ORIGINALARTICLE

Fetal and Neonatal Autopsy: A Morphological Study and Correlation with Prenatal Anomaly Scan

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Abstract:
Background: Congenital malformations are the leading factor of perinatal death and childhood morbidity. Present study was aimed to compare congenital malformations detected prenatally by ultrasonography and postnatally by fetal autopsy and also the quantum of additional information autopsy can provide. *Material and Methods:* Present study was hospital based cross sectional studyof fetal and neonatal autopsies conducted in cases terminated for anomalies, intrauterine fetal demise and stillbirths in the second and third trimester. First trimester cases were excluded. *Results:* Eighty one fetal / neonatal autopsies were studied. Majority were terminated pregnancies before 24 weeks of gestation for congenital anomalies (93 %) and birth weight less than 1000 grams (75.3 %). Ultrasonography(USG) showed concordance with autopsy in 78% cases, discordance in 5% cases and additional findings were seen in 6% cases. Common congenital anomalies were central nervous system (CNS) defects (41.4 %), genitourinary(GU) defects (21.9 %), congenital heart defects (CHD) (4.9%), gastrointestinal(GI) defects (9.75%), musculoskeletal defects (14.6%), respiratory defects (7.3 %), cystic hygroma (1.23%) and fetal hydrops (1.23%). Autopsy added diagnosis in 05 cases (6 %) as bilobed right lung (2), omphalocele (1), anencephaly (1) and horseshoe shaped kidney (1).*Conclusion:* Parents should be encouraged for autopsy in view of counseling for future pregnancies. Anomaly scan predicts the malformations in the fetus but autopsy is necessary to confirm the anomaly and also to look for additional malformations. Thus autopsy can help parents in planning and management of future pregnancies.

Keywords: Fetal autopsy, Perinatal autopsy, Congenital anomalies, Stillbirths.

Introduction:
Congenital malformations are the leading cause of perinatal death and childhood morbidity. Ultrasound screening has been a routine for all pregnant patients to detect structural anomalies, and it is recommended to perform this scan at 18-22 weeks of gestation.[1,2]Intrauterine death is the major indicator of perinatal mortality and therefore suggests the quality of health care in the community.[3] In cases of medical termination of pregnancies for anomalies, intrauterine fetal demise, stillbirths and inevitable or spontaneous abortion perinatal autopsy is recommended to confirm the cause.[4] Although autopsy findings are detectable by ultrasound and vice versa, still the fetal autopsy plays a vital role in spite of available antenatal diagnostic modalities in the conformation as well as identification of congenital anomalies and also for the counselling of the parents, to prevent the fetal congenital anomalies in future pregnancies.[5]Autopsy is also a valuable audit of clinical care and may facilitate learning from adverse events. The present study aimed to compare congenital malformations detected prenatally by ultrasonography(USG) and postnatally by fetal autopsy and also the quantum of additional information autopsy can provide.

Material and Methods:
The present study was a hospital-based cross-sectional study of fetal and neonatal autopsies conducted in the department of Pathology, at Bharati Vidyapeeth medical college and hospital, Pune, India. The study period was from January 2019 to July 2021. Study approval was taken from the institutional ethical committee. All second and third trimester fetal/neonatal autopsies in cases

terminated for anomalies, intrauterine fetal demise and stillbirths were studied. Fetuses with gestational age less than 14 weeks were excluded. All autopsies were conducted as per the standard operating protocol of the department which included external and internal examination along with the photographs.The autopsy was performed after obtaining informed consent from either of the parents regardless of the gestational age.The autopsy protocol included the removal of thoracic, cervical, abdominal, and pelvic organs enbloc[6]. Weight of all the organs was documented and then proper sections were taken and submitted for hematoxylin and eosin (H and E) staining. Sections were taken from heart, lungs, kidneys, adrenals, liver, bowel thymus, stomach, spleen, brain, testis/ ovaries, bladder and skin whereever necessary. Histopathological examination of the placenta, fetal membranes and umbilical cord was also done. Findings of autopsy and antenatal ultrasound examination were compared. Data was collected and compiled using Microsoft Excel, analysed using statistical package for the social sciences(SPSS) 23.0 version. Statistical analysis was done using descriptive statistics.

Results:

Eighty one fetal / neonatal autopsies were studied. Majority were terminated pregnancies before 24 weeks of gestation for congenital anomalies (47.83 %) and birth weight less than 1000 grams (56.52 %). Out of 81 cases,73cases belonged to second trimester and 08 cases were of third trimester.In the present study, common congenital anomalies were CNS defects (41.4 %), genitourinary defects (21.9 %), cardiac (4.9%), gastrointestinal defects (9.75%), musculoskeletal defects (14.6%), respiratory defects (7.3 %), cystic hygroma (1.23%) and fetal hydrops (1.23%). Autopsy added diagnosis in 05 cases (6 %) as bilobed right lung (2), omphalocele (1), anencephaly (1) and horseshoe shaped kidney (1).In present study, Antenatal ultrasound diagnosis was correlated with autopsy findings in 78 % of cases of congenital anomalies, 6% had additional findings in autopsy compared to the antenatal scan. It is almost similar to study conducted by Uma SA et al with additional findings in 37% cases.

Table 1- General characteristics

USG Findings	No. of Cases (n=81)	Percentage (%)
Concordant cases	63	78%
Concordant cases with additional findings	05	6%
Discordant cases	04	5%
Anomaly scan report not received	09	11%

Table 2 – USG findings

USG Findings	No. of Cases (n=81)	Percentage (%)
Concordant cases	63	78%
Concordant cases with additional findings	05	6%
Discordant cases	04	5%
Anomaly scan report not received	09	11%

Discussion:

A total of 81 autopsies were conducted at Bharati Vidyapeeth (deemed to be University) Medical College and Hospital. In the present study, the majority of the cases were medically terminated (43 out of 81) and rest were cases of spontaneous abortion (38 out of 81). Majority of the fetuses belonged to second trimester in this study (90.1%) and rest belong to third trimester (9.9%). Fetuses belonging to firs trimester were excluded from the study. In the present study, majority of the congenital anomalies belong to central nervous system (41.7%) followed by genitourinary defects (21.9%), musculoskeletal defects (14.6%), gastrointestinal defects (9.75%), respiratory defects (7.3%), cystic hygroma (1.23%) and fetal hydrops (1.23%). Placental findings like uteroplacental insufficiency (11.4%), placental infarct (4.3%), chorangiosis (2.9%), chorioamnionitis (1.4%) and thin cord syndrome (1.4%) were noted (Table 3) Ultrasound is the main diagnostic tool in the prenatal detection of congenital malformations. The key to an accurate antenatal diagnosis is careful scanning of the fetus and first-hand knowledge about fetal anatomy and Ultrasound is the main diagnostic tool in the prenatal detection of congenital malformations. The key to an fetus and first-hand knowledge about fetal anatomy and the knowledge of abnormalities that may be associated with a particular

Table 3- System wise distribution of cases and their no. on autopsy

Major Congenital anomalies	Number of cases	Percentage (%)
CNS Defects	17	
Anencephaly	4	4.93%
Spina bifida	2	2.50%
Occipital meningocele	1	1.23%
Arnold Chiari malformation	4	4.93%
Absent corpus callosum	1	1.23%
Lateral meningocele with spina bifida	1	1.23%
Arachnoid cyst	1	1.23%
Diastematomyelia	1	1.23%
Intracranial ventriculomegaly	1	1.23%
Congenital Hydrocephalus	1	1.23%
Genitourinary Defects	**10**	
Glomerulocystic disease of kidney	1	1.23%
Renal agenesis – Bilateral	2	2.46%
Agenesis of genitourinary system	1	1.23%
Bladder outlet obstruction	5	6.17%
Horse shoe kidney	1	1.23%
Cardiac Defects	**2**	
Tetralogy of Fallot	1	1.23%
Pericardial effusion	1	1.23%
Respiratory defects	**3**	
Bilobed right lung	2	2.46%
Hypoplastic lungs	1	1.23%
Musculoskeletal defects	**6**	
Short femur	1	1.23%
Kyphoscoliosis	1	1.23%
Scoliosis	2	2.46%
Two fused metacarpals with absent ulna and rudimentary femur	1	1.23%
3 digits in right lower limb with kyphoscoliosis	1	1.23%
Gastrointestinal defects	5	
Omphalocele	4	4.9%
Gastroschisis	1	1.23%
Cystic hygroma	1	1.23%
Fetalis hydrops	1	1.23%
Placental findings		
Normal for gestational age	55	67.9%
Chorangiosis	2	2.46%

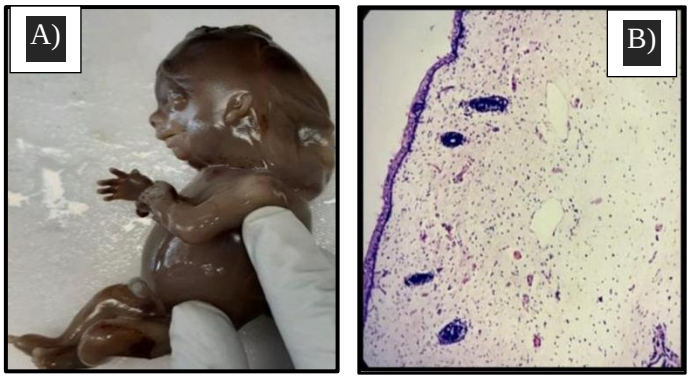

Fig1. A) Fetus with cystic hygroma, B) Histopathology of cystic hygroma (H and E 400x)

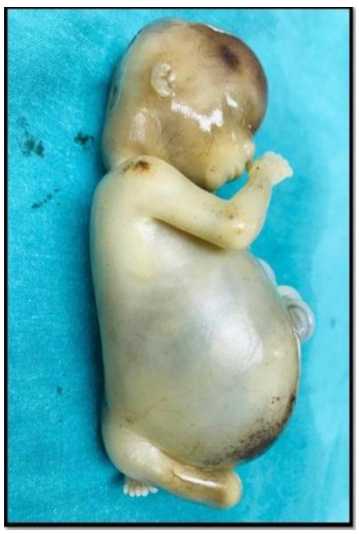

Fig 2: Fetus with Bladder outlet obstruction

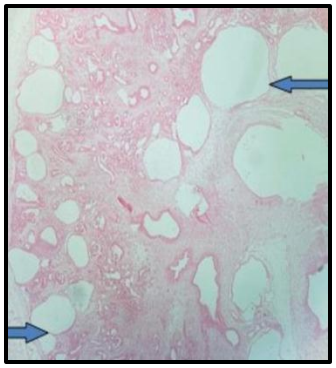

Fig 3: Histopathological image of glomerulocystic disease of kidney showing majority of the glomeruli with cystic change

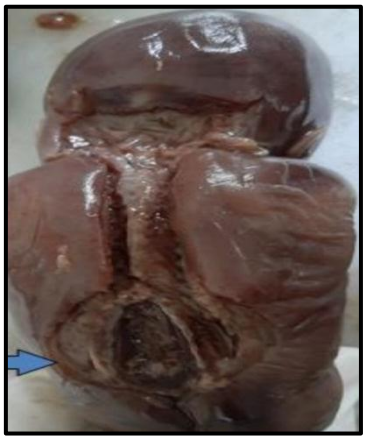

Fig 4: Fetus with spine bifida

Fig 5 A): Fetus with lateral meningeal

Placental infarct	3	3.70%
Uteroplacental insufficiency	8	9.87%
Chorioamnionitis	1	1.23%
Thin cord syndrome	1	1.23%
Not received	11	13.5%

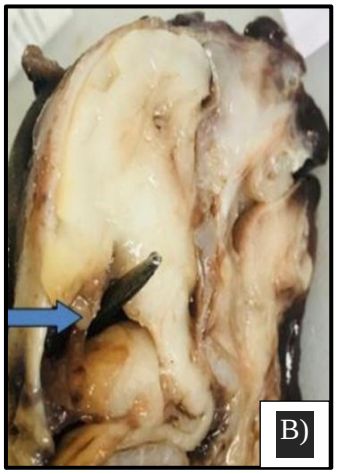

Fig 5 B): Forceps seen communicating at the level of tentorium cerebri through lateral meningocele

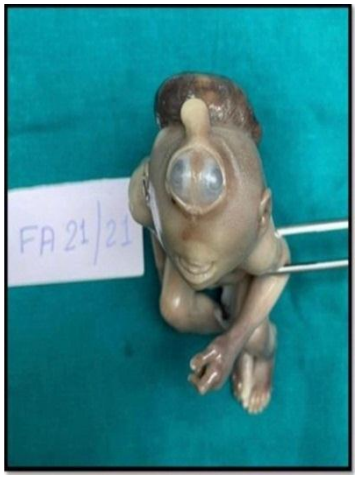

Fig 6: Fetus with anencephaly with fused orbital sockets and bilateral eyes opened

Fig 7: Fetus with omphalocele

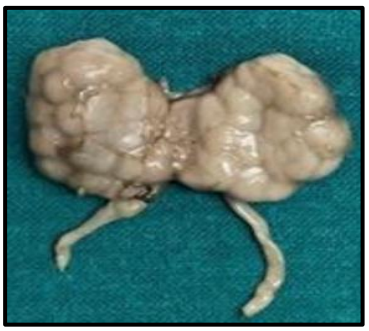

Fig 9: Horseshoe shaped kidney

Fig 8: Fetus with Hypercoiled umbilical cord. Case of Thin cord syndrome

anomaly. In the present study anomaly scan findings showed concordance with the autopsy findings in 78% cases, discordance was seen in 5% cases, additional findings in 6% cases and anomaly scan report was not received in 11%of the cases (Table 2).Out of the 2 cases of meningocele, there was a case of lateral meningocele with spina bifida. The lateral meningoceles were present between the temporal and the occipital bones and were seen communicating at the level of tentorium cerebri(Fig 5A and 5B). The same fetus also showed kyphoscoliosis and bilobed right lung. One case of glomerulocystic disease of kidney was also recorded. The histopathological section showed majority of glomeruli showing cystic change (Figure 3). Bowman's capsule was lined by flattened to low cuboidal lining epithelium and Bowman's space was enlarged. The pelvicalyceal system also appear dilated. In any pregnancy that resulted in fetal loss, be it induced, or in-utero demise, an autopsy should be recommended to be part of the post-mortem examination to verify and revise the prenatal diagnosis which can provide beneficial information for subsequent pregnancies.[7]The false positive diagnosis is quite rare with ultrasonogram. Poor visibility due to oligohydramnios or obesity is an important cause of error in ultrasonogram. However, detection of associated malformations on autopsy may lead to refinement in etiological diagnosis. Risk of recurrence based on ultrasonographic diagnosis of fetus may be erroneous in significant number of cases and hence autopsy of the fetus is essential for genetic counseling. Shanmuga P et al.,[8] noted that fetal autopsy confirmed the ultrasound findings in all 72 cases that were terminated and the pathology-radiology correlation was 100%. Spontaneous fetal losses were 96 in number. Anencephaly and other neural tube defects (27 cases) were the most common malformations noted. Venkataswamy C et al.,[9]studied a total of 66 fetuses, which included 17 intrauterine fetal deaths and 49 pregnancies were terminated because of congenital malformation and increased risk for chromosomal abnormality. In fetuses which showed congenital malformation, multiple anomalies were more common than a single anomaly. The maximum number of

anomalies involved central nervous system (neural tube defect) followed by the genitourinary system, which is similar to this study. Prenatal ultrasound findings were confirmed in all cases except three on autopsy. The USG and autopsy findings showed concordance in 17 cases (39.7%). Additional findings were documented in 25 cases (62.2%) on autopsy. Among these, 15 cases had a significant change of recurrence risk due to altered initial ultrasound diagnosis. In a study by Boyd et al[10], 132 autopsy cases were studied. In 95 (72%) cases the autopsy confirmed the diagnosis which was suspected and did not add further information and in 35 (27%) the autopsy actually added information which led to a subtlety of the risk of recurrence (reduced in 17, increased in 18); in 11 of these 18 cases, it was increased to a one in four risk but two autopsy cases were not classified. In a systematic review, Cristina Rossi et al.,[11] studied 19 articles, where 3534 fetuses underwent autopsy, which confirmed prenatal ultrasound in 2401 (68.0%) fetuses, provided additional information in 794 (22.5%) fetuses, and unconfirmed prenatal ultrasound in 329 (9.2%) fetuses. The latter group consisted of 3.2% false positive and 2.8% false negative cases. The additional findings changed the final diagnosis in 3.8% of cases. The most frequent indication for termination of pregnancy/ stillbirth was CNS anomalies (36.3%), whereas thorax anomalies represented the less frequent indication (1.7%). The highest agreement between autopsy and prenatal ultrasound was observed in CNS (79.4%) and genetics (79.2%), followed by GU anomalies (76.6%), skeleton (76.6%), congenital heart defects (CHD) (75.5%), thorax (69.7%); GI (62.6%), multiple (37.0%), limbs (23.3%). In spite of the high agreement between prenatal ultrasound and autopsy, fetal examination is mandatory because in a minority of cases it discloses additional findings or changes the final diagnosis and genetic counselling. Structurally abnormal fetuses could survive but they are at risk of morbidity throughout their life which greatly impact their families, healthcare systems as well as societies. Primary prevention plays a big role especially in the reduction of the incidence of neural tube defect, and secondary prevention by routine USG examination to all pregnant patients should remain the mainstay of obstetrical screening.[12]Although maternal causes appear to make only a small contribution to fetal deaths, maternal factors may be underestimated because pathologies with a strong maternal component often are attributed to fetal or placental causes. Hypertensive disorders and diabetes are the two most commonly cited maternal diseases associated with 5-8% of stillbirths.[13]While diagnostic imaging techniques is the best available tool to assess fetal anomalies in the prenatal life, it cannot give a complete assessment of the fetal anomalies. Autopsy examination is strongly recommended for identifying the cause of fetal loss.[14]In present study 5 cases showed discordance between anomaly scan and autopsy findings. Findings detected on anomaly scan were Atrial septal defect (ASD)and Ventricular septal defect(VSD) in one, cystic hygroma in one, hypoplastic lungs and kidney in one, craniospinal deformity in one case whereas no any such findings seen on autopsy in all these cases. In present study placental pathology findings has no contributing role for stillbirth or birth defects. In suspected cases of chromosomal anomalies, invasive prenatal diagnostic techniques, including chorionic villus sampling or amniocentesis, can be considered for karyotyping, or preferably the use of a chromosomal microarray or fluorescence in situ hybridization, as appropriate. Inspired by rapid technological improvements, researchers in several countries have been exploring the possibility that medical imaging in particular, MRI and CT scans might substitute a “virtual autopsy” for the more traditional variety.[15] Rapidly advancing Fetal Medicine will soon make fetal surgery a capable modality for the correction of some fetal malformations.

Conclusion:

Fetal and perinatal autopsy is the gold standard pathological investigation and should be performed in all therapeutic terminations of pregnancy or stillbirths. Although the prenatal USG reasonably predicts the malformations, the fetal autopsy is essential to look for additional malformations and to confirm the anomalies diagnosed on USG. Gross examination along with microscopic study helped widely in confirming the antenatal diagnosis and to record additional findings. This study confirms the helpfulness of fetal autopsy in identifying the cause of fetal loss which will help in

counselling of the couple.

Limitations:

Anomaly scan report and placenta for histopathological examination were not received in all the fetuses.

Conflict of Interest - Nil

Sources of Support- Nil

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