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Study of Central Nervous System Malformations of Perinatal Autopsies

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ABSTRACT

Background: Congenital malformations remain a common cause of perinatal deaths accounting for 10-15% in developing countries like India. They are the most severe disorders of the central nervous system. Although antenatal screening for congenital anomalies has been improved over the years, fetal autopsy remains the gold standard for the identification and confirmation of congenital malformations. The present study emphasizes the importance of perinatal autopsy for understanding the cause of death and also conformation of the antenatal diagnosis of the spectrum of various congenital CNS malformations. Methods: We studied 644 perinatal autopsies conducted in our hospital. The duration of the study was 5 years, from 1^{st} August 2015 to 31^{st} July 2020 that included all perinatal autopsies with gestational age of 22 weeks to less than 7 days. Results: Out of 644 perinatal autopsies 125 cases (19.4%) had congenital anomalies, of which 62 cases (9.6%) showed CNS malformations. The most common CNS anomalies encountered were anencephaly 14 cases (22.6%) followed by 10 cases (16.1%) each of spina bifida and meningocele, and 8 cases (12.9%) of meningomyelocele. In the present study, 6 (9.7%) cases of CNS malformations were associated with known syndromes namely Edward syndrome, Potter's syndrome, and KlippelFeil syndrome. Along with CNS in 21 (33.9%) cases we observed associated malformations of other systems with 7 cases involving the musculoskeletal system, 3 cases involving the genitourinary system, and 5 (8.1%) cases showing multisystem involvement. Conclusion: Antenatal screening for congenital anomalies has been improved over the years. Even then fetal autopsy remains the gold standard for the identification and confirmation of congenital malformations. Understanding this gives valuable information that can be further helpful in the genetic counseling of the parents.

KEYWORDS: Perinatal autopsy, Central Nervous System, Congenital malformations, Anencephaly

INTRODUCTION

The frequency of developmental defects ranges from 2% to 3% of all fetuses, 30% of which are related to genetic disorders. Congenital anomalies are the most severe disorders of the central nervous system that account for 40% of deaths of all children in the first year of life and survivors they cause a variety of neurological disorders, mental retardation, or drug-resistant epilepsy. [1] In India, low birth weight, prematurity, sepsis, and infections are still the leading causes. [2]

Sonography is non-invasive, widely available, safe, and has high sensitivity in identifying CNS malformations, autopsy findings are essential to arrive at a definitive diagnosis. The spectrum of CNS malformations includes anencephaly, exencephaly, cranial meningocele, meningomyelocele, spina bifida, Arnold Chiari malformation, syringomyelia, prosencephalies, agenesis of corpus callosum, agenesis of the cerebellum, Dandy-Walker syndrome, congenital hydrocephalus etc. [3]The most common CNS malformation are neural tube defects (NTDs). The perinatal autopsy also helps in identifying any associated anomalies. [4, 5]

METHODOLOGY

This study was done in a tertiary care hospital, where 644 perinatal autopsies with the gestational age of 22 weeks to perinatal day 7 were conducted after obtaining informed consent from the parents. The study was done over a period of 5 years between August 2015 to July 2020. Autopsies were performed following standard protocols. All relevant clinical data were collected. Ethical committee clearance was obtained for the study.

RESULT

Of the total 644 perinatal autopsies, 62 (9.6%) cases showed involvement of CNS. The most common mode of death in perinatal autopsies with CNS malformations was intrauterine death accounting for 46 (74.3%) cases followed by termination. The birth weight of the fetuses ranged from

50g to 2750g. Out of the 62 cases, 32 cases were female showing slight female preponderance.

Diagnosis	No.	Percent
Anencephaly	14	22.6
Meningocele	10	16.1
Spina bifida	10	16.1
Meningomyelocele	8	12.9
Arnold Chairi malformation	3	4.8
Hydrocephalus	5	8.1
Absent corpus callosum	5	8.1
Colpocephaly	4	6.5
Dandy-Walker malformation	3	4.8
Ventriculomegaly	3	4.8
Spinal defect	2	3.2
Encephalocele	2	3.2
Iniencephaly	1	1.6
Schizencephaly	1	1.6
Sirenomelia	1	1.6

Table 1: Spectrum of CNS malformations in perinatal autopsies

The Spectrum also included a single case of Hypoplastic cerebellum, Hypoplastic vermis, Cerebellar agenesis, Choroid plexus cyst, Meningoncephalocele, Microcephaly, Sacrococcygeal teratoma, Dolicocephaly, Unilateral dilatation of occipital horns of lateral ventricle and Absent vermis accounting to1.6%. SeeTable 1.

In the present study, 6 (9.7%) cases of CNS malformations were associated with known syndromes namely Edward syndrome, Potter's syndrome, and Klippel-Feil syndrome (Table 2)

Along with CNS in 21 (33.9%) cases we observed associated malformations of other systems with 7 cases involving the musculoskeletal system, 3 cases involving the genitourinary system, and 5 (8.1%) cases showing multisystem involvement.

DISCUSSION

The major cause of fetal and neonatal deaths as well as disability cases worldwide are congenital malformations. The pattern and prevalence of congenital malformations vary over time and geographical location. These differences can be attributed to the complex interaction of known and unknown genetic and environmental factors like socio-cultural, racial, and ethnic factors. [6]

A significant number of congenital malformations cannot be determined by antenatal investigations such as Ultrasonography (USG), and maternal serum enzyme hormone assays, for which autopsies are a must. [6, 7]

In the present study, the incidence of congenital anomalies is 19.4% which correlated with Naik et al. [7]showing an incidence of 19.6%. The incidence of CNS anomalies in the present study is 9.6% which is closely correlated with the study conducted by Naik et al. [7] showing an incidence of 8.7%. The most common CNS malformation seen in the present study was Anencephaly (Figure 1); 14 cases (22.6%) which is comparable to other studies.

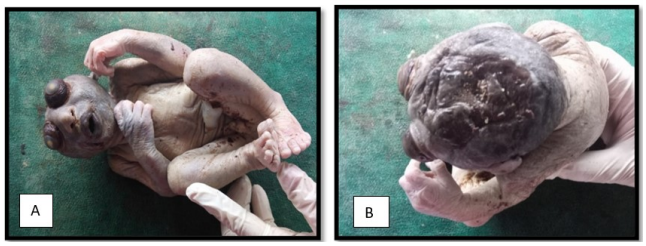

Figure 1: Anencephaly. A)Frontal view, B) Superior view: absent cranium

Other neural tube defects like spina bifida (10 cases), meningocele (10 cases), and meningomyelocele (1 case) were the common CNS malformations seen in the present study which is in accordance with the previous studies (Table 3).

The incidence of iniencephaly was observed to be 1.1% in a study conducted by Pinar et al. [8]Iniencephaly is a rare neural tube defect characterized by extreme retroflexion of the head with the absence of the neck due to spinal deformities. The incidence of iniencephaly is reported to be 1 in 65,000 births in India and is more common in female fetuses.Figure 2 [9]In our study, we encountered one case of iniencephaly accounting for 1.6%. It was associated with a diaphragmatic hernia, poly spleen, bilateral club foot, and single umbilical artery.

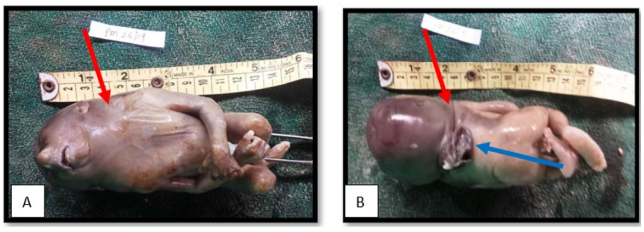

Figure 2: Iniencephaly. A) Absent anterior neck, B)Low hairline (red arrow) and meningomyelocele (Blue arrow)

Dandy–Walker malformation (DWM)Figure 4 is a rare intracranial congenital abnormality that affects the cerebel-

Syndrome	No.	CNS malformations	Other defects
Edward's syndrome	2	Hypoplastic vermis	Strawberry head, low set ears, micrognathia, hypertelorism, shield chest, rocker-bottom foot, hypoplastic lung, diaphragmatic hernia, polysplenia, dilated pulmonary artery with absent ductusvenosus. Figure 3
		Ventriculomegaly	Rocker bottom foot, overlapping of fingers, placental insufficiency.
Klippel Feil Syndrome	2	Meningocele Meningomyelocele	Low hairline and fused neck.
Potter's Syndrome	2	Spina bifida	Cardia shifted to right, hypoplastic left lung, diaphragmatic hernia, the left kidney is hypoplastic.
		Sirenomelia	Depressed nose, low set ears, predominantly increased infraorbital folds, imperforated anus, absent external genitalia, single umbilical artery.

Table 2: CNS malformations associated with syndromes

Type of CNS anomaly	Pinar et al [8] (1998) n=363	Siddesh et al [4] (2017) n=243	Present study n= 62
Anencephaly	86(15.2)	28(11.5)	14(22.6)
Meningocele	31(8.5)	-	10(16.1)
Spina bifida	34(9.3)	69(28.3)	10(16.1)
Meningomyelocele	25(6.9)	-	8(12.9)
Absent corpus callosum	15(4.13)	13(5.3)	5(8.1)
Hydrocephalus	45(12.4)	-	5(8.1)
Dandy-Walker malformation	7(1.9)	23(9.4)	3(4.8)
Arnold Chairi malformation	18(4.9)	-	3(4.8)
Ventriculomegaly	-	63(25.9)	3(4.8)
Encephalocele		19(7.8)	2(3.2)
Choroid plexus cyst	5	4(1.6)	1(1.6)
Iniencephaly	4(1.1)	11(4.5)	1(1.6)
Cerebellar agenesis	3(0.8)	-	1(1.6)
Meningoncephalocele	16(4.4)	-	1(1.6)
Microcephaly	24(6.1)	3(1.3)	1(1.6)

Table 3: Spectrum of CNS anomalies compared with other studies

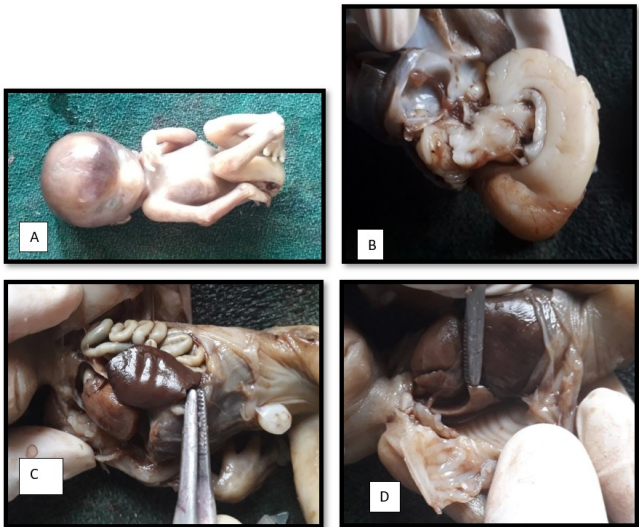

Figure 3: Edward syndrome. A) Strawberry head, lowset ears, micrognathia, hypertelorism, shield chest with long fingers, rockerbottom foot, B) Brain dissectionshowing hypoplastic vermis, C) Diphragmatic hernia, D) Hypoplastic lung

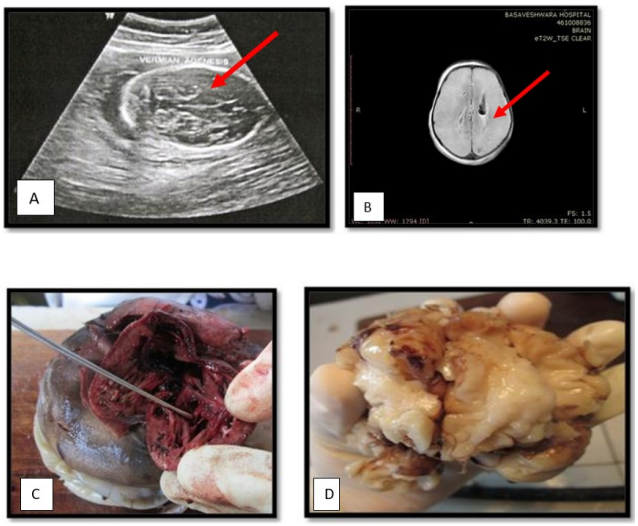

Figure 4: Dandy Walker malformation. A) USG: Vermian-agenesis (red arrow), B) Corpus callosum agenesis (Racing car sign), C) Hypoplastic left heart, D) Corpus callosum agenesis.

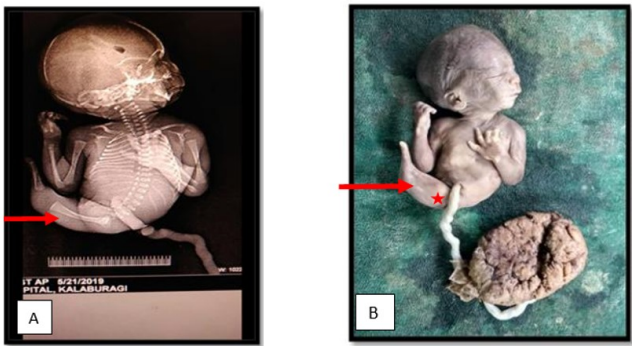

Figure 5: Sirenomelia with Potter's syndrome. A) X-Ray :Hypoplastic lower limb, Sacral agenesis, B) Hypoplastic lower limb (arrow), Absentexternal genitalia (asterisk)

lum and some of its components; particularly the cerebellar vermis, and fourth ventricle, and is characterized by an enlarged posterior fossa. [10]DWM occurs as an autosomal dominant inherited disorder and occurs in one in 25000 – 35000 pregnancies. [10]

DWM is often associated with other CNS and/or extra-CNS abnormalities, with a high frequency of total or partial callosal defect, focal polymicrogyria, heterotopias, and malformed or ectopic inferior olives. In the present study, 3 cases of Dandy-Walker malformation were seen accounting for 4.8%. One case was associated with spina bifida and one case was with a single umbilical artery. Sirenomelia (Mermaid syndrome) is a rare and fatal congenital defect characterized by varying degrees of lower limb fusion, thoracolumbar spinal anomalies, sacrococcygeal agenesis, genitourinary, and anorectal atresia. [11]This condition is found in approximately one out of every 100,000 live births. More than half the cases of sirenomelia result in stillbirth, and this condition is 100 times more likely to occur in identical twins than in single births or fraternal twins. It results from a failure of normal vascular supply from the lower aorta in utero. In this study, we studied 1 case of sirenomelia with Potter's syndrome showing hypoplastic lower limb, sacral agenesis, hypoplastic lower limb, absent external genitalia, dilated anus and rectum, and single umbilical artery.Figure 5

Another rare case seen in this study was acardiac acephalus in a monochorionic monoamniotic twin gestation. The anomalies seen were sacral spina bifida and subcutaneous edema.

Acardiac twin is an extremely rare and bizarre complication of monochorionic twin pregnancy occurring at an incidence of 1 in 34,600 deliveries or 1 % monozygotic twins. [12]Acardiac twins are a result of TRAP i.e., Twin reversed arterial perfusion where one twin is structurally normal called the donor twin and a recipient twin receives all its blood supply from the donor twin through its vascular connections on the surface of the placenta. [13, 14]

schizencephaly is a rare congenital abnormality of the brain affecting 1.48/100,000 live/stillbirths. [15]In schizencephaly the clefts of the brain extend through the hemispheres from the ventricles to the pial surface. One case of schizencephaly was seen in the present study.

CONCLUSION

The present study emphasizes the importance of perinatal autopsy for understanding the cause of death and also confirmation of the antenatal diagnosis. In the present study, we observed that the incidence of neural tube defects was higher compared to other anomalies. With the improve-

ments in socioeconomic conditions, maternal nutrition, maternal health, and health education the incidence of neural tube defects can be reduced. Rare CNS malformations seen in the present study were iniencephaly, schizencephaly, and acardiac acephalous.

Understanding CNS malformations can give valuable information that can be further helpful in the genetic counseling of the parents. Thus, the fetal autopsy is essential to confirm the antenatal diagnosis and also to arrive at a definitive diagnosis.

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