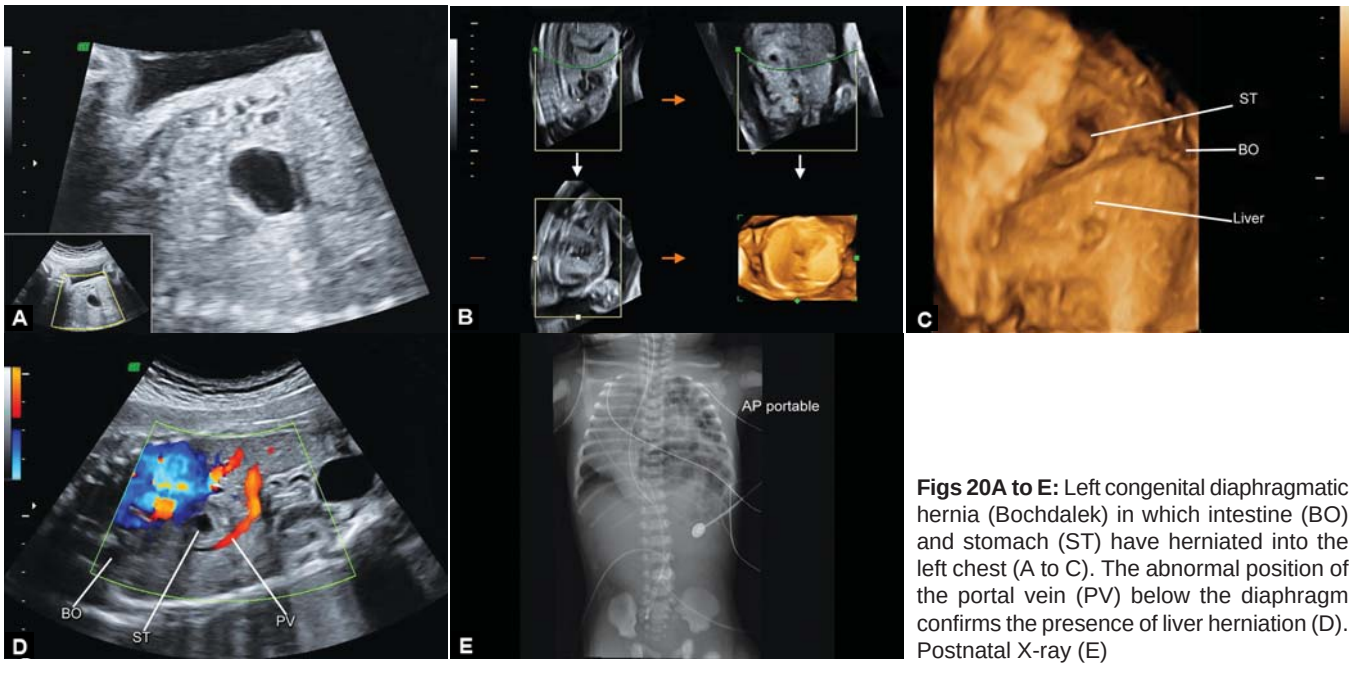


Fig. 19: Postnatal appearance of gastroschisis

Ultrasound was quite accurate in visualizing this abdominal wall defects.[63,68] Prompt surgical repair was performed in all newborn babies and all had normal neonatal development. Due to a small abdominal cavity and large defect of the abdomen, the abdominal wall defect together with eviscerated intestines is covered by a plastic bag which will enable intestines to be gradually pushed back into the abdominal cavity. Immediately after birth, the baby will be prepared for surgical intervention, to be performed with primary closure using Dacron prosthesis.[69-71]

Congenital Diaphragmatic Hernia (CDH)

Prevalence rate of congenital diaphragmatic hernia (CHD) in Europe is 2,71 per 10,000 births.[29] Overhalf of the cases



Figs 20A to E: Left congenital diaphragmatic hernia (Bochdalek) in which intestine (BO) and stomach (ST) have herniated into the left chest (A to C). The abnormal position of the portal vein (PV) below the diaphragm confirms the presence of liver herniation (D). Postnatal X-ray (E)

of congenital diaphragmatic hernia (Figs 20A to E) are diagnosed prenatally.[72] Prenatal assessment aims to rule out associated anomalies in order to make individual prognosis.[72] Prediction of outcome is based on measurements of lung size and vasculature as well as on liver herniation.[72] Visceral herniation into the thoracic cavity during the critical period of lung development when bronchi and pulmonary arteries undergo branching at 5 to 16 weeks, leads to decreased bronchial branching, pulmonary hypoplasia, truncation of the pulmonary arterial tree and to dysfunctional surfactant postpartum.[72] Etiologically defective migration of muscle and nerve cell precursors to the diaphragm during its formation is considered the cause of CDH. The diaphragm develops anteriorly as a septum between the heart and liver, and then grows posteriorly. Final closure is at the left Bochdalek foramen between 8 and 10 weeks gestational age (GA). Bowel migrates from yolk sac to abdominal cavity at 10 weeks. If bowel arrives before the foramen closes then hernia can occur.[73]

Many newborn babies affected by CDH die because of respiratory insufficiency caused by pulmonary hypoplasia.[72] Prenatal intervention percutaneous fetal endoscopic tracheal occlusion by a balloon may be offered in those selected fetuses with CHD that have a predicted poor outcome. The aim of this procedure is to reverse the key determinant of survival—pulmonary hypoplasia. The outcome can be predicted by the gestational age at birth, the lung size before and after balloon placement, and whether the balloon has been removed prenatally. Currently, the added value of prenatal intervention is being investigated in the tracheal occlusion to accelerate lung growth (TOTAL) European and North American trial.[72] High mortality rate (50-80%) of the newborns with CHD suffering severe respiratory insufficiency at birth was significantly reduced by recent improvements of newborn transportation, breathing assistance and intensive care. Introduction of extracorporeal membrane oxygenation (ECMO) enables buying time for further lung growth and maturation. Survival rate is improved if hernia repair is delayed to allow resolution of early pulmonary insufficiency and acute pulmonary hypertension.[74]

A subset of fetuses likely to die in the postnatal period is eligible for a fetal intervention that can promote lung growth. Two randomized trials have shown that fetal surgery using open anatomical repair or tracheal occlusion via hysterostomy has no benefit. Since then, a percutaneous fetoscopic technique has been introduced, which has been shown to be safe and seems to improve survival when compared to historical controls.[72,75] *In utero* fetoscopic treatment by means of tracheal balloon occlusion (FETO) obstructs normal egress of lung fluid, hereby increasing transpulmonic pressure, to create large fluid filled lungs which are supposed to improve lung growth. Lack of lung expansion 2 to 7 days after tracheal occlusion is considered poor prognostic sign.[75]

Postnatal treatment of neonate with suspected CHD is very important because ventilation with bag and mask can cause severe damage to the hypoplastic lungs, and acute shift of the mediastinum by inflating stomach, causing further reduction of survival rates. Immediate endotracheal intubation together with orogastric tube insertion is the method of choice for the resuscitation of those newborns with life-threatening congenital defect.[74]

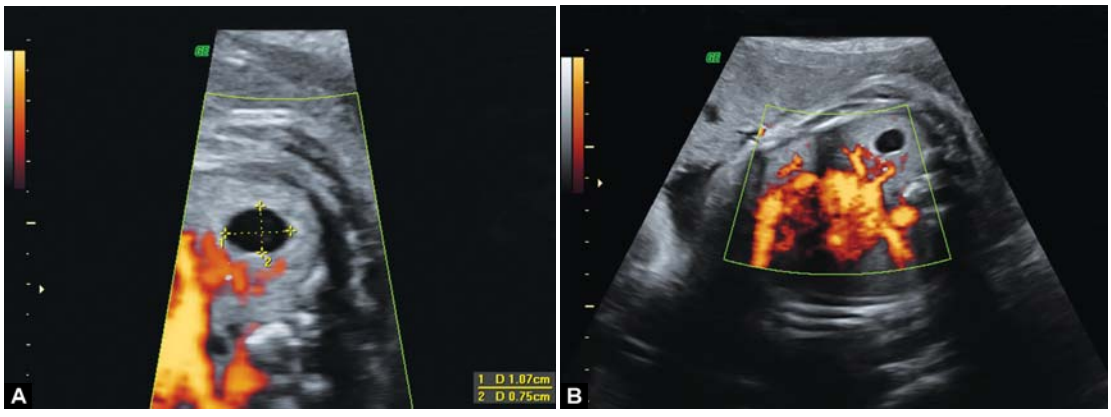
Congenital Pulmonary Anomalies

Congenital cystic adenomatoid malformation (CCAM) and bronchopulmonary sequestration (BPS) are major embryonic pulmonary developmental anomalies.[76,77] Congenital cystic lesions of the lung in children are uncommon but potentially life-threatening and warrant an urgent diagnostic work up. Pulmonary sequestration (PS), CCAM, congenital lobar emphysema (CLE), and bronchogenic cyst (BC) (prenatal finding Figs 21A and B) are the four major congenital cystic lesions, but they share similar embryologic and clinical characteristics. A meaningful percentage of CCAM joins to PS and CLE; instead the BC is generally isolated.[76,77]

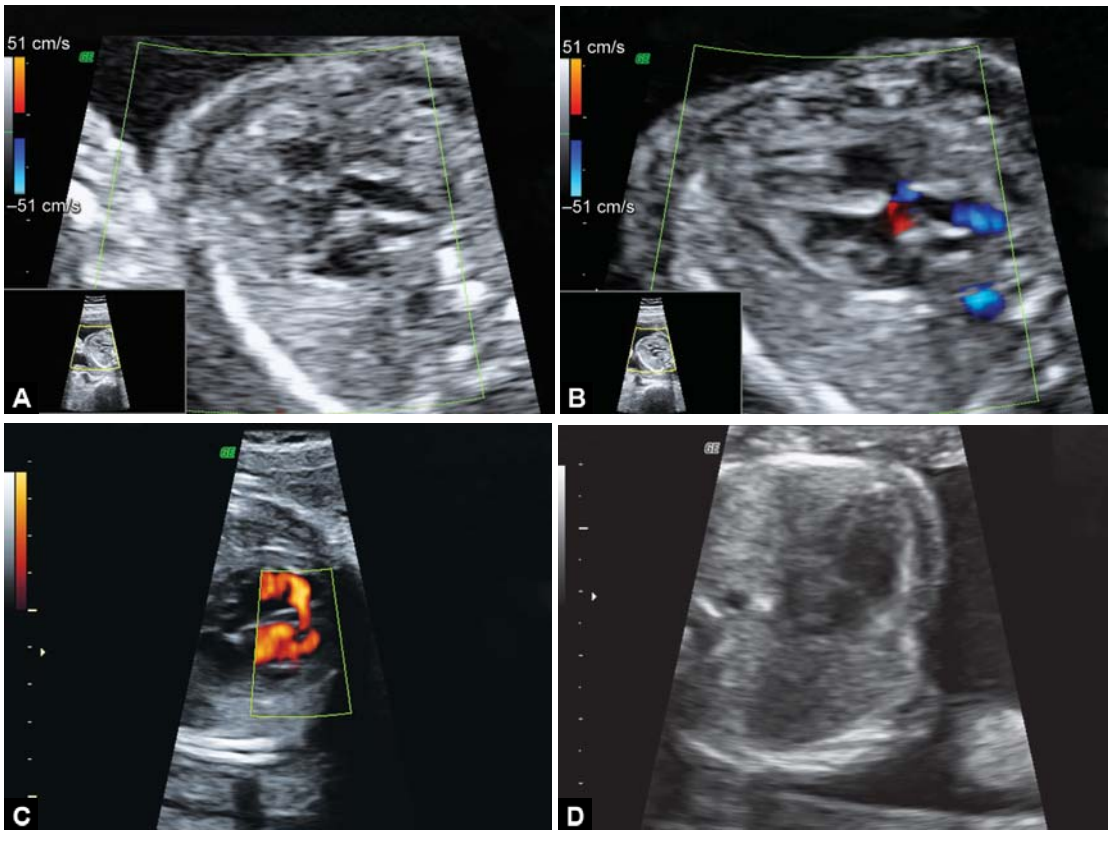
The treatment of these lesions is surgical: CCAM (type I-II) and CLE should be treated promptly in newborns for respiratory distress and pneumothorax, early surgical resection within 1 month of age is safe in symptomatic patients. CCAM (type II) and BC become symptomatic gradually and expose to degenerative risk; intralobar PS generally becomes symptomatic and surgery prevents the risk of infections. Extralobar PS and the asymptomatic BC are not exempted by surgical approach whenever, accidentally described as masses of uncertain nature. Asymptomatic cysts in children should be resected, to avoid later complications of the cysts, which could make operation more difficult. Conservative anatomic resections should be attempted to preserve functional lung tissue. Careful histological examination of the resection specimen is mandatory to identify occult malignancy.[76,77]

Congenital Heart Defects

CHD have an overall incidence of about 1% in live-born infants, and account for 20% of all stillbirths and 30% of neonatal deaths due to congenital anomalies. The prevalence rate in Europe is 80.62 per 10,000 of which 20.15 are severe



Figs 21A and B: Bronchogenic lung cyst: (A) 2D, (B) power Doppler assessment



Figs 22A to D: (A) Membranous ventricular septal defect (VSD), (B) color Doppler: membranous ventricular septal defect (VSD), (C) power Doppler: muscular VSD, (D) hypoplastic left heart syndrome (four chamber view)

CHD. The etiology of CHD includes maternal diseases, such as diabetes mellitus, phenylketonuria, exposure to substances (anticonvulsants, lithium), infections (parvovirus, rubella), chromosomal anomalies (trisomies 21 and 18) and specific mutant gene defects. However, there are many unknown causes. The for aneuploidy of the fetus with CHD is 30%.[78-80] The recurrence risk of cardiac anomalies in the absence of a known genetic syndrome is 2 to 4%, and with two previously affected siblings it is 10%.[80] Major CHD have an estimated prevalence of 2 to 4 per 1,000 live births and are either lethal or require surgical repair or intervention within the first year of life.[80] The division of the heart into a four-chamber structure is achieved by 8 weeks of gestation. It was possible 16 years ago at gestational age of 13 to 15 weeks using a high-resolution transvaginal transducer to obtain satisfactory images of the four-chamber view and the outflow tracts in the majority of fetuses (Figs 22A to D prenatal diagnosis of congenital heard defects).[81]

Management of Surgically Correctable Fetal Anomalies

Prenatal Management

The goal is to offer noninvasive screening for fetal malformations and fetal aneuploidy (trisomy 13, 18, 21) to all pregnant women. Invasive prenatal diagnosis would be offered to women who screen above a set risk cut off level on noninvasive screening or to pregnant women whose personal, obstetrical, or family history places them at increased risk.[82] Currently available noninvasive screening options include maternal age combined with one of the following: (1) First-trimester screening (nuchal translucency, maternal age, and maternal serum biochemical markers), (2) Second-trimester serum screening (maternal age and maternal serum biochemical markers), or (3) 2-step integrated screening, which includes first- and second- trimester serum screening with or without nuchal translucency (integrated prenatal screen, serum integrated prenatal screening, contingent and sequential).[82] We found useful recommendations from Canada which are given as citation.[82]

1. All pregnant women in Canada, regardless of age, should be offered, through an informed counseling process, the option of a prenatal screening test for the most common clinically significant fetal aneuploidies in addition to a second-trimester ultrasound for dating, assessment of fetal anatomy, and detection of multiples (level of evidence: I-A).
2. Counseling must be nondirective and must respect a woman's right to accept or decline any or all of the testing or options offered at any point in the process (III-A).
3. Maternal age alone is a poor minimum standard for prenatal screening for aneuploidy, and it should not be used a basis for recommending invasive testing when noninvasive prenatal screening for aneuploidy is available (II-2A).
4. Invasive prenatal diagnosis for cytogenetic analysis should not be performed without multiple marker screening results except for women who are at increased risk of fetal aneuploidy (a) because of ultrasound findings, (b) because the pregnancy was conceived by *in vitro* fertilization with intracytoplasmic sperm injection, or (c) because the woman or her partner has a history of a previous child or fetus with a chromosomal abnormality or is a carrier of a chromosome rearrangement that increases the risk of having a fetus with a chromosomal abnormality (II-2E).
5. At minimum, any prenatal screen offered to Canadian women who present for care in the first-trimester should have a detection rate of 75% with no more than a 3% false-positive rate. The performance of the screen should be substantiated by annual audit (III-B).
6. The minimum standard for women presenting in the second-trimester should be a screen that has a detection rate of 75% with no more than a 5% false-positive rate. The performance of the screen should be substantiated by annual audit (III-B).
7. First-trimester nuchal translucency should be interpreted for risk assessment only when measured by sonographers or sonologists trained and accredited for this service and when there is ongoing quality assurance (II-2A), and it should not be offered as a screen without biochemical markers in singleton pregnancies (I-E).
8. Evaluation of the fetal nasal bone in the first-trimester should not be incorporated as a screen unless it is performed by sonographers or sonologists trained and accredited for this service and there is ongoing quality assurance (II-2E).
9. For women who undertake first-trimester screening, second-trimester serum alpha fetoprotein screening and/or ultrasound examination is recommended to screen for open neural tube defects (II-1A).
10. Timely referral and access is critical for women and should be facilitated to ensure women are able to undergo the type of screening test they have chosen as first-trimester screening. The first step of integrated screening (with or without nuchal translucency), contingent or sequential screening are performed in an early and relatively narrow time window (II-1A).
11. Ultrasound dating should be performed, if menstrual or conception dating is unreliable. For any abnormal serum screen calculated on the basis of menstrual dating, an ultrasound should be done to confirm gestational age (II-1A).
12. The presence or absence of soft markers or anomalies in the 18 to 20-week ultrasound can be used to modify the a priori risk of aneuploidy established by age or prior screening (II-2B).
13. Information, such as gestational dating, maternal weight, ethnicity, insulin-dependent diabetes mellitus, and use of assisted reproduction technologies should be provided to the laboratory to improve accuracy of testing (II-2A).
14. Health care providers should be aware of the screening modalities available in their province or territory (III-B).

15. A reliable system needs to be in place ensuring timely reporting of results (III-C).
16. Screening programs should be implemented with resources that support audited screening and diagnostic laboratory services, ultrasound, genetic counseling services, patient and health care provider education, and high quality diagnostic testing, as well as resources for administration, annual clinical audit and data management. In addition, there must be the flexibility and funding to adjust the program to new technology and protocols (II-3B).

In order to optimize fetal outcome, there should be an interdisciplinary approach, including specialists in maternal-fetal medicine, neonatology, genetics, pediatric surgery and pediatric cardiology.[83-85] Social work services may provide important support to the family before as well as after birth. Such team approach is the best way to address the important issues of where, when, and how the infant should be delivered, as well as the role of invasive fetal therapy.[85]

Postnatal Counseling and Management

Congenital anomalies are among leading causes of infant mortality (Fig. 23) and an important contributor to childhood and adult morbidity. It is estimated that about 20 to 30% of neonatal deaths could be attributed to major congenital malformations.[86] Major congenital anomalies are abnormalities which are severe enough to reduce life expectancy or compromise normal function.[6] If major malformations cause stillbirth or infant death in more than 50% of cases, they are considered lethal. If newborn infant with major malformation can not survive without medical intervention, than malformation is considered severe.[6]

Fetuses and neonates with congenital anomalies can be divided into six groups:[87]

1. Those who have the potential for total recovery;

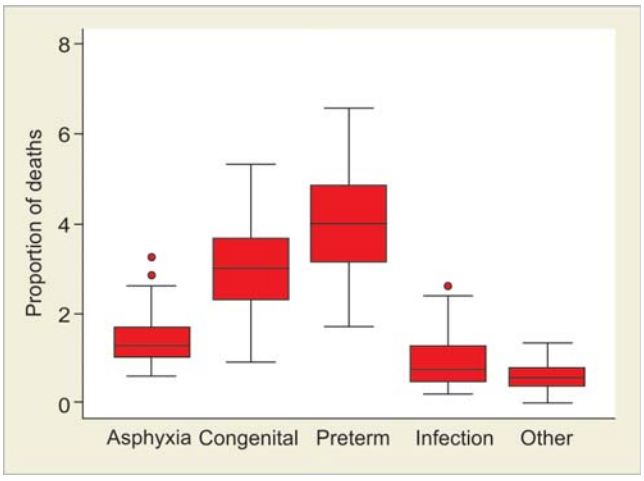


Fig. 23: Box plots showing the proportional distribution of causes of neonatal mortality for the vital registration data (44 countries)[86]

2. Those with anomalies that would allow for a nearly normal life;
3. Those with malformations requiring permanent supervision and/or medical care;
4. Those with somatic rest defect and subnormal mental development;
5. Those with serious somatic and mental damage; and
6. Those with anomalies that are incompatible with life.

The physician should lower the anxiety of the parents, should follow the morals of a civilized society, should act according to the law, and finally, should convince himself to be a solution to a problem and not to be a cause of any.[87]

According to the American Academy of Pediatrics, there are three possibilities concerning the treatment with intensive care in decision-making process based on the infant's prognosis:[88]

- The intensive care is indicated, if survival is likely and the risk of severe morbidity is low.
- The intensive care is not indicated, if the survival is not likely and would be accompanied by severe unacceptable morbidity and suffering.
- In some cases the situation could be in between those two situations and prognosis is not certain, but very likely to be very poor. In that situation parental desires should determine the treatment approach.

In the first situation of 'normality', where child affected with deformation is interpreted as 'normal child', which means that the disorder is curable and the infant can lead a normal life thereafter. This group of infants includes those with single defects, such as cleft lip, some congenital heart defects, pyloric stenosis, hexodactyly, etc. Parents should be informed that the child is normal, with a small problem which is curable and can be easily and adequately solved. The statement that the infant is normal is very important as well as the information that the condition is correctable. Such approach to the counseling can help parents with realistic acceptance of the problem. In case when physicians fail to make acceptance of infant's condition, than relations between parents and their child may develop in two undesirable directions: Rejection or overprotection.[88]

In the second group when dealing with severely malformed infant-like anencephaly, severe neural tube defects, hydranencephaly, holoprosencephaly, the trisomy 18 and 13 syndrome, the 4p-syndrome, the Meckel-Gruber or Potter syndrome, the physician must give parents the option of no medical intervention.[88] All mentioned disorders are severely limiting infant's capacity to survive and function even with full medical support including intensive care.[88] The doctor should say that even if the life will be

preserved for some time, the baby has no capacity for continued survival. In the case of intervention the functional capability of the baby will be very limited.[88] The physician should state that the kindest approach to the infant is that of no medical intervention, and ask for the permission for such an approach. In such way parents are informed about the basic course of the problem, helped to interpret the situation, and given the option of no medical intervention in the best interest of the child.[88] They should be aware that the baby will be provided with compassionate care and that suffering will be minimal. Sometimes when parents are faced with end-of-life decisions, they will need psychological or social worker help to overcome their problem.[89] Parental complaints are more likely to occur due to misunderstanding, confusion and tension among staff and parents as a result of a failure to have in place or to implement agreed protocols.[90]

When dealing with intermediate situation, the counseling of the parents is very complicated and individualized, depending on the nature and the severity of the handicap. The accurate information is again very important, including facts relative to the cause of the problem, the usual range of functional and other limitations, and what can be done in order to help the child to adapt to the problem. In this situation the parents should be helped to accept their child with the problem, informing them that there are other families with the same or similar problems.[89-91]

Generally, this counseling process is very hard working and time consuming. Any medical professional who is counseling parents of malformed newborns should be aware that parents may need several meetings to accept the situation and to understand it.[89-91] Sometimes the same information rephrased is well-accepted, and on another occasion the parents do not even notice the problem. Some parents are almost incapable of accepting a handicapping disorder of their child, while the others can develop deep parental love for a malformed and handicapped child.[88,89,91]

CONCLUSION

Antenatal diagnosis together with the improvement of surgical and postoperative care of newborns with severe surgically correctable congenital anomalies enabled better survival of live-born infants and more effective prenatal prevention in case of preventable anomalies. Nevertheless, congenital malformations continue to be important cause of perinatal mortality rate in developed and in developing countries. In order to optimize fetal outcome, there should be an interdisciplinary approach, including specialists in maternal-fetal medicine, neonatology, genetics, pediatric surgery, pediatric cardiology and neurosurgery. More attention should be paid to the primary, secondary and tertiary prevention of surgically correctable congenital anomalies whenever possible.

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ABOUT THE AUTHORS

Sanja Zaputovic (Corresponding Author)

Department of Obstetrics and Gynecology, Medical School University of Zagreb, Clinical Hospital 'Sveti Duh', Sveti Duh 64, 10000 Zagreb Croatia, Phone: 00385-1-3712316, Fax: 00385-1-3745534 e-mail: sanjazaputovic@yahoo.com

Milan Stanojevic

Department of Obstetrics and Gynecology, Medical School University of Zagreb, Clinical Hospital 'Sveti Duh', Zagreb, Croatia

Ulrich Honemeyer

Department of Obstetrics and Gynecology, Welcare Hospital, Dubai UAE

Tanja Turudic

Department of Obstetrics and Gynecology, Medical School University of Zagreb, Clinical Hospital 'Sveti Duh', Zagreb, Croatia

Asim Kurjak

Department of Obstetrics and Gynecology, Medical School University of Zagreb, Clinical Hospital 'Sveti Duh', Zagreb, Croatia