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OUTCOME OF FOETAL AUTOPSY AND INTERESTING CONGENITAL ANOMALIES DETECTED IN SECOND AND THIRD TRIMESTER OF PREGNANCY IN CORRELATION WITH IMAGING FINDINGS.

Pathology

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ABSTRACT

Introduction: In the present era of target imaging for foetal anomalies (TIFFA), more and more cases of congenital anomalies were detected at the early gestational age and terminated medically. Foetal autopsy will help to ascertain the imaging findings and to find out the cause of intrauterine foetal death.

Aims & objectives: To analyse various congenital anomalies detected during foetal autopsy in correlation with antenatal imaging findings and to identify cause of intrauterine death during second and third trimester of pregnancy.

Materials and Methods: Foetal autopsies were performed as per standard protocol on all foetuses received in the Department of Pathology over a period of 5 years from June 2013 to June 2018.

Results: Total of 54 foetal autopsies from 52 mothers were performed over a period of five years. Of the 54 cases, the predominant cause of foetal loss were found to be due to MTP following congenital anomalies in 34 cases (65.3 %) and one case (1.9%) of SLE on methotrexate, followed by intrauterine deaths due to uteroplacental insufficiency in 17 cases (32.7%), and twins complicating pregnancy in 3 cases (5.7%). Among the 34 congenital anomalies, central nervous system defects were seen in 9 cases (26.4%) followed by musculoskeletal defects in 8 cases (23.5%), cardiac vascular anomalies in 7 cases (20.5%), foetal hydrops in 3 cases (8.8%) and congenital syndromes in 3 cases (8.8%).

Conclusion: The organized post-mortem examination of the foetus is superior in identifying the cause of death along with appropriate antenatal history and radiological findings.

KEYWORDS

Foetal autopsy, congenital malformations, IUFD

INTRODUCTION

Foetal death is defined as death prior to the complete extraction or expulsion from its mother of a product of conception irrespective of the duration of pregnancy. It is divided as early (<22 weeks of gestation), intermediate (between 22 and 27 weeks of gestation) and late (> 28 weeks of gestational age). Of these, early are designated as abortions whereas intermediate and late are known as stillbirths [1]. In the present era of target imaging for foetal anomalies (TIFFA), more and more cases of congenital anomalies were detected at the early gestational age and terminated medically. Congenital anomalies affect approximately 1 in 33 infants and result in approximately 3.2 million birth defects related disabilities every year [2]. An estimated 270,000 new-borns die during the first 28 days of life every year from congenital anomalies [2]. Foetal autopsy is the single most useful investigation to ascertain the clinical/imaging diagnosis and to find out the additional anomalies and cause of intrauterine foetal death (IUFD) [3]. It is also a valuable audit of antenatal care and may facilitate learning from adverse events.

AIM & OBJECTIVE:

To analyse various congenital anomalies detected during foetal autopsy in correlation with antenatal imaging findings and to identify cause of intrauterine death during second and third trimester of pregnancy.

MATERIALS AND METHODS

This is a descriptive analytical study done in the department of pathology for a period of 5 years from June 2013 to June 2018 at Alluri Sitarama Raju Academy of Medical Sciences (ASRAMS), Eluru. Inclusion criteria: Foetal autopsies received in the department of pathology were included in the study. Exclusion criteria: Foetuses which are macerated were excluded from the study. Antenatal ultrasound findings were collected in available cases. Consent for the autopsy was taken from the parents/ relatives on a proforma prepared according to guidelines provided by the Institutional Ethics Committee. The foetuses were fixed in 10% formalin. Autopsies were performed as per Guidelines on autopsy practice followed by The Royal College of Pathologists. Apart from ultrasound findings the following data is collected: Age of the mother, antenatal history, and medical conditions complicating pregnancy, gestational age and gender of the foetus, full anthropometric profile, and external examination, gross and microscopic evaluation of different organs, placenta, umbilical cord and membranes. During autopsy procedure, photographs were taken for unusual gross and microscopic findings. Post mortem radiographs of abnormal features were taken whenever required.

Statistical analysis

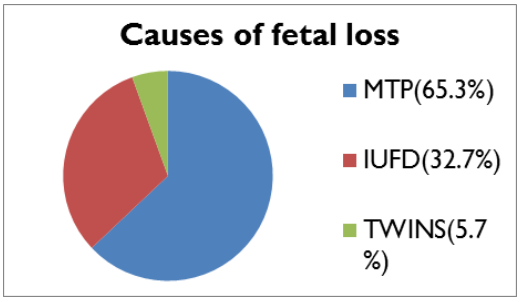
Data was compiled by using Microsoft excel sheet 2010 (Microsoft Corporation, Seattle, WA, United States). Simple descriptive statistics were used and data represented in the form of pie charts, bar diagram and tables.

RESULTS

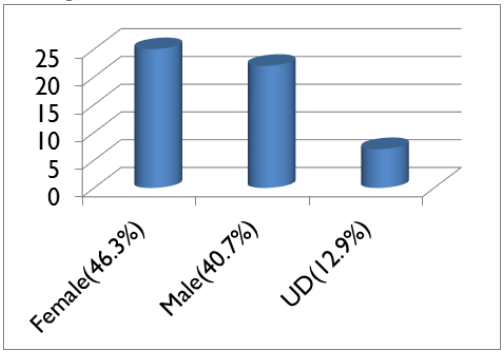
Total of 54 foetal autopsies were performed from 52 mothers over a period of five years. As shown in table/figure 1, the predominant cause of foetal loss was due to medical termination of pregnancy (MTP) following detection of congenital anomalies by ultrasound in 34 cases (65.3%) and one case (1.9%) of SLE on methotrexate, followed by intrauterine deaths due to uteroplacental insufficiency in 17 cases (32.7%). Twin gestation is seen in 3 cases (5.7%). One of the foetuses among the twins is live male baby without anomalies and doing well. The mean and median age of the mothers with foetal demise was 24 years with a standard deviation±3.75). As shown in table/figure 2, there were 25 female (46.3%), 22 male (40.7%) foetuses and gender is undetermined in 7 (12.9%) foetuses. Age of the mothers ranged from 16 to 31 years. Gestational age of foetuses ranged from 13 to 38 weeks. Second trimester foetus loss (11^{+0}-23^{+6} weeks gestation) was seen in 30 cases (57.6%) and third trimester (≥24 weeks gestation) foetal demise was seen in 22 (42.3%) cases. As shown in table/figure 3, among the 34 congenital anomalies, central nervous system defects were seen in 9 cases (26.4%) followed by musculoskeletal defects in 8 cases (23.5%), cardiac vascular anomalies in 7 cases (20.5%), renal defects in 4 cases

(11.7%), foetal hydrops in 3 cases (8.8%) and syndromes in 3 cases (8.8%).

Table/Figure 1: Demonstrates causes of foetal loss.



Table/Figure 2: Gender wise distribution of foetuses along with gestational age in weeks.



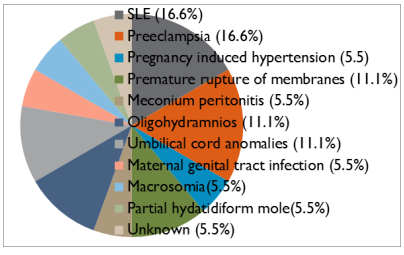
Table/figure 3: Shows various congenital anomalies and syndromes detected in foetal autopsy.

Sl.no	Age	Gestational age	Gender of the foetus	Major anomaly	Associated anomalies / abnormalities
Central Nervous System defects (26.4%)					
1	19	Primi with 22 weeks of gestation	F	Exencephalus.	Nil
2	30	G2P1 with 28 weeks of gestation	M	Spina bifida occulta	Nil
3	24	Primi with 21 weeks+ 3 days gestation.	F	Spine bifida (closed) with ventriculomegaly	Congenital talipes equinovarus
4	19	Primi with 18 weeks of gestation	M	Occipital encephalocele	Bilateral Polycystic kidney
5	29	Primi with 18 weeks of gestation	Small genital tubercle	Iniencephaly (Anencephaly + Rachischisis + Absence of neck)	Gastrischisis
6	30	G3P2L1D1 with 21 weeks 2 days gestation	F	Spina bifida with myelomeningocele, cerebellar hypoplasia, bilateral ventriculomegaly and corpus callosal agenesis	Nil
7	31	Primi with 17 weeks of gestation	M	Spina bifida with myelomeninogocele	Nil
8	28	20 weeks 4 days, 3rdconsanguineous marriage	F	Sacrococcygeal teratoma, Type IV.	Nil
9	30	G3P2L1D1 with 20 weeks of gestation	M	Cyclopia (alobar holoprosencephaly)	Nil
Cardiovascular defects (20.5%)					
10	30	G4P1D1A2 with 30 weeks of gestation	M	Dextrocardia	Right lung hypoplasia
11	22	G2P2L1 with 24 weeks of gestation	F	Dextrocardia	Diaphragmatic hernia, Ectopic left kidney and single umbilical artery
12	21	Primi with 28 weeks of gestation	F	Dextroposition of heart	Asplenia with chorangiosis of placenta
13	27	Primi with 21 weeks of gestation	Undetermined with small genital tubercle	Hypoplastic left heart syndrome	Pulmonary hypoplasia
14	24	Primi with 20 weeks of gestation	F	Dextrocardia with atrioventricular septal defect	Marginal insertion of umbilical cord
15	25	G2P2L1 with 22 weeks of gestation	F	Dextrocardia	Congenital diaphragmatic hernia.
16	25	G3A1L2 with twin pregnancy. Delivered a normal baby boy at 38 weeks and an abnormal foetus.	Undetermined	Acardiac amorphous twin with Twin Reversed Arterial Perfusion (TRAP) sequence.	Small umbilical cord is seen feeding this limb.
Renal defects (11.7%)					
17	26	G3P3D2 with 28 weeks of gestation	M	Bilateral Renal agenesis and intrauterine growth retardation.	Nil
18	26	Primi with 26 weeks of gestation	Indistinguishable	Unilateral renal agenesis.	Pes valgus deformity foot, neck webbing and Single umbilical artery
19	22	G2P1L1 with 34 weeks gestational age	undetermined sex	Unilateral renal agenesis.	Atrophy of bladder, ambiguous genitalia and Chorangiosis of placenta
20	22	G1P1 with 29 weeks of gestation	F	Unilateral renal agenesis	Cystic atrophy of bladder along with infectious aetiology of liver, small and large intestine.
Musculoskeletal defects (23.5%)					
21	19	Primi with 18 weeks of gestation	M	Omphalocele	Nil
22	25	G2P1L1 with 19 weeks of gestation.	Unknown	Gastroschisis,	Kyphosis of Spine, short umbilical cord and single umbilical artery

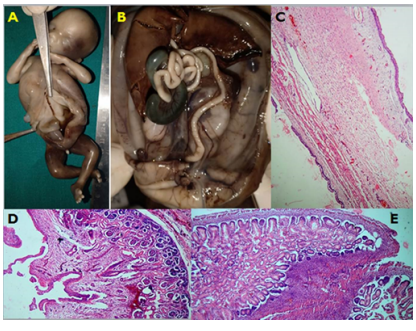
23	28	G3P2D2 with 23 weeks of gestation, consanguinous marriage for 2 generations	M	Macroglossia Prematurity.	Nil
24	24	Primi with 13 weeks of gestation	Small genital tubercle seen	Scoliosis Spine	Pulmonary Hypoplasia
25	18	Primi with 25 weeks of gestation	M	Arthrogryposis multiplex congenita	Nil
26	22	G2P1 with 24 weeks of gestation. Nonconsanguinous marriage. First normal baby used many tablets for vomitings.	F	Phocomelia	Nil
27	21	Primi with 18 weeks of gestation.	M	Bilateral congenital talipes equinovarus deformity, Genu valgum of knees.	Chronic villitis, Funisitis and Chorioamniotis
28	23	Primi with 21 weeks gestational age	M	Right diaphragmatic hernia with herniation of liver and bowel loops into the thorax.	Nil
Foetal hydrops (8.8%)					
29	24	G2P1L1 with 21 week gestation	M	Cystic hygroma / lymphangioma	Nil
30	24	G2P1L1 with 22 weeks 4 days gestation.	M	Cystic hygroma/ Lymphangioma of foetus	Nil
31	16	Primi at 21weeks gestational age.	F	Cystic hygroma thorax	Placental insufficiency
Congenital Syndromes (8.8%)					
32	24	6 months amenorrhoea, 24 weeks gestation, Twin pregnancy	females	Atrial septal defect is in normal looking foetus. Congenital cystic hygroma and polymalformative syndrome in abnormal looking foetus.(Fetal hydrops+facial dysmorphia + webbed neck + micromelia + clubfoot + hypoplastic lungs + absent liver and spleen)	Umbilical cord coiling and Velamentous insertion. Short umbilical cord and Velamentous insertion. Diamniotic monochromic Placenta with extensive intervillous haemorrhage.
33	20	G3P2D2 with 35 weeks 2 days gestation	M	Otocephaly -absence of the mandible (agnathia), ventromedial displacement and often fusion of the auricles (synotia), and hypoplasia of the oral cavity (microstomia).	Situs inversus totalis
34	25	Primi with 17 weeks of gestation, oligohydramnios	M	Megacystis with bilateral hydroureteronephrosis and micro colon –Intestinal hypoperistalsis syndrome (Berdon syndrome).	Umbilical cord: Shows marginal insertion. Placenta: Shows maternal floor infarct

Abbreviations: G-Gravida, P-Para, L-Live, D-Death, M-Male, F-Female

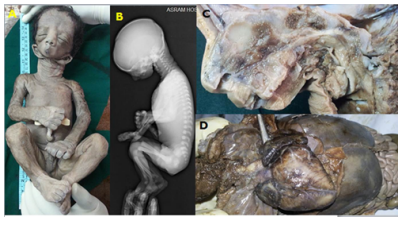
Table /figure 4: Causes of uteroplacental insufficiency in intrauterine death foetuses without anomalies.



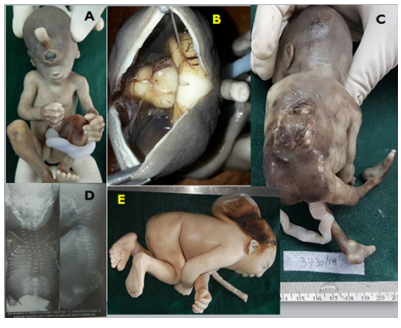
Table/ figure 5: A. 17 week's foetus with Megacystis B. Bilateral hydroureteronephrosis and micro colon and dilated bile tinged small bowel C. Microphotograph of dilated urinary bladder with underlying smooth muscle (H&EX40). D. Microphotograph of Kidney with dilated pelvicalyceal system (H&EX40). E. Microphotograph of Micro colon with absence of ganglion cells (H&EX40) (Berdon syndrome).



Table/figure 6: A. 35 weeks 2 days foetus with small head (Microcephaly), absent mandible (Agnathia), ventrally displaced midline fusion of external ears in the neck (Synotia), small mouth (microstomia), absent tongue (aglossia), hypertelorism and obliterated external auditory meatus. B. Fetogram shows absent mandible. C. Cut section shows agnathia. D. Situs inversus totalis (Otocephaly with situs inversus totalis).

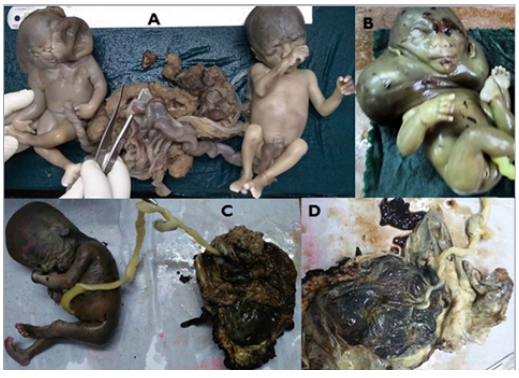


Table/figure 7:A.20 week's foetus having single median orbit with a partially divided eye (synopthalmic), absent nose (Arhinia), proboscis present above the eye and microstomia (Cyclopia). B. Cranial cavity shows single midline forebrain ventricle, fused thalami and absence of midline structures such as corpus callosum and falx cerebri. C.17 week's foetus having Spina bifida with myelomeningocele D. Fetogram showing spina bifida. E.18 week's foetus with occipital encephalocele.

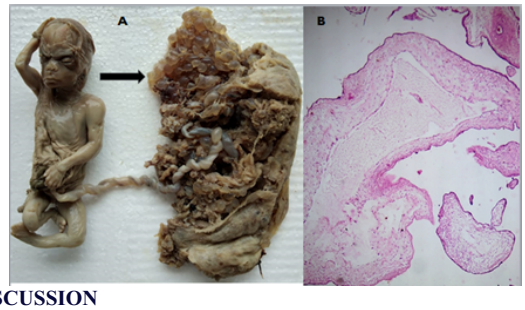


Table/figure 8:A.18 week's foetus with Omphalocele B. 19 week's foetus with Gastroschisis C. 24 week's foetus with Phocomelia

Table/figure 9: A. 24 week's twin gestation with atrial septal defect in normal looking foetus and Congenital cystic hygroma and polymalformative syndrome in abnormal looking foetus Note umbilical cord hypercoiling and velamentous insertion. B. 22 week's 4 days foetus with bilateral retromandibular cystic hygroma. C. 18 week's foetus with umbilical cord knot and extensive intervillous haemorrhage of placenta. D. Shows marginal insertion of umbilical cord.



Table/ Figure 10: A. 18 week's 5 days foetus with Partial hydatidiform mole of placenta showing grape like vesicles (arrow mark) B. Microphotograph of placenta showing avascular chorionic villi lined by cytotrophoblasts and hydropic degeneration with central cavity (cisterns) formation (H&EX40).



DISCUSSION

With the advent of TIFFA scan with high resolution, more number of congenital anomalies was detected on antenatal scan and they are terminated medically. Perinatal autopsy still remains the gold standard in detecting the cause of death in IUFD and confirming the anomalies detected on ultrasound [4]. The present study focuses on highlighting the interesting congenital anomalies detected during foetal autopsy and causes of IUFD.

In the present study, major indication for foetal autopsy was termination of pregnancy for congenital anomalies (57.7%) which is higher than studies done by Venkataswamy et al [5] and Kale et al [6]. IUFD was seen in 36.5% of cases due to maternal, umbilical cord and placental insufficiency which is slightly lower than Venkataswamy et al (41.1%) [5].

Twins with IUFD was seen in 3 cases (5.7%), in one case one live baby was born at 38 weeks of gestation by caesarean section and other was Acardiac amorphous foetus with Twin Reversed Arterial Perfusion sequence and small umbilical cord. Similar type of rare case was reported by Alexandru et al [7]. One case of foetal hydrops with polyformative syndrome was reported in twin pregnancy and similar cases were reported by Ries et al [8] and McClain [9].

The most common defects were of Central Nervous System (26.4%) in our study which correlates with studies done by Andola [10] and Sankar [11]. Among the CNS defects we are reporting an interesting case of Cyclopia which is very rare and reported by Salama et.al [12]. Musculoskeletal defects are the second most common defects in our study (23.5%) which is comparable with study done by Kale et al (21.08%) [13]. Apart from anterior abdominal wall defects, we encountered a rare case of Phocomelia which was attributed to thalidomide administration in early pregnancy [14].

Congenital syndromes observed in our study are Otocephaly with Situs inversus totalis; Megacystis-Micro colon-Intestinal Hypoperistalsis Syndrome (Berdon syndrome) and similar type of rare syndromes are reported by Kandala [15] and Mehmet et al [16].

Among 54 cases of foetal autopsy antenatal ultrasound findings are correlated in 35 cases from available records. The antenatal ultrasound findings are correlated with autopsy findings in 62.8% of cases, autopsy findings are added to the diagnosis in 28.5% of cases and in 8.8% cases there is a change in the ultrasound diagnosis.

Table/ Figure 11: Correlation of antenatal ultrasound findings with autopsy findings and comparison with other studies.

Studies	Total number of cases	No change in diagnosis	Added to diagnosis	Change in primary diagnosis
Uma S Andola et al [10] (2012)	35	50%	29.54%	9.09%
Grover et al [17] (2017)	40	32.5%	42.5%	25%
Venkataswamy et al [5] (2018)	45	37.7%	22.2%	33.3%
Present study (2019)	35	62.8%	28.5%	8.5%

As shown in table/figure 11, our study is compared with other studies and it is nearar to Uma S Andola et al [10] in change in the primary diagnosis whereas Grover et al [17] and Venkataswamy et al [5] reported a slightly higher percentage in the change in the primary diagnosis after autopsy.

CONCLUSION

The organized post-mortem examination of the foetus is superior in identifying the cause of death due to maternal, foetal, umbilical / placental factors along with appropriate antenatal history and radiological findings. Autopsy not only plays an essential role in accurate diagnosis and helps in appropriate genetic counselling. The present study reemphasizes the need for foetal autopsy even in the era of advanced imaging techniques.

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Nil.

Conflicts of interest

Nil.

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