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Correlation of fetal autopsy with prenatal ultrasound findings: Study in a tertiary care teaching hospital

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Abstract

Aim: To present a comprehensive analysis of autopsy findings in 168 fetuses in a tertiary care teaching hospital and to assess the clinical utility in reaching a final diagnosis. This is essential for counseling regarding the risk of recurrence in cases of congenital anomalies. We also performed autopsy in fetuses that were terminated based on the ultrasonogram that confirmed the malformation and were correlated to evaluate the potential benefit of radiological investigation.

Materials and methods: Retrospective review of perinatal autopsy records in a tertiary care centre in South India during three year period (2005-2008) was made. Our study comprises of 168 fetuses, 42 terminated after detecting an anomaly in ultrasonogram and 126 were spontaneous fetal losses. In all cases, fetal autopsy was carried out and internal organs were studied. All fetuses with malformations confirmed by ultrasound findings were compared with autopsy findings.

Results: Fetal autopsy was able to provide a definite final diagnosis in 100% of cases. Fetal autopsy correlated very well with the ultrasound findings in all cases.

Conclusion: This study helps to analyse the importance of fetal autopsy in identifying the cause of fetal loss that will help in the genetic counseling of the couple.

Keywords: Congenital anomalies, Fetuses, Ultrasonogram.

Introduction

Congenital malformations remain a common cause of perinatal deaths and account for 25-30% in developed countries and 10-15% in developing countries like India.[1,2] Incidence of major congenital malformation is 3% and that of multiple congenital malformations is about 0.7%.[3] One such mishap creates anxiety in the parents for the fear of similar recurrence in future pregnancies. The recurrence risk of these disorders varies from negligibly low to 25% depending on the genetic component in the disorder. In order to avoid such fetal losses appropriate genetic counseling is mandatory. There are only few studies on fetal autopsy, especially concerning genetic etiology of fetal loss.[4]

Anomaly scan during antenatal period has become a routine in all pregnancies and the ideal time to detect malformations is at around 18 weeks. Ultrasonogram can give fairly accurate diagnosis but some malformations may go undetected by routine ultrasonogram and should be followed by examination of the terminated fetus for associated anomaly to confirm the diagnosis and look for associated malformations. This helps in diagnosing the cause of fetal loss and is therefore a prerequisite for genetic counseling. The objective of the present study was to review and evaluate fetal autopsy of stillbirths/fetal losses and confirm the malformations that were diagnosed by radiology.

Materials and Methods

168 fetuses, over a period of 3 years (2005-2008), referred to department of pathology for autopsies were included in this study. This comprises of 72 therapeutic abortions after the recognition of some congenital malformation on ultrasonographic examination or of genetic disorder on invasive prenatal diagnosis. We also examined 96 fetal losses, which included spontaneous abortions, intrauterine deaths and stillbirths. Each fetus was examined according to a predesigned protocol. This included a photograph, external and internal examination, histopathological examination of all tissues including placenta. Autopsy was carried out after obtaining proper written consent by the parents or relatives who brought the fetus.

In cases terminated after prenatal diagnosis of malformations, the ultrasound diagnosis and post mortem diagnosis were compared to look for agreement. Additional findings at post-mortem examination were considered significant if these findings affected the final diagnosis or brought a change in the recurrence risk.

Results

Fetal autopsy confirm the ultrasound findings in all 72 cases that were terminated. Thus the pathology-radiology correlation was 100%. Spontaneous fetal losses were 96 in number. The cause of death were divided into fetal, maternal and placental (Fig. 8). Anencephaly and other neural tube defects were the most common malformations in our study.(Table 1, Fig. 6, Fig. 7)

Table 1: Post mortem diagnosis of single anomaly (n=58)

1.	Central nervous system	27
	Anencephaly	15
	Spina bifida	7
	Spina bifida with Arnold chiari malformation	2
	Dolicocephaly	2
	Lissencephaly with CMV inclusions	1
2.	Renal malformations	14
	Infantile polycystic kidney	5
	Bilateral multicystic dysplasia	2
	Unilateral Cystic renal dysplasia	2
	Renal agenesis	2
	Horse shoe kidney	2
	Urethral atresia	1
3.	Cardiovascular malformations	8
	Transposition of great vessels	2
	Tetrology of Fallot	2
	PDA,ASD with biventricular hypertrophy	2
	Hypoplastic RV and TV	2
4.	Respiratory system	9
	Congenital lung hypoplasia	4
	Congenital cystic adenomatoid malformation	2
	Holoporencephaly	1
	Lymphangiectasia with hyaline membrane disease	1
	Concentric laminar intimal fibrosis with early plexiform lesions(PHT GR3-4)	1

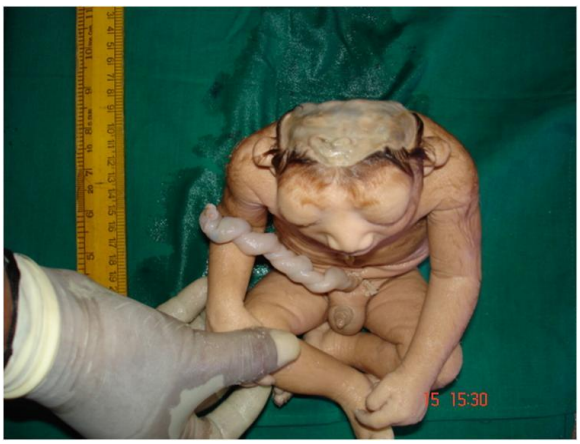

Fig. 1: Gross photograph of 19 weeks fetus with absence of cranial vault (Anencephaly)

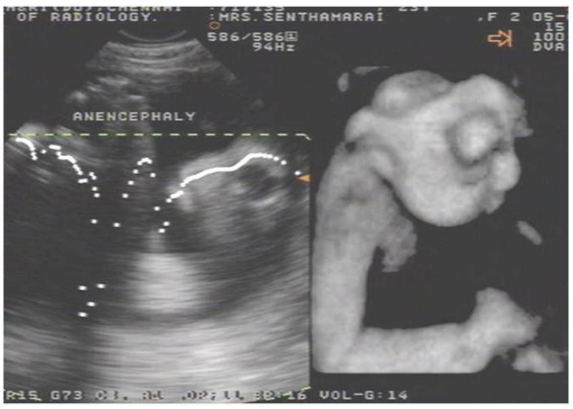

Fig. 2: MRI of 19 weeks fetus with no cranial vault (Anencephaly)

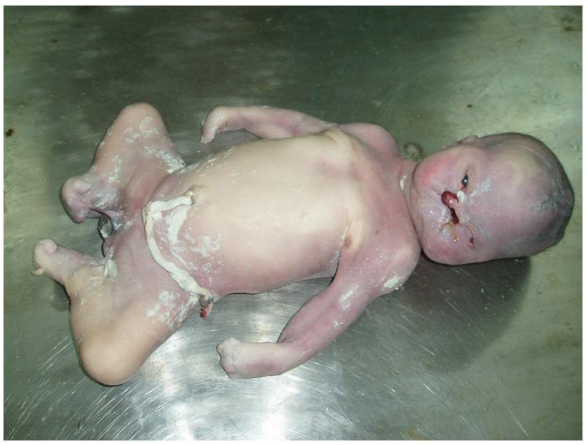

Fig. 3: Gross photograph of 22 weeks fetus with short upper and lower limbs (Phocomelia)

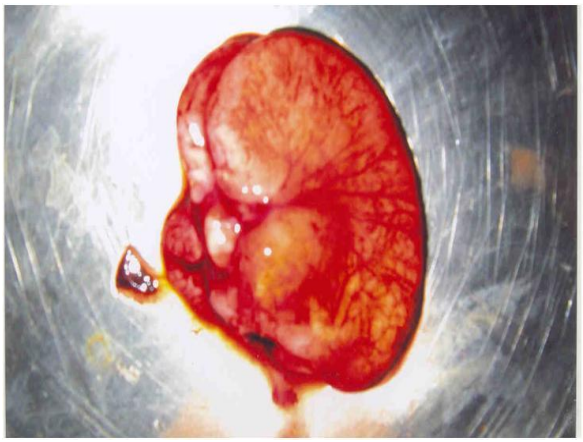

Fig. 4: Gross photograph of smooth brain (Lissencephaly)

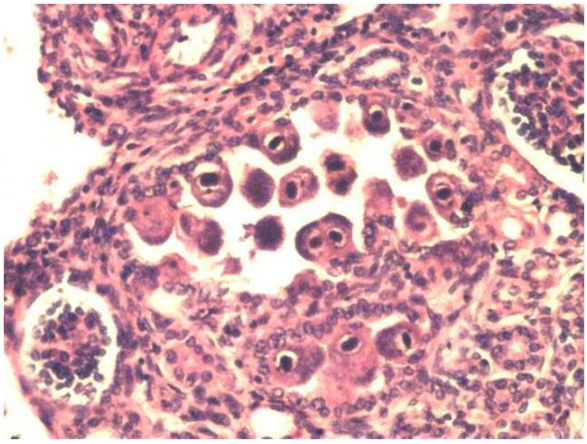

Fig. 5: Microphotograph of renal parenchyma with CMV inclusions in the tubules (Hand E, x 200)

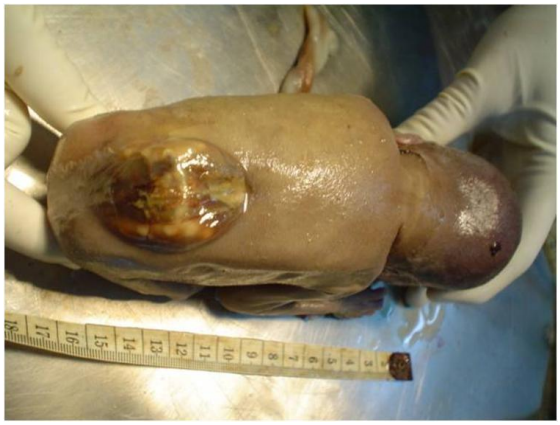

Fig. 6: Gross photograph of 18 weeks fetus with meningocoele

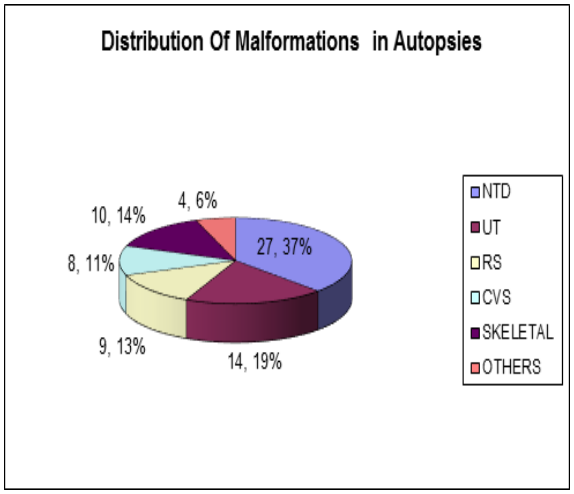

Fig. 7: Distribution of malformations in autopsies

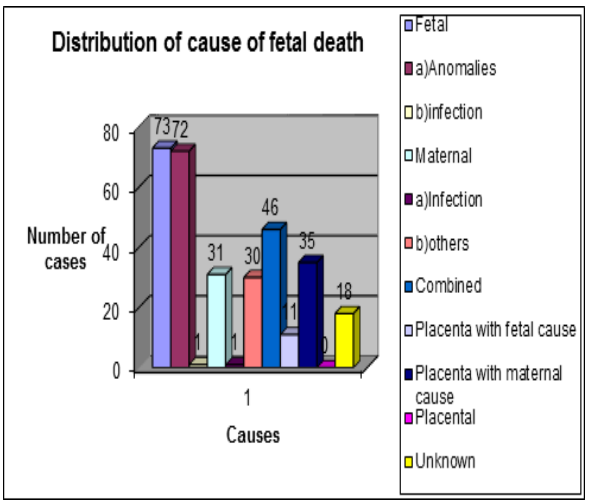

Fig. 8: Distribution of cause of death in fetuses

Discussion

Fetal loss is a common clinical problem and the family needs to know the cause of the loss of a foetus. The future reproductive decision of the couple depends on the cause of the fetal loss, that will predict the recurrence risk and may prevent similar losses.[4,5] The investigations to be performed for analyzing fetal loss includes radiograph, chromosomal analysis, fetal autopsy, investigations for infections and genetic metabolic causes, histopathology of placenta and other fetal tissues as indicated.[5,6] Chromosomal analysis should be performed not only for major malformation but also in fetal hydrops, intrauterine growth retardation, oligohydramnios, macerated fetus and unexplained fetal loss. Skeletal radiograph helps in detecting skeletal dysplasia both prenatally and following termination.[6,7] (Fig. 3, Table 2) Detecting anomalies and malformation prenatally helps in reducing the risk of recurrence which could be otherwise upto 25%. An alternative method to assess the malformations is by performing "limited autopsy" wherein a photograph and radiograph of the fetus alone will suffice.

Table 2: Distribution of multiple malformations(n=14)

1.	Skeletal dysplasia	10
	Rocker-bottom feet	3
	Multiple digital congenital anomalies(overriding, accessory fingers, fused fingers)	3
	Polydactyly	1
	Arthrogryphosis multiplex congenital (Phocomelia)	1
	Short long bones	1
	Congenital talipus equinovarus of left foot	1
2.	OEIS (Omphalocele, Extrophy, Imperforate anus, Spine	1

	deformity.	
3.	Downs syndrome	1
4.	Diaphragmatic hernia	1
5.	Cleft lip & palate	1

Histopathological examination should be carried for all the fetal organs.[6] Renal cystic diseases may be missed by ultrasound scan due to associated oligohydramnios that can be confirmed by histopathology. Moreover, other renal pathology including infantile (autosomal recessive) polycystic renal disease (recurrence risk-25%) and cystic renal dysplasia (recurrence risk-3%) is based on histopathology.[5,6,7] Henceforth genetic counseling is also essential in such cases. We had 10 cases with oligohydramnios. Of these two cases were diagnosed as polycystic renal disease. The rest were due to urorectal malformations and bladder outlet obstruction. Placental examination is very important in fetuses without malformations as it may provide the cause of death in fresh stillbirths or neonatal death. In our series, out of 168 placentas 48 showed features of chorioamnionitis, 49 showed features of infarction and 1 showed chorangioma.The rest of the placenta showed no significant pathology.

Saller et al[8] have analysed 124 cases of perinatal deaths to assess the clinical utility of autopsy. In their study number of perinatal deaths comprises of 75.8% and fetal deaths about 62.3%. Similar study done by Sankar et al proved that the number of cases of fetal deaths were 59%.[17] Our study included 72 anomalous and 96 non-anomalous fetuses (Table 3). Out of 168 fetuses, karyotyping was done in only for two cases and showed no chromosomal abnormality. Documentation of malformation helps greatly in genetic counseling and prenatal diagnosis in the subsequent pregnancy. In cases without any specific diagnosis, some malformations can be looked for in subsequent pregnancies by ultrasound evaluation. Maternal causes can also lead to placental insufficiency. This includes causes like immunological, infections, maternal illnesses and factor V Leiden. Placental examination can also give useful information.

Table 3: Distribution of total number of cases

Total number of cases	168
Terminated after prenatal diagnosis	72
Spontaneous abortion	96

Non-immune hydrops fetalis can be due to chromosomal anomalies, hematological disorders, metabolic disorders and cardiovascular disorders.[9,13] Structural cardiac anomalies, abnormalities of the rhythm and cardiomyopathies have been reported to account for 50% of cases. The other common causes of hydrops are chromosomal(5-33%) and infections(12-16%).[10,11] Fetal hydrops can be associated with congenital malformations, fetal akinesia syndromes and skeletal dysplasia, hematological conditions like alpha-thalassemia, pyruvate kinase deficiency and glucose 6-phosphate dehydrogenase deficiency. The prevalence of alpha-thalassemia in fetal hydrops in south East Asia accounts to 28.2% and metabolic causes accounts to 5-15%.[11,12,13] In our study, out of 10 cases of fetal hydrops, no definite cause was obvious. Better laboratory services are needed to identify these causes of fetal hydrops.The combination of examination of the fetus and placenta with the results of microbiological, cytogenetic and metabolic investigations provides an etiological diagnosis for non-immune fetal hydrops in 65-85% cases in various previous studies.[9,12] The low diagnostic yield in hydrops fetalis in our study is possibly due to incomplete investigative work up for infective and metabolic disorders.

Out of 72 fetuses with malformations central nervous system malformations were the most common indication for therapeutic abortions. The most frequent anomalies were neural tube defect (Fig. 1, 2, 6) and all were correctly identified prenatally. There was an interesting and a rare case of lissencephaly associated with Cytomegalovirus infection (Fig. 4, 5). Lissencephaly was first described by Owen in 1868 that means "smooth brain". It is a developmental disorder of the brain characterized by lack of normal convolutions due to defective neuronal migration. An accurate diagnosis of Lissencephaly and CMV infection is mandatory as appropriate preventive measures may be instituted in high –risk pregnancies[14]. A fetus diagnosed to have neural tube defect(recurrence risk 3-5%) by ultrasonogram, had additional findings like polydactyly and renal malformations on fetal autopsy. In our study post-mortem examination confirmed the ultrasonogram findings in 100% of cases, which is comparable to previous studies.[13] The false- positive diagnosis is extremely 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. Even though autopsy is the best method to detect the cause for perinatal death, there has been a decline in autopsy rate[7,18]. The various options available for investigations in this situation was reviewed in an article. Post mortem imaging has a useful role in providing structural information of the central nervous system in fetuses and stillbirth neonates.[15,16] Another promising alternative approach used in adult post-mortem investigation is the use of limited laparoscopic autopsy, which can be tried in perinatal autopsy that is relatively costly. This retrospective study of 168 cases confirms the utility of fetal autopsy in identifying the cause of fetal loss. There is a need to educate the

relatives about the need of fetal autopsy for genetic counseling. Our data showed that fetal autopsy results in Indian scenario are similar to that reported in the Western literature. Fetal autopsy facilities can be established collaborating with pediatricians. Better investigative facilities for chromosomal analysis, metabolic disorders and infections will definitely increase the diagnostic yield, especially in intrauterine death and fetal hydrops when autopsy is not possible because of ethical and religious reasons, careful examination, a photograph and a radiograph may provide diagnostic information.

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