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Congenital Malformations in Perinatal Autopsy with Special Emphasis on Syndromes: A Study of 100 Cases

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Abstract

Background: Perinatal autopsy is an important tool to look out for various congenital malformations and its impact on perinatal morbidity and mortality. Though radiological intervention has reduced the incidence, perinatal autopsy is essential for confirmation of diagnosis and to look out for additional information.

Objectives: To emphasize the importance of perinatal autopsy in diagnosing and confirmation of congenital malformations and to compare it with prenatal clinical findings.

Materials and Methods: The present study comprises 100 consecutive perinatal autopsies after approval from the Institutional Ethics Committee. Prior consent from parents were taken and autopsy was done using standard protocols. Prenatal radiological findings were compared with the autopsy findings wherever available.

Results: Out of 100 perinatal autopsies studied, 45 cases shows congenital anomalies, which included 26 males, 13 females and 6 cases with ambiguous genitalia. Among the 45 cases, 21 were therapeutic terminations, 15 still births and 09 cases of Intrauterine Deaths. The most common timing of therapeutic termination encountered was between 12–20 weeks. Out of 45 cases, anomalies were present in 16 cases of central nervous system (CNS), 5 of lung, 4 from kidney, 2 of heart, 7 cases of syndromes, 5 cases with multisystem involvement and 5 cases of miscellaneous group.

Conclusion: Perinatal autopsy is essential to confirm congenital malformations and to look for additional findings. Also, it helps to counsel the parents to prevent such complications in future pregnancy.

Keywords: Fetal autopsy; Still birth; Sirenomelia; Meningomyeloencephalocele.

Introduction

Congenital malformations remains one of the most common cause of perinatal morbidity and mortality accounting for approximately 10–15%, but actual numbers may vary widely due to under reporting of cases in India.[1]

Congenital malformations is the least focused areas of disease surveillance as other important rampant issues like low birth weight, prematurity, sepsis and infections are the leading causes of perintal mortality in India. In western countries congenital malformations are the leading cause of infant mortality, due to high standards in accurate reporting, proper and regular antenatal check-ups and carrying out perinatal autopsy of demise fetuses.[2,3]

The present study was carried out to emphasize the role of perinatal autopsies, which can be studied to prevent futher perinatal mortalities. In spite of recent advances in antenatal diagnostic modality, fetal autopsy plays a very vital role in the confirmation of clinical diagnosis and also to look for additional associated malformations or lesions and to report incidental findings. This helps in

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counselling of the parents and to prevent the fetal congenital anomalies in future pregnancies.[3]

Materials and Methods

This study was carried out in department of pathology, over a period of one year from January 2018 to December 2018 and 100 consecutive autopsies were studied. Approval from the Institutional Ethics Committee was obtained prior to commencement of studies. Informed consent from the parents were taken prior to autopsy.

All fetuses with gestational age of 12 weeks to 39 weeks were included in the study and all autolysed fetuses and fetus with gestational age less than 12 weeks and more than 39 weeks were excluded. Each fetus was examined according to standard protocol and external and internal examination was done. The autopsy protocol included the removal of thoracic, cervical, abdominal and pelvic organs en block and subsequently dissected into organ blocks.

Results

Out of 100 perinatal autopsies studied, 45 cases shows congenital anomalies, which included 26 males, 13 females and 6 cases with ambiguous genitalia. Among the 45 cases, 21 were therapeutic terminations, 15 were still births, 09 cases of Intrauterine Deaths. The most common timing of therapeutic termination encountered in this study was between 12–20 weeks (Table 1).

Table 1: Gestational Age Wise Distribuation of Congenital Anomalies Cases.

Gestational age (in weeks)	Number of cases	Percentage (%)
< 20	19	42.22%
21- 25	11	24.45%
26-30	06	13.33%
31-36	07	15.56%
>36	02	04.44%
Total	45	100%

Table 2: Birth Weight Wise Distribution of Cases.

Birth weight (g)	Total cases	Percentage (%)
<500	20	44.44%
500-1000	13	28.89%
1001-2000	05	11.11%
2001-3000	06	13.34%
>3000	01	02.22%
Total	45	100%

Each case was classified on the basis of gestational age and birth weight. Congenital malformations were common between 12–20 weeks and birth weight range was less than 500 gms (Table 2). Out of 45 cases, congenital anomalies was most common from CNS system which includes 16 cases. Other cases were 5 from lung, 4 from kidney, 2 of heart, 7 cases of syndromes, 5 cases with multisystem involvement and 5 cases were of miscellaneous group. Multiple congenital anomalies were seen in most of the syndromes (Table 3).

Table 3: System Wise Distribution of Cases.

Congenital anomalies	Associated anomalies	Number of Cases (n=45)
1. Central Nervous System Defects		**16**
Hypoplastic cerebellum with absent vermis		1
Absent corpus collosum with ventriculomegaly		1
Absent corpus collosum with colpocephaly		1
Corpus collosum agenesis with spina bifida	cleft lip	1
Anencephaly with spinabifida		1
Anencephaly	fused jaw and chest	1
Anencephaly		3
meningomyeloence phalocele		1
meningoencephalocele with dilated ventricle	lemon skull	1
meningocele		2
Meningomyelocele with spina bifida		1
Sacrococcygeal teratoma		1
2. Genito-Urinary Defects		**04**
Right Renal cystic dysplasia	Absent left kidney	1
Bilateral polycystic kidney		1
Left renal agenesis	Absent left adrenal	1
Bilateral renal agenesis	Absent ureter and bladder	1
3. Lung Defects		**05**
Congenital cystic adenoid malformation		
Type I	Multicystic renal dysplasia and low set ears	1
CCAM - Type II	Single umbilical artery	2
CCAM - Type III		1
Lung Atelectasis		1
4. Heart Defects		**02**
• Over-riding of aorta with pulmonary artery stenosis		1
• Tetralogy of Fallot with achondroplasia		1

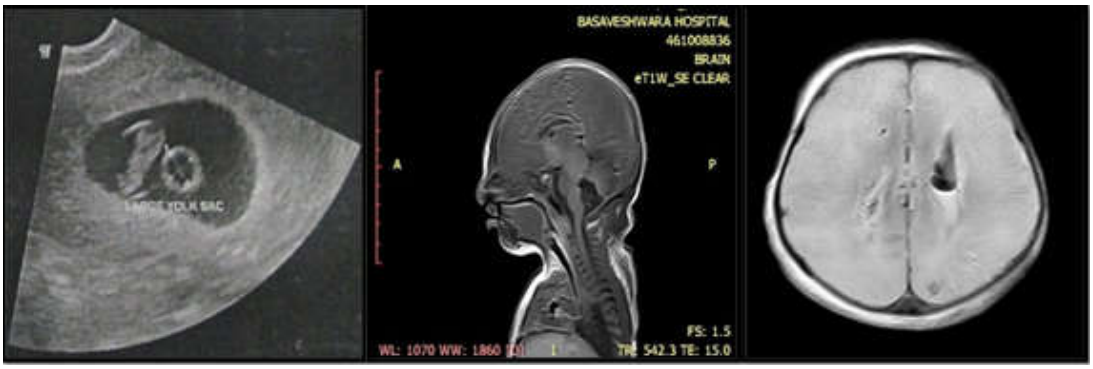
4. Multiple Congenital Anomalies		**05**
Low set ear and cleft lip	absent stomach	1
Absent left lung with hypoplastic left ventricle	mitral valve atresia	1
Anencephaly with encephalocele		1
Cleft palate with microtia and low set ears	polycystic kidney meningocele with hemangioma	1
Hydrocephalus with absent corpus collosum	club foot	1
5. Syndromes		**07**
Potters syndrome with sirenomelia		1
Edward syndrome		1
OEIS COMPLEX		1
Holoprosencephaly with hypoplastic heart syndrome		1
Dandy walker syndrome		1
Kleppel feil syndrome		1
Meckel gruber syndrome		1
6. Miscellaneous		**05**
Cystic hygroma		3
Omphalocele		1
CMV inclusions in Adrenal gland		1

In CNS, most common anomaly was anencephaly followed by meningocele. Rare case like absent corpus collosum with colpocephaly was also encountered. Anomalies of lung includes congenital cystic adenomatoid malformation (CCAM) type I, II and III and lung atelectasis. Two cases of heart malformation includes pulmonary stenosis with over-riding of aorta and Tetralogy of Fallot. Renal anomalies includes polycystic kidney disease and renal cystic dysplasia. One case of bilateral renal agenesis associated with absent ureter and urinary bladder was also encountered.

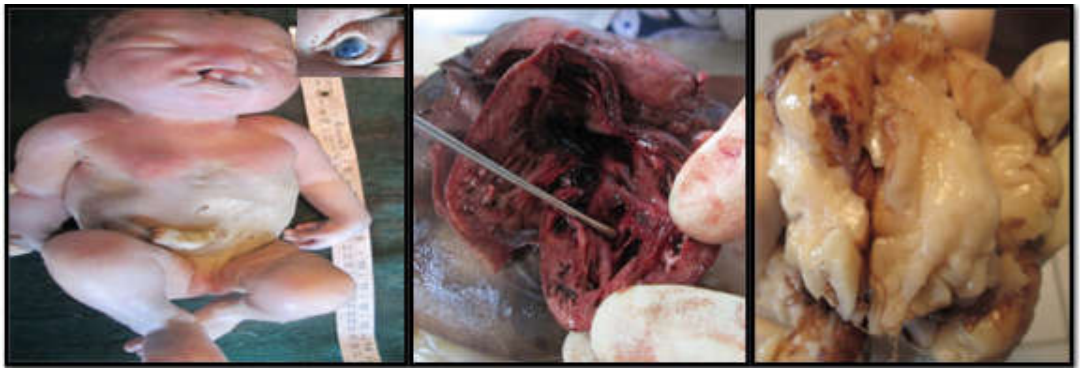
Multi-system involvement with congenital malformations include cases like absent lung with hypoplastic left ventricle and mitral valve atresia and another case like anencephaly with encephalocele associated with polycystic kidney. One case of hydrocephalus with absent corpous collosum and clubfoot was also reported.

Interesting cases of syndromes include each case of Potter's syndrome with sirenomelia, Edward syndrome, OEIS complex, Dandy Walker syndrome, Holoprosencephaly with hypoplastic left heart syndrome, Klippel Feil syndrome and Meckel Gruber syndrome.

Miscellaneous cases includes three cases of cystic hygroma, one case of omphalocele and one case showing cytomegalovirus like inclusions in adrenal and calcification in foetal liver.

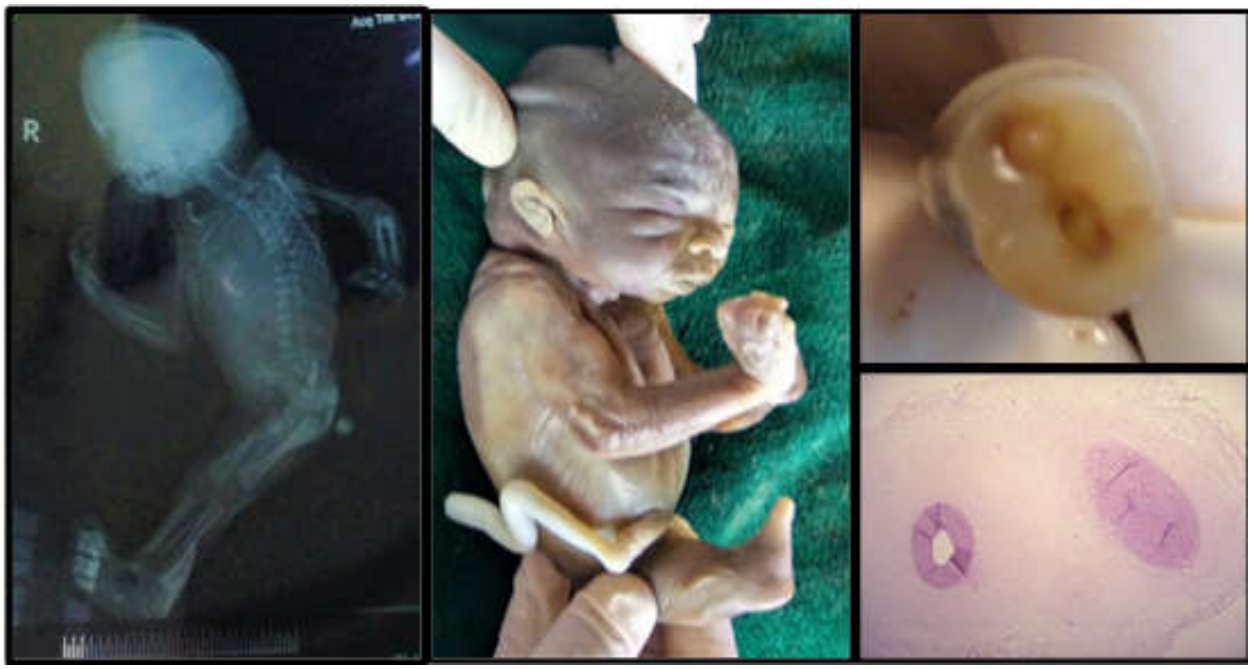


Large Yolk Sac | Hypoplastic Cerebellum | Corpus Callosum Agenesis



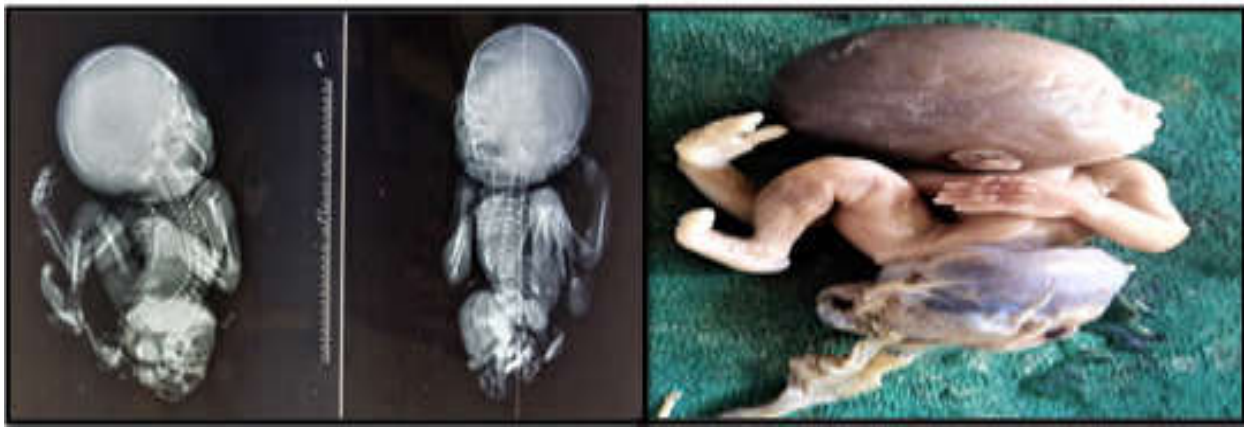
Cleft Lip and Cleft Palate with Congenital Glaucoma | Hypoplastic Left Heart | Corpous Callosum Agenesis

Fig. 1: Dandy Walker Syndrome.



X-Ray Showing Fused Lower Limbs | Hypoplastic Lower Limbs | Umbilical Cord with two Vessels

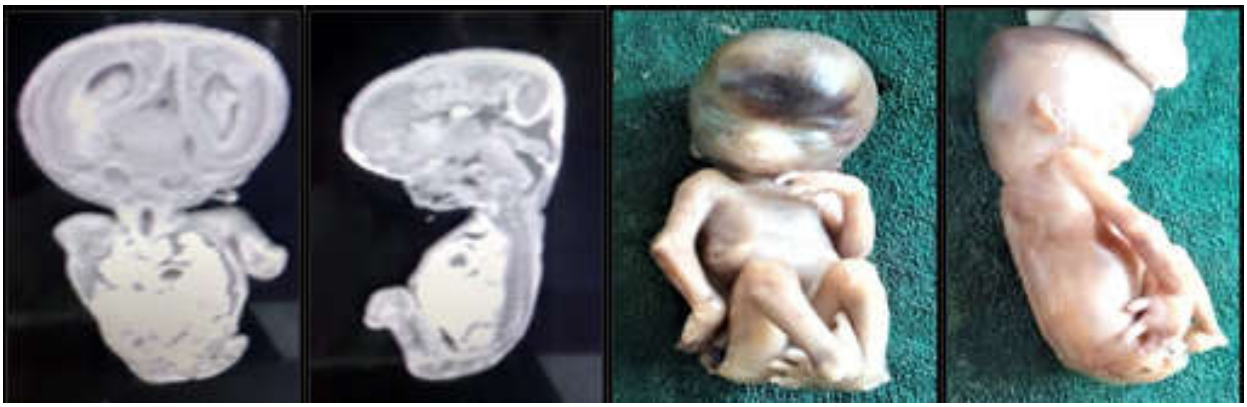
Fig 2: Sirenomelia (Mermaid Syndrome).



X-Ray Showing Omhalocele with Curved Spine | Grossly Protusion of Abdominal Contensts

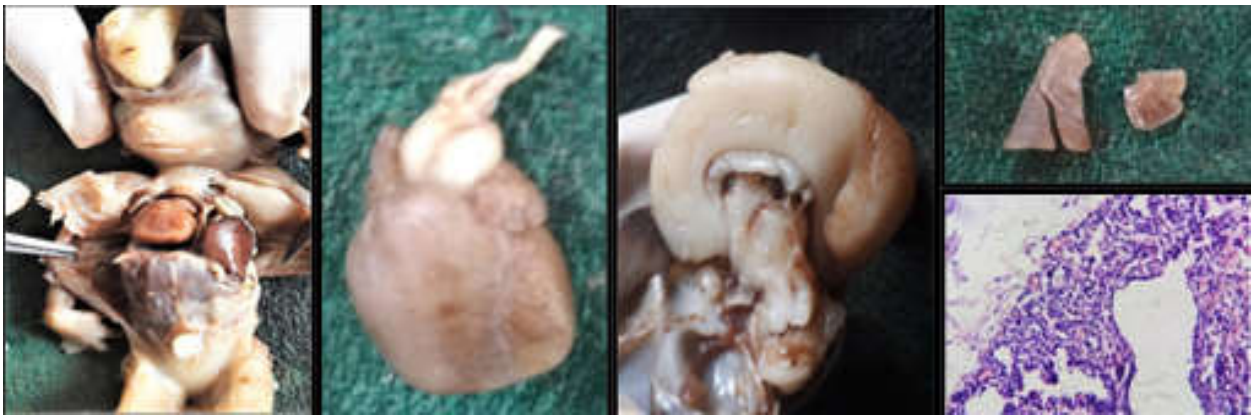
Hypoplastic Lower Limb and Imperforate Anus | Dextrocardia

Fig. 3: OE is Complex.



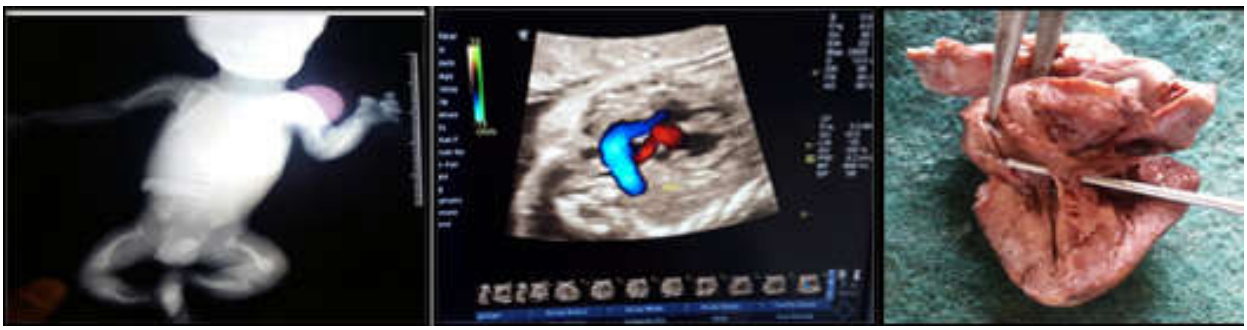
Mri- Blake Pouch Cyst, Hypoplastic Vermis, Diaphragmatic Hernia and Depressed Nasal Bone

Gross-Pointed Frontal Bones, Flat Occiputlow Set Ears, Hyertelorism, Shield Chest and Rocker Bottom Foot



Diaphragmatic Hernia | Dilated Pulmonary Trunk | Hypoplastic Vermis | Hypoplastic Left Lung

Fig. 4: Edward Syndrome.



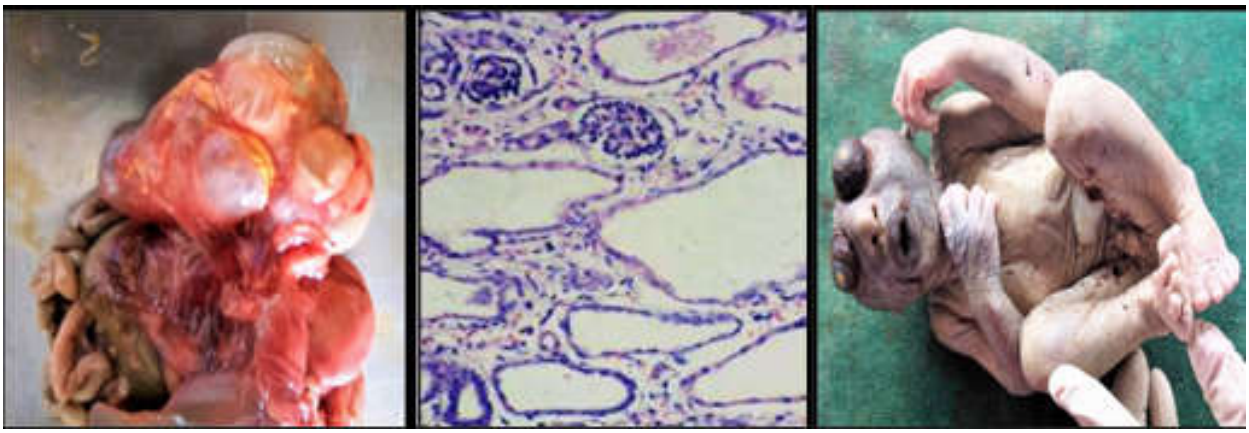
X-Ray showing Achondroplasia with Sqauring of Pelvis and Short Femur

Ventricular Septal Defect on Doppler and Gross

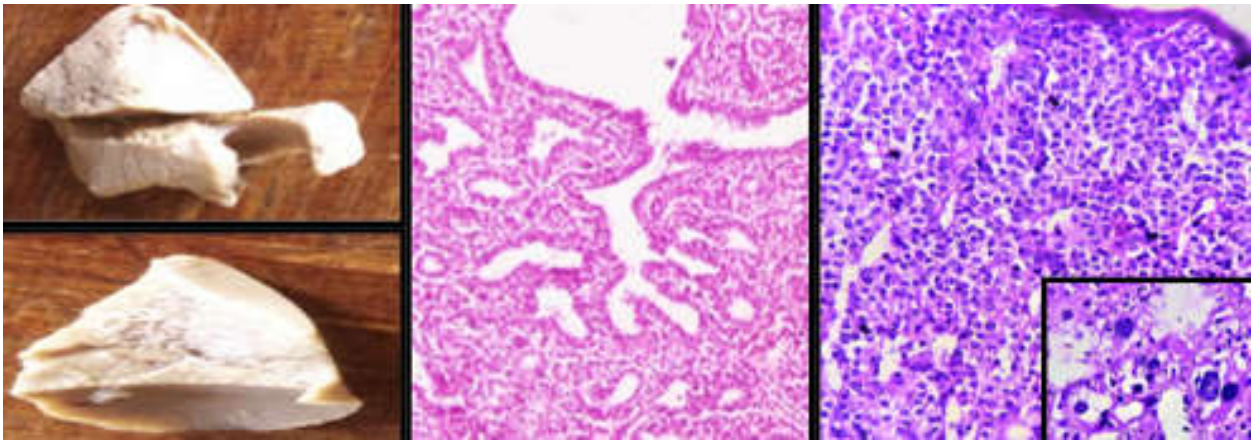
Over Riding of Aorta

Pulmonary Artery Stenosis

Fig 5: Tetralogy of Fallout with Achondroplasia



Gross and Microscopy of Polycystic Kidney Disease | Anencephaly



Gross and Microscopy of Congenital Cystic Adenomatoid Malformation Type-III | CMV Like Inclusions in Adrenal

Fig 6: Various Congenital Anomalies.

Discussion

Congenital anomalies constitute a major cause of perinatal morbidity and mortality . Perinatal autopsy plays an important role in diagnosing and confirming the various congenital malformations. In this study CNS malformations constitute the majority of the cases.[1,2]

One case of Dandy Walker syndrome was reported were 26 year female presented with 8 weeks of amenorrhaoe. On subsequent scans large yolk sac, cystic hygroma, cerebellum showing vermis agenesis, mega cistern magna, spina bifida and fetal hypoplastic left heart was noted. Grossly facial dysmorphic features, low set ears, congenital glaucoma, Cerebellar hypoplasia and ventricular septal defect was noted. (Fig. 1).

The Dandy – Walker complex is a rare congenital intracranial malformation that comprises a spectrum of abnormalities of the posterior fossa with cystic dilatation of the 4th ventricle, complete or partial agenesis of the cerebellar vermis and enlarged posterior fossa and mega-cisterna magna . The incidence being 1 in 30000.[4]

Another case of Mermaid syndrome / sirenomelia was reported were dead fetus of 26 weeks gestation with history of severe oligohydramnios and on USG, bilateral renal agenesis with hypoplastic lower limbs was observed and was confirmed on autopsy with umbilical cord showing two vessels.[5] (Fig. 2).

Serinomelia or Mermaid syndrome is a deadly birth defect in which the two lower limbs of the newborn are fused together . Incidence is 1 in 1 lakh births. It represents a severe developmental defect of the posterior axis caudal blastema and associated with agenesis or hypoplasia of diverse organs.[6]

One case of OEIS complex was also reported. Carey et al; in 1978 gave the name OEIS complex to a combination of defects comprising omphalocele, exstrophy of the cloaca , imperforate anus , and spinal defects. Incidence is 1 in 2 lakh births. Usually cases are sporadic but can be multifactorial like teratogenic exposure to alcohol, diazepam,

valproic acid, smoking, heparin, misoprostol, maternal history of diabetes and obesity. (Fig. 3) Chromosomal aberrations possibly associated are 47 XXX , 47 XXY, 45 XO / 46XX (mosaic) , Trisomy 18.[1,7]

One case of Edward syndrome were also seen, where history of primigravida with 18 weeks of gestation and II degree consanguineous marriage. On ultrasonography Posterior fossa shows absent vermis, blake pouch cyst, absent nasal bone, diaphragmatic hernia, dilated pulmonary artery, Absent ductus venosus, bilateral club foot, syndactyly and rocker bottom foot. MRI of the foetus was done before autopsy which shows Cystic lesion seen in posterior fossa suggestive of blake's pouch cyst and hypoplastic vermis . Cardia shifted to right side, strawberry skull, rocker bottom foot with congenital talipes equino verus (CTEV) bilaterally , and diaphragmatic hernia . On autopsy, grossly pointed head with flat occiput, low set ears , micrognathia , hpertelorism , shielded chest and rocker bottom foot was noted. On internal examination hypoplastic lung, diaphragmatic hernia with stomach and bowel loops protruding into thoracic cavity, two spleens (polysplenia), dilated pulmonary artery with absent ductus venosus was noted . The diagnosis was confirmed by kayotyping.[8]

Edward syndrome first reported in 1960 by John Hilton Edwards et al; is common chromosomal disorder due to the presence of an extra chromosome 18, either full, mosaic trisomy, or partial trisomy 18q. Karunakaran and Pai reported the first case in the Indian literature in 1967 . It is second most common autosomal trisomy syndrome after trisomy 21. The live born prevalence is estimated to be 1/6,000 - 1/8,000 births, but the overall prevalence is higher (1/2500–1/2600) due to the high frequency of foetal loss and pregnancy termination after prenatal diagnosis. The recurrence risk for a family with a child with full Trisomy -18 is about 1% and increases with increased maternal age.[9] (Fig. 4)

One case of Tetralogy of Fallot with acondroplasia was seen where primigravida presented with 28 weeks gestation and on antenatal scan short limb dysplasia, Tetralogy- of –Fallot and hypoplastic nasal bone was noted. Components in Tetralogy- of- Fallot includes infundibular pulmonic stenosis, ventricular septal defects, aortic valve dextroposition (overriding of aorta), and right ventricular hypertrophy. It constitutes 10% of congenital heart diseases and most common cyanotic heart disease with incidence of 1:4000 births (Fig 5).[10]

Other cases encountered in our study includes bilateral polycystic kidney disease, congenital cystic adenoid malformations of Type I , II and III of lung. Also seen was cytomegalovirus like inclusions in the adrenal gland possibly suggestive of TORCH infections in the mother. (Fig 6).[12, 13]

Conclusion

Perinatal autopsy plays a vital role in many ways. In a country like India where Government has taken many steps to decrease the perinatal morbidity and mortality, study of perinatal autopsies becomes more important for targeted approach.[11] The aim of perinatal autopsy is not only to confirm clinical and radiological diagnosis but to look for additional incidental findings. Autopsy findings along with genetic karyotyping will help in counseling the couples in future pregnancies and in minimizing the recurrences.

Acknowledgement: Nil

Conflict of Interest: Nil

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