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Reviewed causes of death in 145 perinatal autopsies at King Chulalongkorn Memorial Hospital during October 2002 to December 2006

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Objective : *To evaluate cause of death in perinatal autopsies*

Design : *Retrospective descriptive study*

Setting : *Department of Pathology, King Chulalongkorn Memeorial Hospital, Bangkok, Thailand.*

Materials and Methods : *One-hundred and forty-five perinatal autopsies from October 2002 to December 2006 were recruited under criteria.*

Results : *Most causes of death were congenital anomaly (36.6%), placental or cord pathology (23.4%) unexplained causes (17.9%) and other explicable causes (17.2%). The most common systemic congenital anomaly was cardiovascular system (23.5%).*

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Conclusions : *Perinatal death is an important problem for parents who have lost their babies. Perinatal autopsy has a momentous role. The most common cause of death is congenital anomaly. About 82.1% of the autopsies can demonstrate the problem, wherease the others cannot due to severe maceration.*

Keywords : *Perinatal death, Autopsy, Causes of death.*

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วีระนุช เอี่ยมพรรัตน์, สิริสรรพางค์ ยอดอาวุธ, นฤมล คล้ายแก้ว. การพิจารณาสาเหตุการเสียชีวิตในกลุ่มที่มีการตายปริกำเนิดที่ได้รับการส่งชันสูตรศพ 145 รายในโรงพยาบาลจุฬาลงกรณ์ ระหว่างเดือนตุลาคม 2545 ถึง ธันวาคม 2549. จุฬาลงกรณ์เวชสาร 2551 พ.ย. – ธ.ค.; 52(6): 407 – 20

วัตถุประสงค์ : *ในการวิจัยนี้เป็นการศึกษาเพื่อหาสาเหตุของการเสียชีวิตในกลุ่มการตายปริกำเนิดที่ได้รับการผ่าชันสูตรศพ*

รูปแบบการวิจัย : *การวิจัยเชิงพรรณนาแบบเก็บข้อมูลย้อนหลัง*

สถานที่ทำการศึกษา : *ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ โรงพยาบาลจุฬาลงกรณ์ กทม. ประเทศไทย*

ตัวอย่างและวิธีการศึกษา : *ศพของกลุ่มที่มีการตายปริกำเนิด และได้รับการผ่าชันสูตรจำนวน 145 ราย ในภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ โรงพยาบาลจุฬาลงกรณ์ ที่เข้าได้กับเกณฑ์ การศึกษาวิจัยระหว่างตุลาคม 2545 ถึง ธันวาคม 2549 ทุกศพจะได้รับการผ่าชันสูตรตามแนวทางการผ่าชันสูตร และตามหนังสือตำรามาตรฐานการผ่าชันสูตร*

ผลการศึกษา : *ผลการศึกษาพบว่าสาเหตุการเสียชีวิตโดยส่วนใหญ่มาจากความพิการแต่กำเนิด (36.6%) รองลงมาคือการเสียชีวิตจากพยาธิสภาพที่รกและสายสะดือ (23.4%) สาเหตุอื่นๆ ที่สามารถอธิบายได้ (22.1%) และกลุ่มที่ไม่สามารถอธิบายสาเหตุการเสียชีวิตได้ (17.9%) และนอกจากนี้ยังพบว่าความพิการของระบบหัวใจและหลอดเลือดเป็นสาเหตุที่พบมากที่สุด (23.5%) เมื่อเทียบกับความพิการระบบอื่นๆ*

สรุป : *การตายปริกำเนิดเป็นปัญหาที่สำคัญของทั้งบิดาและมารดา สาเหตุการเสียชีวิตโดยส่วนใหญ่มาจากความพิการแต่กำเนิด โดยพบความพิการระบบหัวใจและหลอดเลือดมากที่สุด เมื่อเปรียบเทียบกับความพิการระบบอื่น ๆ การผ่าชันสูตรศพสามารถอธิบายการเสียชีวิตได้ถึง 82.1% กลุ่มที่ไม่สามารถอธิบายถึงสาเหตุการเสียชีวิตได้นั้น ส่วนหนึ่งเกิดจากการที่ศพเน่าจนไม่สามารถสืบหาสาเหตุได้*

คำสำคัญ : *การตายปริกำเนิด, การผ่าชันสูตรศพ, สาเหตุการเสียชีวิต*

Abortions and stillbirths are common problems that suffer parents. The facts about the cause death of the baby and preventions are required in order to release they from the misery. The perinatal mortality rate indicates the health of the mothers and fetal heath status. According to the WHO's definition [1], perinatal mortality rate means the number of perinatal deaths per 1,000 live births. The perinatal period starts as the beginning of fetal viability (28 weeks gestation or 1,000 g) and ends at the end of the7th day after delivery. Perinatal deaths are the sum of stillbirths plus early neonatal deaths. The National Vital Statistic System, according to the United States of America (U.S.A.), reported incidence of perinatal mortality rate (PMR) has been declining since 1950.[2] However, Thailand, a developing country, has a higher rate (11.84 per 1,000 live births)[3-4] than the U.S.A. (7.6 per 1,000 live births).[2]

There are many systems that classify the causes of perinatal death such as the Nordic-Baltic [5], the Aberdeen [6], the Wigglesworth [7], and the Fundamental. [8,9] The leading causes of death were composed of congenital malformations, infections, perinatal asphyxia and inborn errors of metabolism.[10] However, the rest are called others were unexplained causes.

In this study, the authors aimed to review the incidence and causes of death in perinatal autopsy with Wiggleworth's classification. It is a simple and forms the basis for perinatal mortality analysis by functional subgrouping without consideration conditions in pregnancy, during labor and or in the neonatal period.

Materials and Methods

All perinatal autopsy cases, during a five-year period (from October 2002 to December 2006) were identified from the autopsy files of the Department of Pathology of King Chulalongkorn Memorial Hospital.

All of them were performed according to the guidelines and standards given in the textbooks of autopsy.[12-17] Shortly, the external appearances were described, including body weight, length, head circumferences, chest circumferences, abdominal circumferences, crown-lump length, crown-heel length and foot length. The visceral organs were eviscerated and examined. All visceral organs were weighed, serially dissected and processed. Gross anomalies were analyzed and divided in systems as follows:

1. Nervous system: such as alobar holoprocencephaly and hydrocephalus.
2. Cardiovascular system: such as ventricular septal defect, atrial septal defect, patent-ductus arteriosus and coarctaion of aorta.
3. Respiratory system: such as pulmonary hypoplasia and CCAM.
4. Digestive tract and hepatobiliary system: such as gastroschisis, omphalocele and liver hypolobation.
5. Genitourinary system: such as hydroureter and renal agenesis.
6. Craniofacial system: such as cleft lips, cleft palate, low set ear and absent nose.
7. Skeletal system: such as club foot, syndactyly and polydactyly.

Some cases had multiple anomalies, but divided in all systemic anomalies and ignored the causative system for death. Then a number of

systemic anomaly was higher than number of cases. Microscopic examination, including special stains, was used for giving the final diagnosis.

Placental and umbilical cord examinations were important to identifing the cause of death. Pathologic findings were classified into three groups as follows [18-19]:

1. **Inflammation** : such as acute chorioamnionitis and villitis.
2. **Utero-placental pathology** : such as abruption placenta, intervillous infarction and villous fibrosis
3. **Umbilical cord pathology** : such as true knots, cord torsion, abnormal length of cord (including short and long cord) and nuchal cord.

The data were analyzed using SPSS program. The analyses were two tailed. Catergorial variables were reported in number and percentage.

Results

There were 74 females and 71 males consecutive perinatal autopsies. The minimum gestational age was approximately 28 weeks whereas the maximum gestational age was approximately 43 weeks (Table 1). The median body weight was 2,050 g (ranged from 460 to 4,580 g). The median maternal age was 30 years (ranged from 13 to 44 years old). Maternal diseases were usually detected in elderly pregnancy.

Table 1. Correlations between maternal ages and pathologic findings of perinatal autopsies.

	Number	Maternal age (years)				
		≤ 19	20 - 24	25 - 29	30 - 34	≥ 35
BW (grams) ≤ 999	9	1	2	1	4	1
1000 - 1499	28	4	3	10	5	6
1500 - 1999	32	3	3	5	9	13
2000 - 2499	27	2	5	5	12	2
2500 – 2999	28	5	6	9	4	4
3000 – 3499	15	2	2	3	4	4
3500 - 3999	4	0	0	1	1	2
≥ 4000	2	0	0	0	2	0
Total	145	17	21	34	41	2
Causes of death						
- Congenital anomaly	53	4	7	11	13	18
- Placental or umbilical cord pathology	34	5	5	7	10	7
- Unexplained death	26	4	5	8	5	4
- Other*	25	2	3	7	10	3
- Traumatic lesions	4	1	1	0	2	0
- Intrauterine infection	3	1	0	1	1	0
Total	145	17	21	34	41	32
Gestational age (weeks)						
- 28 to 33	67	7	10	19	17	14
- ≥ 34	78	10	11	15	24	18
Total	145	17	21	34	41	32

* = Tumors, hemoglobinopthy, immaturity and storage diseases

The data and finding were analyzed and classified them according to Wigglesworth system (Table 2). The leading causes of death were, namely: congenital malformation (36.6%), placental or umbilical cord pathology (23.5%) and unexplained causes (17.9%). Multiple anomalies may be related to chromosomal abnormality, syndrome and sequences (Fig.1, 2 and 3). This study, 13 of 53 cases were identified as chromosomal abnormalities related to congenital malformations. The common congenital systemic anomaly was cardiovascular system (23.5%) such as atrial septal defect (Fig.4), ventricular septal defect (Fig. 5) and patent-ductus arteriosus (Table 3).

Table 2. Causes of death in perinatal autopsy according to the Wigglesworth perinatal death classification.

Cause	Number (cases)	Percent
Congenital malformations[a]	53	36.6
Placental or umbilical cord pathology[b]	34	23.5
Unexplained death	26	17.9
Others[c]	25	17.2
Traumatic lesions[d]	4	2.8
Intrauterine infections	3	2.1
Total	145	100

a = Classified systemic congenital anomaly, see Table 3

b = For detailed information regarding placental or umbilical cord pathology, see above text

c = Tumors, hemoglobinopathy, immaturity and storage diseases

d = Traumatic lesions occurred during delivery, including intracranial hemorrhage, rupture of subcapsular hematoma of the liver

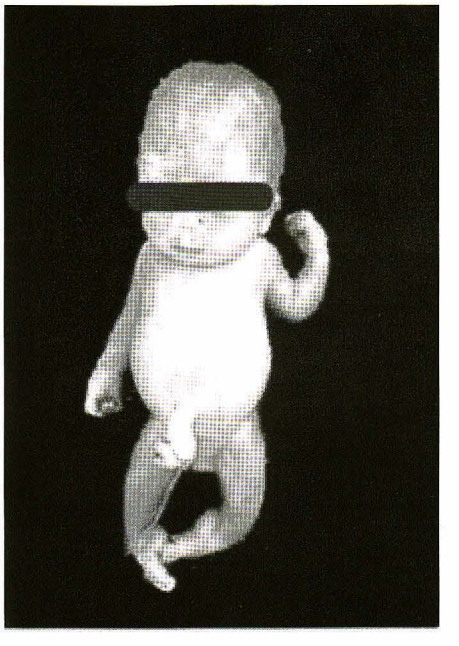

Figure 1. A fresh stillbirth fetus had short both upper and lower extremities.

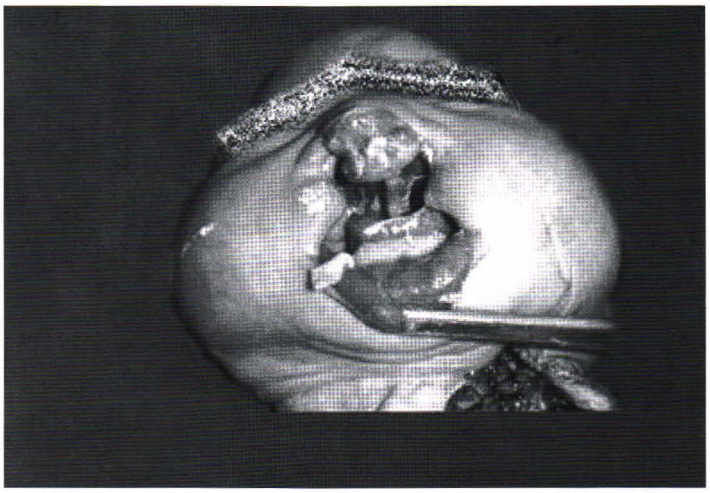

Figure 2. A stillbirth was complete cleft lips and palates. This case has a trisomy18 karyotype.

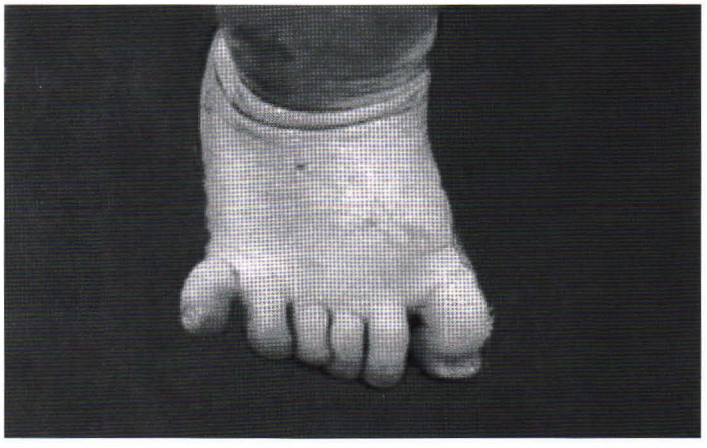

Figure 3. This foot showed polydactyly (number of fingers or toes more than the normal), and usually be found in trisomy13 karyotype.

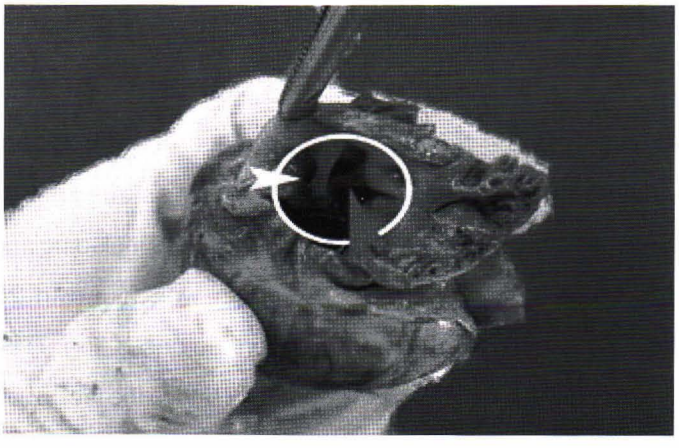

Figure 4. The atrial septal defect (arrow head), common congenital heart anomaly, closed to foramen ovale (arrow).

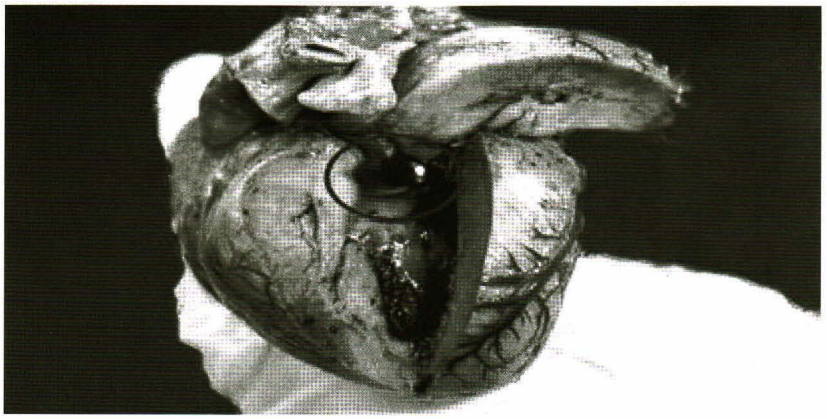

Figure 5. Ventricular septal defect was a common congenital heart anomaly.

Table 3. Classified systemic congenital anomaly.

System	Frequency[a]	Percent
- CVS	31	23.5
- Respiratory system[b]	23	17.4
- Skeletal system	19	14.4
- Craniofacial system[c]	19	14.4
- Genitourinary system	16	12.1
- CNS	13	9.9
- Digestive tract including Hepatibiliary system	11	8.3
Total	145	100

a = In fifty-three cases, each patient had multiple anomalies which were classified into systemic anomaly

b = Including diaphragmatic hernia

c = Including cleft lip, cleft palate and low set ear

This study found 15 elderly and 4 teenage mothers who had anomalous dead fetuses. At a time, 13 of 17 teenage pregnant women had a history of the first baby (76.47%) and 8 of 32 elderly pregnant women had a history of the first baby (25%), too. Furthermore, 4 of 17 teenage and 5 of 32 elderly pregnant women developed complications during their antenatal care.Twenty-one out of 34 cases in the placental and cord lesion group had umbilical cord lesion, such as true knot, cord torsion (Fig. 6), short and long cords including nuchal cord. Unknown cause of death was found in 26 cases, comprising 14 macerated cases (Fig. 7) and 4 incomplete cases of autopsy due to the lack of placenta examination. Eight out of 14 macerated cases (57.1%) were preterm newborns death (GA $\leq$ 36 weeks).

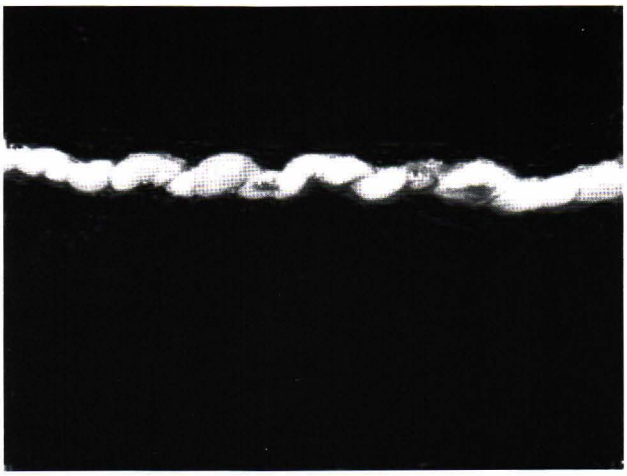

Figure 6. A hypercoiled umbilical cord was an occurrence to fetal death in utero.

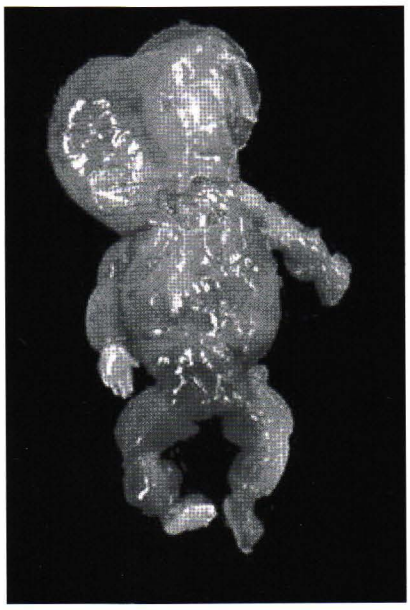

Figure 7. A macerated fetus was generalized skin blebs with skin edemas and cystic hygroma.

Discussion

A perinatal mortality rate is an indicator of health status. In Thailand, a perinatal motality rate (PMR) was 11.84 per 1,000 live births[4] in 1995. Sanker VH and Phadke SR[20] analyzed 135 fetuses with multiple malformations: 81 cases had isolated malformation and 54 cases had multiple malformations. Central nervous system malformations were the most common indication for therapeutic abortion. A previous study of Tannirandorn Y and Jatuparisuth N[21] showed 640 stillbirths out of 120,998 total births (5.3 per 1000 live births) at King Chulalongkorn Memorial Hospital. One hundred and fourteen cases had congenital anomalies, and the most common anomalies were in the central nervous system. Whereas Ratanasiri T and Anukoolprasert T[22] reported, that gastrointestinal system was the most common for major congenital anomalies; other systems namely cardiovascular, musculoskeletal and central nervous systems were in decling orders, respectively. But in this present study,

a cardiovascular system was the most common congenital anomaly. Other systems such as respiratory, musculoskeletal and craniofacial were less common.

Progress in science and technology has always given updated medical data and new instruments which have been raising values in parental counseling, planning, detecting and correcting. Especially, an ultrasonography is safe and possesses high sensitivity and specificity. Then, it is used as a routine prophylactic antenatal care. Usually helps demonstrated congenital abnormalities and elevates number of therapeutic abortions. From the above, these are influence factors for difference results from previous reports.

Some previous studies, intracardiac echogenic foci detected the increase of incidences in fetus associated with trisomy 13, 18 and 21, and 45,XO.[23] Atrial septal defects and ventricular septal defects were common cardiovascular anomalies.[24] The reported were similar to this study. Some genetic abnormalities cannot be prevented after conception, but early detection can be done. This results in optimal management for such complicated cases.

Not only, that prematurity, an intrauterine retardation and multiparity were high risk factors for antenatal and perinatal death[14], but also maternal aging increases the risk of adverse pregnancy outcomes.[22] In consequence of multiple factors, such as genetic abnormality, mutation of chromosome, toxic substances and unknown, elderly mother had higher chances. Compared to this study, both elder and younger mothers did not mark more influence on congenital anomaly than appropriate group, but elderly group had higher number of occurrence than teenage group.

The minimum maternal age, related to placental and cord pathology cause, was 17 years whereas the maximum age was 41 years. The mode maternal age ranged from 30 to 34 years (10 cases). Four of this causative death (3 cases of uteroplacental insufficiency and 1 cord pathology) were associated with maternal diseases. Maternal age is not associated with placental and cord pathology until the development of the diseases.

Fetal deaths before 24 weeks of gestation were often due to infection or congenital malformation. From 24 to 36 weeks of gestation, the predominant causes were asphyxia, hydropic fetus and anemia.[14] Whereas at the 36 weeks of gestation, the causes of death were often unknown. Many unexplained cases display evidences of chronic hypoxia. Fifteen cases of unexplained group had gestational age of at least 36 weeks, this is in concordance with previous reports.[25]

In our study, approximately 33.80% of the pregnancies were of inappropriate age, 75% were elderly mothers who had multipara whereas 76.47% were from teenage group who had the first fetus. About 25% of maternal diseases were hemoglobinopathy and 80% of them did not receive antenatal care; these diseases were, for example, thalassemia which is a common problem in Thailand and in South East Asia.[25] It is associated with hydropic fetuses leading to serious fetal complications. Furthermore, about 40% of others causative death group were hydropic fetuses with fathers and/or mothers were thalassemia, too. Tumors and lung immaturity were found in this others group.

The diagnosis of hydrops was generally made when a fetus presents with excess fluid in more than one body cavity. The affected pregnancy was generally complicated by polyhydramnios and the fetus exhibits one or more of the following: generalized skin thickening over five millimeters, ascites, pleural effusions, pericardial effusion, and placentomegaly.[26] Parents should understand their causes, preventions and must know affects their babies.

Teenage pregnancies had insufficient income, had fewer consultations with health personal, did not plan their pregnancy. They were pregnant for the first time, and delivered babies with low birth weight. [27-30] The results showed that the majority of people have little knowledge. They could be drawn to believe unwholesome values which were connected to low education, poor socio-economic status, bad service utilization and low incomes. This increases the problem of higher unwanted child and many more. Thus, this highlights the importance of educated family planning.

The Nova Scotia Atlee Perinatal Database analyzed pregnancy outcomes in 1988 - 2001 and it was used to evaluate the relationship between fetal trauma and type of labor and method and mode of delivery. There were three major traumas, brachial plexus injury, intracranial hemorrhage and compresses skull fracture, and minor traumas, such as linear skull fracture, facial palsy and cephalhematoma.[31] Furthermore, the risk of significant fetal trauma in terms of pregnancy was very low and has been associated with labor and with assisted vaginal delivery. Four in the 145 cases were preterm babies (gestational age less than 30 weeks). A preterm baby has high incidence of asphyxia which induces premature bleeding, hypovolumic shock and finally death. Currently, an increased number of preterm labors is due to high growing science and technology that increases the number of preterm babies, asphyxia and die later. On the other hand, the number of preterm infants with accidental hemorrhage declines due to the progress in science and technology.

Congenital infections found in 3 cases. Among the 145 cases, one was cytomegalovirus infection, another was congenital rubella, and in the other no specific organism could be identified. Traditionally, congenital infections were known as TORCH infections, referring to toxoplasmosis, others (such as syphilis), rubella, CMV and herpes/ hepatitis.[14] The commonly observed virus infections in full-term neonatal infants were due to cytomegalovirus, herpes simplex, coxsackie and other enteroviruses.[10] Bacterial infections associated with neonatal sepsis were Group B *Streptococcus* (GBS), *Escherichia coli*, coagulase negative *Staphylococcus*, non-typable *Haemophilus influenza*, enterococci and occasionally, *Listeria monocytogenes*.[10] Compared to this study, TORCH infection has presented in developing countries because the low incidence they might not send dead fetuses for autopsy and no specimen or inappropriate specimen were studied.

Examination of placenta and umbilical cord specimens is very informative in cases with intrauterine death. Unfortunately, one-fifth of our cases with unexplained death, the placenta were not sent for autopsy. Nevertheless, a success of perinatal autopsy may be affected by incomplete clinical data at the time of the autopsy, severe autolytic changes caused by maceration or prolonged post-mortem interval. Eight out of fourteen cases with unexplained death in the present study were complicated by autolysis. But,

routine histologic examination of the major organs can provide useful information, even in macerated stillbirths. It contributes to assessment of gestational age and can provide evidence of fetal hypoxia without suspected gross morphology.

Today, teenage and elderly pregnancies have higher frequencies. By the virtue of unwanted child, unrealized antenatal cares including mother's illnesses, and many justifications developed might cause avoidance for proper antenatal care until true labor pain appears. This destroys a chance to evaluate the pregnancy which is crucial to identify the problem and providing optimal management. This partly contributes to high rate of perinatal death. And, it also helps a mother to decide whether to keep, her baby or to terminate the pregnancy.

Conclusion

In conclusion, the perinatal autopsy may be useful for evaluation in three ways: 1) the confirmation of ante-mortem diagnoses; 2) the identification of unexpected disorder; and 3) exclusion of other death. Identification of perinatal death is a significant helping for parents who have lost their babies. In our series, 82.1% of perinatal autopsy can demonstrate the cause of death, but others cannot be discovered. Congenital anomaly is the most common causes of death in proportion to others. It is related to multiple factors such as genetic abnormality, mutation of chromosome, toxic substances, and unknown. Progress in science and technology helps in routine antenatal care, discovers new medicines and new instruments for assisting in deliver-procedures. That can detect intrauterine fetal anomaly and increases number of congenital anomaly, whereas traumatic lesions and intrauterine infections were declined. Our understanding of neonatal complications in preterm infants and how they manifest during pregnancy may be possible by the pathological assessment of the tissue. This also has research implications into the mechanism of tissue damage. At any rate, perinatal autopsy including clinical data analysis can answer the questions but this is may not be successful in every case.

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