International Journal of Research in Medical Sciences
Aswathy P et al. Int J Res Med Sci. 2022 Jun;10(6):1302-1308
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20221486

Original Research Article

Pathological features in perinatal autopsy and its relation with clinical and antenatal sonography findings

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Received: 05 April 2022
Accepted: 29 April 2022

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ABSTRACT

Background: Perinatal mortality is considered as a yardstick of obstetric and maternal care before and around the time of death. Perinatal autopsy is an inevitable procedure which helps to ascertain the cause of death, identify rare diseases, supplements clinical diagnosis and provide risk estimates for future pregnancies. The aim of the study was to describe the pathological features in perinatal autopsy specimens and to compare the pathological features with clinical and antenatal sonography findings.

Methods: A descriptive study was conducted among 43 perinatal autopsy cases. A thorough perinatal autopsy was done. Detailed maternal medical and obstetric history including the laboratory and USG findings were collected. Collected data analysed using Statistical package for social sciences (SPSS) software.

Results: The results were grouped into fetal, maternal and placental findings. Congenital anomalies were detected in 20% cases. That included gastrochisis, ebstein anomaly, isolated dextrocardia, hypoplastic left heart syndrome, cleft lip and palate, prune belly syndrome, club foot. Placenta findings observed were chorioamnionitis, placental thrombotic vasculopathy and placental findings in COVID-19 positive cases. The most common maternal comorbidity was hypertension (20.9%). Perinatal mortality was high in those cases with past history of abortions and history of infertility treatment. Full agreement between perinatal autopsy and antenatal USG findings was detected in 36.36% cases. Additional anomalies detected on autopsy was 54.54%.

Conclusions: A thorough clinical history, prenatal ultrasonography and perinatal autopsy features could be described in detail in all the cases. Comparison of finding at autopsy with antenatal ultrasonography finding indicate that ultrasonography finding have only a reasonable value in assessing fetal status. Advanced radiology techniques could be maximum helpful.

Keywords: Perinatal death, Perinatal autopsy, Congenital anomaly, Maternal comorbidity, COVID-19

INTRODUCTION

Diseases originating in the perinatal period accounts for significant morbidity and mortality in low and middle income countries. Perinatal period extends from 28th week of gestation (or more than 1000gm) to the 7th day of life (early neonatal period). In view of increasing survival of babies weighing less than 1000 gm in many centers as a result of improvement in perinatal care, the concept of extended perinatal period has been introduced. This period extends from 22nd week of gestation (or more than 500 gm) to 7th day of life.[1]

The leading causes of death during perinatal period includes congenital anomalies, prematurity, low birth weight,infections, maternal risk factors.[2] The most common cause of fetal and perinatal mortality in developed countries is congenital anomaly. In addition to fetal problems, obstetric complications are also implicated in more than half of perinatal and neonatal deaths. So adequate maternal health and antenatal care

can have a significant role in reducing perinatal and neonatal morbidity and mortality.[3] Different classification systems were introduced to subdivide the causes of perinatal death. It includes WHO International Classification of Disease- Perinatal Mortality (ICD -PM), ReCoDe system and Tulip classification. The most widely accepted system is WHO ICD-PM which describes the causes of perinatal mortality under 3 subheadings namely antepartum (before the onset of labour), intrapartum (during labour but before delivery) or neonatal (upto day 7 of post natal life).

Though nothing can make up for the loss of a fetus or a newborn, a thorough examination of the fetus and placenta following death is essential for arriving at a definitive diagnosis.[4] Perinatal autopsy remains the best method for investigating perinatal deaths. However, there is a decline in autopsy rates now a days. This may be due to the reluctance of parents to give consent for the autopsy of their babies who don't have any obvious abnormalities. But the information provided by perinatal autopsy has important implications both for families and remains the best method of investigating fetal loss, still birth and neonatal death.[5]

In most circumstances, the information obtained during the pathological autopsy of a still born is significant since it will extend the clinical diagnosis. Antenatal anomaly scan has become a standard element of obstetric care, and the ideal time for a fetal malformation scan is about 18 weeks. Eventhough ultrasonogram can provide a fairly accurate diagnosis, it is still necessary to examine the dead fetus for accompanying defects in order to confirm the diagnosis and to rule out any associated malformations.[5] Only a few studies have comparatively examined prenatal ultrasound findings and perinatal autopsy results. The combination of antenatal sonogram and perinatal autopsy may detect the majority of fetal anomalies, but confirmation of genetic abnormality requires invasive prenatal genetic tests and subsequent genetic workup in families. The invasive prenatal genetic tests includes chorionic villous sampling, amniocentesis and percutaneous umbilical blood sampling. These genetic tests are indicated when couples have an increased risk of having a baby with genetic abnormality. Genetic testing can provide only limited information about inherited conditions. The utility of genetic testing is frequently limited by a lack of treatment options and financial constraints. With the available resources, the present study aims to describe the pathological features in perinatal autopsy specimens and to compare the pathological features with clinical and antenatal sonography findings.

METHODS

A descriptive study was conducted on 43 perinatal autopsy cases recieved in the Department of pathology, Govt. Medical College, Kottayam from November 2019 to April 2021. The study was approved by the institutional review board of Government Medical College, Kottayam. Detailed medical and obstetric history of each case and the antenatal ultasonography reports/ findings were collected from medical records library and request forms. Fetal autopsy specimens with gestational age between 28 completed weeks and within 1 week after birth were included in the study and severely autolysed fetus were excluded. Among the 43 cases, 2 were twin pregnancies and the remaining were singleton pregnancies. Hence the total perinatal specimens examined was 45 in number. In each case the autopsy was performed according to the standard protocol in the following order. Anthropometry, external examination, internal examination, examination of the placenta and the umbilical cord.[2]

Anthropometry

Includes body weight and external measurements such as head circumference, chest circumference, abdominal circumference, crown rump length (CRL), rump heel length (RHL) and foot length (FL).

External examination

External surface of the fetus was examined for evidence of maceration, cyanosis, injury and skin lesions. The orifices were examined for patency, exudation or other abnormalities. All major and minor anomalies including facial anomalies were recorded.

Type of incision

Inverted 'Ý shaped incision starting from chin to mid-inguinal points.

Internal examination

Initially the body cavities were examined for the presence of effusion, blood, pus or fecal material. Then insitu examination of abdominal organs were done followed by examination of thoracic structures including thymus. After completing the examination of both body cavities, evisceration was done. The viscera was dissected from posterior surface. Heart was examined by inflow outflow technique. Brain was dissected by Rokintansky's method. Tissue bits from every organ was taken for histopathological study.

Placenta

Weight, measurement, completeness of cotyledons were noted. Colour and fetal surface of membranes were examined. Placenta should be sliced at approximately 1 cm intervels.

After the completion of autopsy, all the organs were returned into the respective body cavity followed by suturing of the incision lines and the bodies were properly disposed.

The clinicopathological variables studied include maternal age, consanguineous marriage history, infertility treatment and abortion history, maternal comorbidities, gestational age, gender distribution of fetuses, birth weights of the preterm fetuses, antenatal ultrasonography findings, congenital anomalies detected in each case, placental findings, relation between perinatal autopsy findings and antenatal sonography findings.

Analysis was done using Statistical package for social sciences (SPSS) software (version 26). Descriptive data was presented in the form of frequency, proportion and percentage.

RESULTS

Perinatal autopsy was performed under standard protocol and the pathological findings were analyzed. Among the 43 cases, 2 were twin pregnancies and the remaining were singleton pregnancies. Hence the total perinatal specimens examined was 45 in number. The average gestational age of the fetuses was 33 weeks 2 days. 37 (86.04%) were preterm gestations (Table 1).

Table 1: Gestational age of fetuses.

Gestational age (weeks)	N (43)	%
Preterm (<37 completed weeks)	37	86.04
Term (37 completed weeks)	6	13.96
Total	43	100

Table 2: Relation between perinatal autopsy findings and antenatal sonography findings.

Relation between perinatal autopsy and antenatal sonography findings (N=11)	N	%
Full agreement	4	36
Disagreement	6	55
Inconclusive	1	9
Total	11	100

Among the 45 fetuses, 26 (58%) were males and 17 (38%) were females. Ambiguous genitalia was observed in 2 (4%) cases. Majority of the fetuses fell under adequate for gestational age category 28 (66.6%). 8 (20.5 %) were small for gestational age and 3 (7.5 %) were large for gestational age.

The average maternal age of the study population was 27 years. Minimum age was 20 and maximum age was 35 years. The most common maternal comorbidity identified was hypertension 9 (20.9%) followed by maternal infections 6 (13.9 %). Past history of abortions, history of infertility treatment and consanguineous marriage were associated with increased risk of perinatal mortality. (Figure 1 and 2)

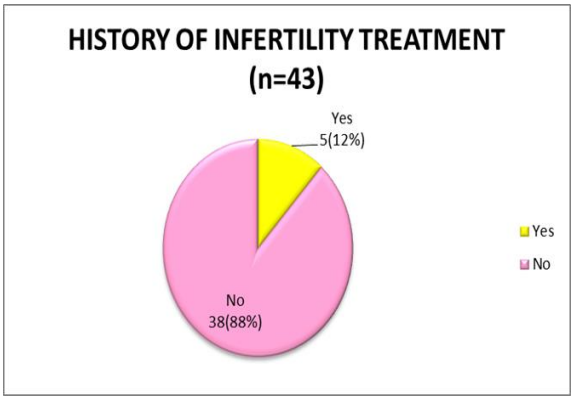

Figure 1: Infertility treatment history in parents.

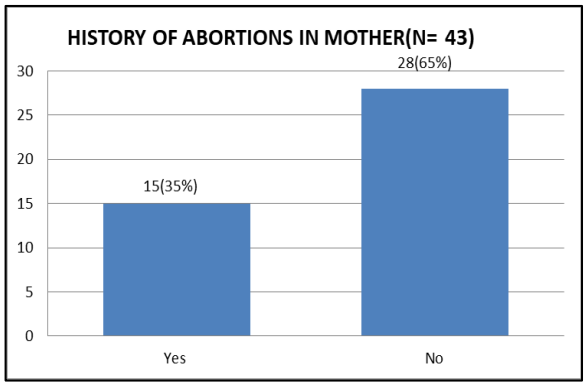

Figure 2: Past history of abortions in mothers.

Figure 3: Prune belly syndrome- atrophy of muscles of the anterior abdominal wall, undescended testis with bilateral hydronephrosis distended bladder and hydroureter.

The congenital anomalies detected on autopsy was 20% and following antenatal ultrasound was 15.55%. Multiple anomalies were more common than single anomaly. The anomalies detected during autopsy were gastrochisis, Ebstein anomaly, isolated dextrocardia, cleft lip and palate, and a single umbilical artery.

Figure 4: Gastrochisis - presence of large and small bowel, liver outside abdominal cavity with adherent placenta and cord not covered by membranes.

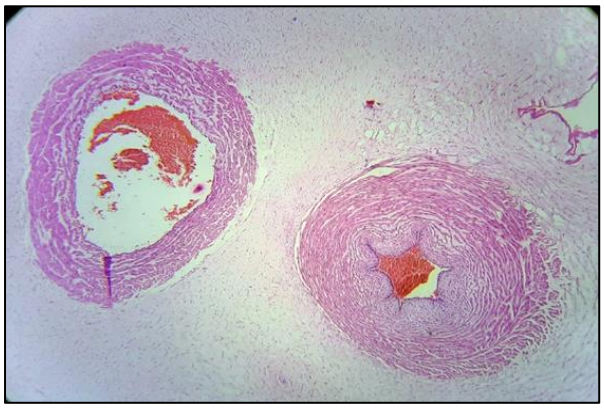

Figure 5: Single umbilical artery - cut section of umbilical cord shows single umbilical artery and vein (hematoxylin and eosin stain, 10 X).

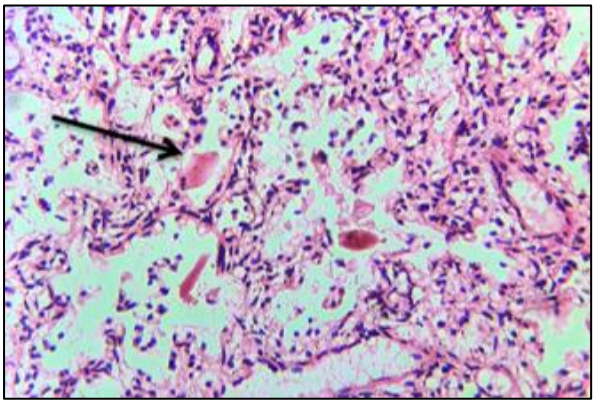

Figure 6: Meconium aspiration lung - presence of squames (arrow) and pigment laden macrophages in alveolar spaces of lung (hematoxylin and eosin stain, 40X).

A combination of findings was observed in 3 cases during autopsy (Figure 3, 4 and 5). A combination findings such as club foot and foetal hydrops, Prune belly syndrome, hypoplastic left heart syndrome and foetal hydrops were also detected during perinatal autopsy. Placenta findings observed were chorioamnionitis, placental thrombotic vasculopathy, twin twin transfusion syndrome and placental findings in COVID 19 positive cases (chronic villitis, placental infarction, decidual arteriopathy, increased intervillous fibrin deposits). A single case of meconium aspiration syndrome was also observed (Figure 4).

Full agreement between perinatal autopsy and antenatal USG findings was detected in 4 (36.36%) cases. Additional anomalies detected on autopsy in 6 (54.54%) cases. Single case of vanishing twin detected on antenatal sonography was not verified in autopsy (Table 2).

DISCUSSION

Perinatal deaths are a reflection of maternal and fetal health care during pregnancy, as well as the success of our health care system in reducing foetal morbidity and mortality. The incidence of perinatal autopsies are reducing now a days. People are ignorant of the significance of autopsy, which can reveal the exact cause of death and help parents make decisions about future pregnancy planning. The underlying causes of perinatal mortality can be broadly categorized as fetal, maternal and placental.

Table 3: Comparison of congenital anomalies detected in different studies.

Variables	Present study (n=43) (%)	Brahmanandan et al (n=431)[13] (%)	Kale et al (n=223)[19] (%)
Frequency of congenital malformations	9 (20)	72 (16.7)	53 (23.7)
Most common system affected	Cardiovascular system and gastrointestinal system	Central nervous system	Musculoskeletal system

In the present study, the mortality in males 26 (58%) is higher compared to that of females 17 (38%). Male and female mortality were equal in a study conducted by Parthan et al in 2013.[6] The incidence of ambiguous genitalia in the present study population is 4% due to unknown reasons. The gestational age can be calculated from last menstrual period (LMP), crown rump length, foot length and from antenatal sonography (dating scan). In the present study, gestational age was calculated from last menstrual period. In this study, the average gestational age is 33 weeks 2 days. This is comparable

with the retrospective cohort study conducted by Dehbalaie et al in 2014.[7] However, previous studies have demonstrated that the risk of perinatal mortality increases as gestational age approaches term.[8,9]

Table 4: comparison of placental findings in COVID 19 positive cases in different studies.

Placental findings in COVID 19	Present study (n= 2)	Menter et al[23] (n=5)	Baergeneta et al[24] (n=10)
Signs of maternal malperfusion			
Infarction	Present	Present	Absent
Increased intervillous fibrin deposits	Present	Present	Absent
Decidual vasculopathy	Present	Present	Absent
Intervillous thrombus	Absent	Present	Absent
Signs of fetal maperfusion			
Thrombus in fetal circulation	Absent	Present	Present
Avascular villi	Absent	Absent	Absent
Chorangiosis	Present	Present	Present
Inflammatory changes			
Chorioamnionitis	Absent	Present	Absent
Chronic villitis	Present	Present	Absent
Other findings (chronic deciduitis , subchorionitis, choriovasculitis, fetal vasculitis)	Absent	Present	Present

The single most important determinant of a baby's chance of survival is its birth weight.6In the present study, out of 45 stillborns 39 babies were preterm. 66.6% of the preterm babies had adequate weight for gestational age, 20.5% were small for gestational age and 7.5% were large for gestational age. A study conducted by Unterscheider et al found that fetal growth restriction is an important risk factor for perinatal mortality in non anomalous babies.[10]

Preterm delivery was associated with a greater rate of perinatal mortality in multiple studies, accounting for roughly two-thirds of all perinatal deaths.[11-13] In the present study, preterm babies accounts for 86.04%. In our study, no abnormality was detected in 73% of cases. But it was found that those cases were associated with multiple maternal comorbidities which might have contributed to the perinatal death. Congenital anomalies accounts for 20% of perinatal death. Brahmandan et al in their study from Kerala described that prematurity is the most common cause of perinatal death which accounts for 44.1% of all perinatal deaths and the study conducted by Allanson et al also revealed similar results.[13,14]

Advanced maternal age is one of the risk factor for perinatal mortality and development of anomalies in fetuses. Consanguineous marriage is associated with increased risk of still birth. The history of consanguineous marriage was identified in 4.65% of cases in the present study. In study by Maghsoudlou et al found out that the association of consanguineous marriage associated still birth is more in preterm than in term pregnancies.[15]

The most common maternal comorbidity detected in the present study was gestational hypertension (20.9 %). This finding was comparable with the study conducted by Brahmanandan et al 21.7%.[13] In the present study, maternal infections such as congenital our study history of abortion was obtained in 34.88% of cases.[16] A study by Yirgu et al revealed mothers with no previous history of abortion have a lower risk of losing their new born for perinatal mortality as compared to those who had history of abortion.[17] The most common malformation observed in the study by Kalyani et al was those involving alimentary system (20.31%).[18] The study done by Kale et al revealed musculoskeletal system being the most common system affected (19.3).[19] However in the present study, cardiovascular and alimentary systems were equally affected (33.33%) (Table 3). The anomalies detected were Ebstein anomaly, hypoplastic left heart isolated dextrocardia, gastrochisis, prune belly syndrome, cleft lip and palate and fetal hydrops.

Most of the placental causes of fetal deaths are nonspecific. In the present study, single case of chorioamnionitis and placental thrombotic vasculopathy was observed. A study on placental pathology by Korteweg et al observed placental infarction and fetal thrombotic vasculopathy in 79.4% and 2.8% cases respectively.[20] Another study by Kidron et al in 120 stillbirth found out that inflammatory lesions accounts for 12% of placental abnormalities.[21] In our study, COVID 19 related findings such as villitis, perivillous fibrin deposits, arteriopathy, chorangiosis, focal placental infarction were identified in the placental tissue in 6.66% cases (Table 4).

In the present study, one case became inconclusive. The additional autopsy findings were gastrochisis, club foot, isolated dextrocardia and cleft lip and palate. In the present study, complete agreement between autopsy and antenatal USG was detected in 36.36%, disagreement was detected in 54% cases. In our literature search,

disagreement between autopsy and antenatal sonography was observed in 36.7% in study conducted by Pradhan et al, 29.54% in study by Andola et al.[6,22]

CONCLUSION

A thorough clinical history, prenatal ultrasonography and perinatal autopsy features could be described in detail in all the cases. Comparison of finding at autopsy with antenatal ultrasonography finding indicate that ultrasonography finding have only a reasonable value in assessing fetal status. Advanced radiology techniques could be maximum helpful. In comparison to ultrasonography findings, while searching for a cause for fetal loss, the following factors are equally or more important. This includes: maternal comorbidities, full perinatal autopsy, screening for infection, assessment of prematurity by better technique, history of consanguinity, abortion history and infertility treatment history.

ACKNOWLEDGEMENTS

I express my sincere and heartfelt gratitude to Dr. Sankar, Professor and HOD, Dr. Lilly Kutty Pothen, Additional Professor and Dr. Renu Thambi, Associate professor (CAP) for the guidance and the lab technicians for their technical support. I would like to acknowledge Kerala University of Health Sciences for providing the opportunity for performing the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Aswathy P, Pothen L, Thambi R, Sankar S. Pathological features in perinatal autopsy and its relation with clinical and antenatal sonography findings. Int J Res Med Sci 2022;10:1302-8.