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Perinatal Autopsy: A 3 year Study of Central Nervous System Anomalies.

*Kambala GM[1], Natta BR[2], Undavalli VK[3].
[1]*Dr.Grace Madhuri kambala, Assistant Professor of Pathology, Siddhartha Medical college, Vijayawada.*
[2]*Dr,Bharat Rao Natta, Professor and Head of the department of Pathology, Siddhartha Medical college, Vijayawada.*
[3]*Dr.Vamsi Krishna Undavalli, Assistant Professor of Community Medicine, Dr Pinnamaneni SIMS & RF, chinna Avutapalli.*
* *Corresponding Author: Dr. Grace Madhuri Kambala,*

Abstract
Background:
CNS anomalies are due to defective closure of neural tube.It is associated with other systemic anomalies in most of the cases. This study was undertaken to determine the incidence of CNS anomalies among congenital malformations at autopsy, associated systemic anomalies, maternal age and sex of the fetus.
Objectives:
To determine the incidence of central nervous system anomalies among congenital malformations at perinatal autopsy.
Methods:
The present study comprises 62 consecutive perinatal autopsies conducted after obtaining consent from the parents/guardians. In cases where prenatal ultrasound findings were available they were compared with the autopsy findings.
Results:
Out of 62 perinatal autopsies, 27 cases showed congenital anomalies with M:F = 1.2:1. The malformations involving the central nervous system were commonest, seen in 9 cases (33.3%). Anencephaly is the most common type of anomaly seen in 6(66.6.%) cases.
Conclusion:
This study highlights the importance of perinatal autopsy in confirming the diagnosis of congenital anomalies by prenatal ultrasound findings. Pathological examination of the fetus is essential to document associated anomalies.

Keywords: *CNS Anomalies, Fetal Autopsy,Anencephaly, Spinabifida, Omphalocele.*

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I. Introduction

The term 'autopsy' derives from the ancient Greek word 'autopsia' that means 'to see for oneself' derived from (Autos- 'oneself') and (Opsis-'eye').[1] . The major objectives of the autopsy are to evaluate pregnancy and birth, determine gestational age, document growth and development, detect underlying abnormalities(anomaly, infection, metabolic defect, other), evaluate diagnoses and therapy, and determine cause of death.[2,3] Congenital anomalies contribute a significant proportion of morbidity and mortality, as well as fetal mortality. They account for 8-15% of perinatal deaths and 13-16% of neonatal deaths in India[4]. Unlike the situations in developed countries, where congenital malformations are leading cause of infant mortality, in India low birth weight, prematurity, sepsis and infections are still the leading causes. Perhaps for this reason not much attention has been paid to the problem of congenital malformations in India[5]. In spite of the availability of various antenatal diagnostic modalities fetal autopsy plays the vital role in the conformation , identification of congenital anomalies and also for the counseling of the parents, to prevent them in further pregnancies. Central nervous system(CNS) anomalies account for about one third of congenital anomalies identified during perinatal period. They are the second most common severe congenital anomalies after cardiac anomalies. CNS anomalies can be considered as the part of an isolated or systemic syndrome. CNS anomalies are the reasons for 75% of fetal deaths and 40% of childhood deaths.[6]

II. Materials and Methods

This is a prospective study, conducted in Siddhartha medical college, vijayawada between January 2016 to Dec 2018. This study includes the perinatal death i.e. the death of a fetus weighing 500 gm or more at 22 or more weeks of gestation and the death of an infant between birth and at the end of the neonatal period. After the delivery, informed and written consent was taken from the parents or guardian, for a fetal autopsy procedure. They were told that such a procedure will help diagnose the cause of fetal death, and also will be useful in assessing the risk of recurrence.

Detailed maternal medical and obstetric history including the laboratory and ultrasonographic reports were reviewed. In each case the autopsy was done according to the Standard Protocol in the following order: Anthropometry, External examination, internal examination, Examination of the placenta and umbilical cord, Tissue taken for Histopathological study. In case of suspected skeletal dysplasia radiologic study was done. After autopsy was completed all the organs were returned into the respective body cavities and the incision lines were sutured and preserved in the containers.

III. Results

A total of 62 fetal and neonatal (Perinatal) autopsies were performed during the period of study. In 62 autopsies performed 51 (82%) were fetal deaths, 11 (18%) were early neonatal deaths. In a total of 62 fetuses, there were 34 male and 28 female babies.

Congenital anomalies were seen in 27(43.5%) cases. Of them 9(33.3%) cases showed CNS anomalies.(Table 1) Anencephaly is the most common type of anomaly seen in 6(66.6.%) cases.

Age: Minimum age of the mother with CNS anomalies observed in our study was 19 years and maximum was 28 years with mean of 23 years.

Table 1: Case Wise Presentation of Central Nervous System Anomalies.

Case No	Age of The Mother (Yrs)	Parity	Sex of The Fetus	Gestational Age (Weeks)	CNS Anomaly	Associated Anomalies
1.	21	Primigravida	M	23	Anencephaly	Spina bifida
2	26	Gravida 2	F	Full Term	Holoprosencephaly	
3	22	Primigravida	F	24	Anencephaly	
4	23	Primigravida	F	27	Anencephaly	Spinabifida,Omphalocele
5	28	Gravida 2	M	22	Anencephaly	
6	19	Primigravida	M	32	Lissencephaly	
7	23	Gravida 2	F	25	Anencephaly	Single umbilical artery
8	28	Primigravida	F	30	Myelomeningocele	
9	24	Primigravida	M	24	Anencephaly	

Parity: Out of 9 mothers 6 were primigravida (66.6%), three were gravida 2 (33.3%),

Sex: Out of 9 fetuses, four were male and five were female.

Gestational Age: Gestational age ranged from 22 weeks to full term.

Head Circumference: It ranged from 9 to 14 cms with mean of 11.4 cms.

Associated Anomalies: Out of 9 cases, one case showed both anencephaly and spina bifida. 2 cases showed association with other systemic anomalies. One showed anencephaly with omphalocele, other showed anencephaly associated with single umbilical artery.

IV. Discussion

Fetal autopsy significantly contributes to the diagnosis of Intrauterine fetal death and congenital anomalies are a major cause of perinatal death [7]. Congenital malformation remains a common cause of perinatal death and accounts for nearly 25-30 % in developed countries and 10-15 % in developing countries like India [8,9]. CNS anomalies were observed in 33.3% of cases in the present study which correlates with the study of Kaiser et al[10], Tomatir et al[11], Uma et al[12]. However Sankar and Phadke et al[13] reported even higher incidence of 74.2%.(Table 2)

The most common defect was Anencephaly seen in 6 cases (66.6%), which was accurately diagnosed with Ultrasonography. Antenatal AFP levels were raised in all the 6 cases. Associated Spina bifida was seen in two cases of anencephaly (Fig 1,2&3). In a study by Panduranga et al[14] spina bifida was the most common associated anomaly seen in 26.8% of cases. Other associated anomalies observed in the present study were Omphalocele (Fig 1), single umbilical artery which were also observed in various studies done by Panduranga et al[14], Tan et al[15], Taksande et al[16].

Table 2: Comparitive Analysis of Central Nervous System Anomalies.

S.No	Authors	Year	Number/Total	Percentage (%)
1	Kaiser et al [10]	2000	45//121	37
2	Sankar and Phadke[13]	2006	60/81	74.2
3	Tomatir et al [11]	2009	57/183	31.1
4	Uma S Andola [12]	2012	15/44	34.09
5	Present Study	2016	9/27	33.3

Figure 1: Anencephaly associated with omphalocele, spina bifida, short umbilical cord.

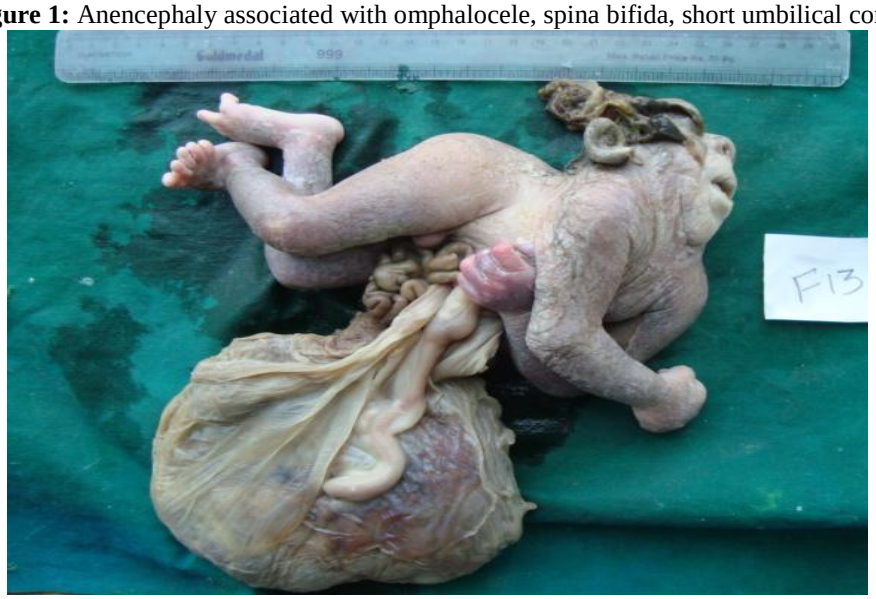
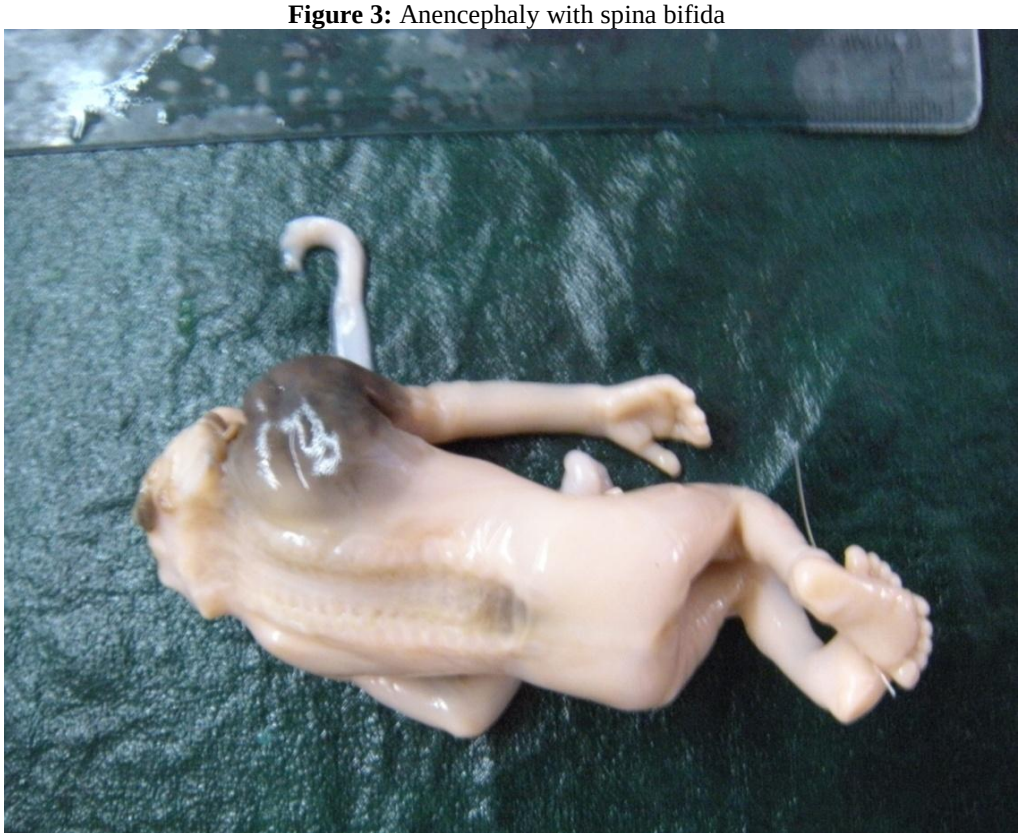


Figure 2: Anencephaly with spina bifida

Figure 3: Anencephaly with spina bifida



Panduranga et al[14] in their study on 41 cases of Anencephaly reported a female preponderance, however in the present study we could not observe any sex predilection as male to female ratio was 1:1. There was a higher incidence of anencephalic pregnancy among primigravidae(66.6%) similar to the study of Tan et al[15]. The age group of mothers with anencephalic pregnancies in this study was between 20 and 29 yrs and was consistent with Panduranga et al[14]. In contrast, Caffey et al[17], Edward et al[18] and Golalipur et al[19] observed the prevalence in mothers aged above 35 yrs.

Wenghoefer et al[20] in his study on 51 cases of holoprosencephaly reported higher incidence of anomaly in female fetuses. Cleft lip, cleft palate, cyclopia, maxillofacial malformations were the most common associated anomalies. In 63%, the diagnosis of holoprosencephaly led to a termination of pregnancy. Ten percent of the fetuses were born alive. One case of alobar type of holoprosencephaly was seen in a full term female child in the present study who died shortly after birth.(Figure 4&5) There were numerous associated craniofacial anomalies like Hypoplasia & Synostosis of Frontal Bone (Single hypoplastic Frontal Bone with absence of metotic sutures), Anophthalmia (Eye balls replaced by rudimentary soft tissue mass), Hypoplasia of Maxillae, Arrhinia , Cleft Palate, Central Hare Lip, Hypotelorism. Karyotyping revealed trisomy 18. In a case report by coleta et al[21] a low birth weight male newborn presented with holoprosencephaly , microcephaly, midline cleft.

Figure 4: Fetus with Hypoplasia & Synostosis of Frontal Bone, Arrhinia, cleft Palate central hare lip (Holoprosencephaly)

Figure 5: Fetus of holoprosencephaly with Single hypoplastic frontal bone with absence of metopic sutures and anopthalmia (Eye balls replaced by rudimentary soft tissue mass)

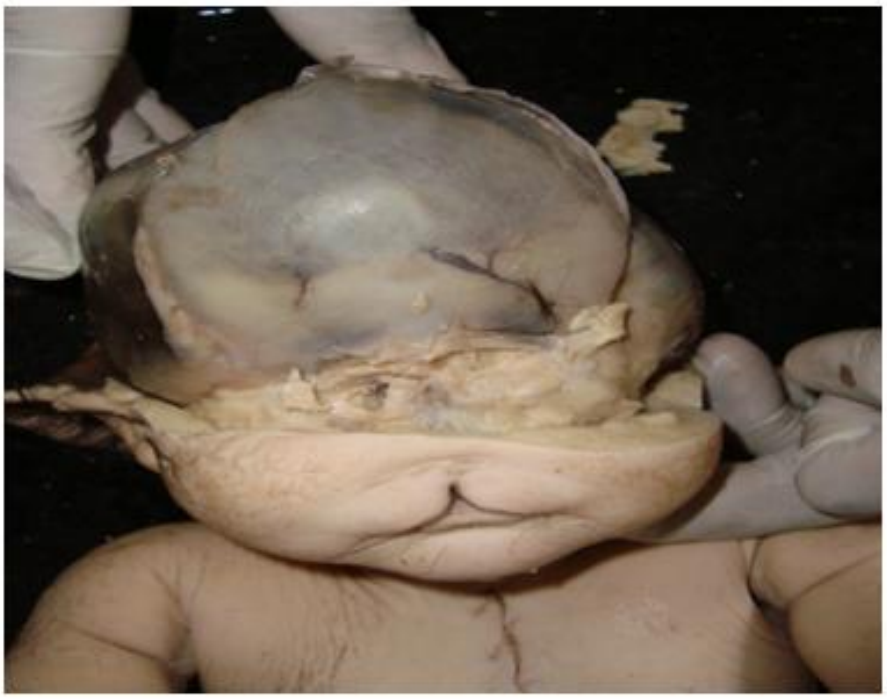
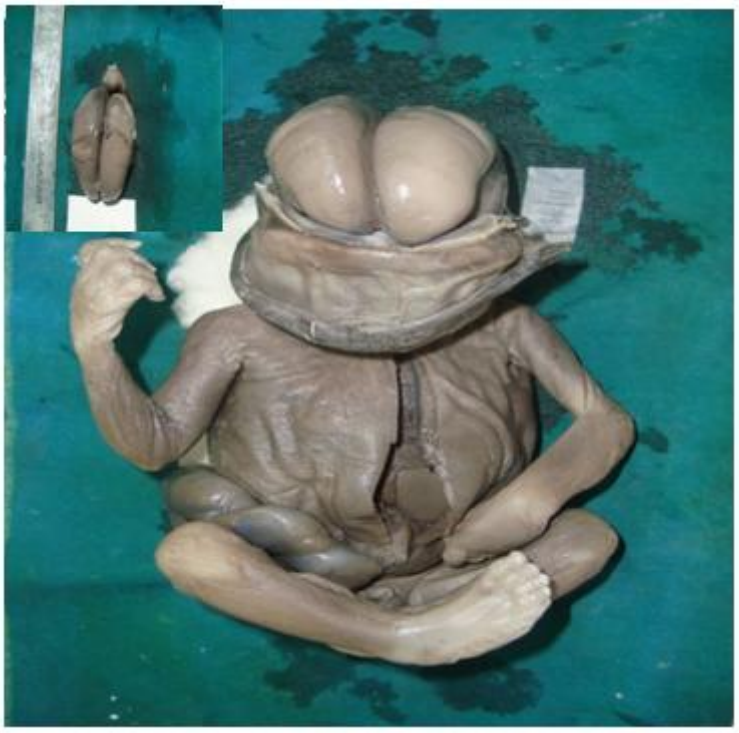


Figure 6: Fetus with Lissencehaly(agyria)



Occipital Encephalocele was observed in a 30 weeks female fetus died in utero and there were no associated anomalies observed. Karyotyping was normal. Caviness et al[22] reported a case of newborn female fetus with occipital encephalocele who died on the fourth postnatal day.

Lissencephaly is associated with Miller – Deiker syndrome and chromosomal deletions in a study by Fong et al[23]. However in the present study Lissencephaly of type 1 was seen in a 32 wks male fetus (Figure 6). It was diagnosed antenatally by Ultrasound and there were no associated anomalies. Karyotyping was done which revealed no abnormality. Greco et al[24] observed a female fetus with lissencephaly who was delivered in 39th week of gestation. The child survived for 2 days and died of seizures.

V. Conclusion

We conclude from our study that CNS anomalies are the most common among congenital anomalies. Anencephaly contributes the majority of cases seen in women with 20-29 yrs of age. Most commonly noticed in the primigravida with equal sex distribution of the fetuses. Central nervous system anomalies are the commonly associated anomalies. Anencephaly is efficiently diagnosed by ultrasound examination (USG) during early days of pregnancy, but pathological examination of the abortus is needed, as in most cases anencephaly is also associated with other systemic anomalies.

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