CLINICO-PATHOLOGICAL CORRELATION IN NEONATAL AUTOPSIES

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ABSTRACT

Of the 253 neonates admitted to a neonate intensive care unit during the period Jan 91 to Sep 93, 43 neonates died. Autopsy was done in 23 of these (53%). The mean duration of stay of the neonates in the intensive care unit prior to death was 5.6 days (range 2 hours to 10 days). Antemortem diagnoses included asphyxia neonatorum (4), meconium aspiration syndrome (2), septicemia (5), prematurity (3), birth trauma (2), congenital anomalies (2), hypoxic ischemic encephalopathy (1), and non-specific diagnosis (4). There were 6 major autopsy findings that, if known prior to death, would have altered clinical management and might have resulted in cure or prolonged survival. There were 8 additional major findings that, if known prior to death, would not have altered management. There were 14 minor findings related to major diagnoses but unrelated to the primary cause of death.

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KEY WORDS : Autopsy; Cause of death; Perinatal mortality.

Introduction

For the obstetrician, paediatrician, and parents, the anticipated outcome of pregnancy is a normally formed healthy infant and the possibility of perinatal death is not seriously entertained. In the event of such a mishap, the parents want to know where and how things went wrong without necessarily wanting to attach blame to a particular individual or institution. For the paediatrician, a greater concern is the need to know the risks of recurrence and means of prevention if any.

Autopsy, once an integral part of medical practice is now infrequently performed. Recent estimates place the autopsy rate at only 15%, down from a peak of 50% in the years following World War II [1]. The decline has been attributed to economic considerations, loss of interest in both clinicians and pathologists, and difficulties in obtaining consent. Many physicians now assume that the premortem evaluation has 'made the diagnosis', and that autopsy is obsolete. In a non-academic setting the autopsy may be viewed as a time-consuming chore. It is but natural that when no cause is obvious in a perinatal death, conjectures and

unscientific conclusions are drawn. It is in this context that perinatal autopsy becomes important.

To explore this vital issue, we conducted a study to examine the correlation between clinical diagnosis and autopsy findings in neonates dying in a neonatal intensive care unit.

Material and Methods

This study is based on the clinical and autopsy findings of neonates dying after admission to the neonatal intensive care unit of Command Hospital Air Force during the period from Jan 91 to Sept 93.

All newborns delivered after a high risk pregnancy and requiring admission to the NICU were evaluated in detail. Antenatal, natal, and postnatal events were recorded for each neonate. Clinical, examination relevant investigations, and record of therapeutic measures in all neonates was profiled. Autopsy, including relevant histopathological examination, was carried out after obtaining consent from either of the parents. Final diagnoses were categorized according to the criteria of Goldman et al [2]. Major diagnoses were defined as the basic

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underlying diseases which were the primary cause of death. The primary cause of death refers to that process which was the direct cause of death, and it excludes terminal events (eg. cardiac arrest). Minor diagnoses were defined as conditions that contributed to death and unrelated diseases.

Unexpected findings on autopsy were divided into 4 classes. Class I included major findings that, if known before death, would have altered clinical management and might have resulted in cure or prolonged survival. Class II included major findings that, if known before death, would not have changed clinical management either because specific therapy was unavailable, the patient had received appropriate therapy, or the parents had refused further treatment. Class III included minor findings related to major diagnoses but unrelated to the primary cause of death. Class IV included minor findings that were unimportant and unrelated to diagnosis [3].

Result

During the study period, there were a total of 3390 deliveries. Of these, 253 neonates required admission to the NICU. There were 43 neonatal deaths. The mean duration of stay of these neonates in NICU was 5.6 days (range 2 hours to 10 days). Autopsy was performed in 23 neonates (53%), 13 males and 10 females.

Antemortem diagnoses in these 23 neonates are summarized in Table 1. Diagnosis of septicemia in 5 neonates was made on the basis of positive sepsis screening. Blood culture was negative in all 5 cases. Birth trauma in 2 neonates was diagnosed on the basis of difficult labour and evidence of shock at birth. Of the 2 cases of congenital anomalies one was a case of cyanotic congenital heart disease (specific diagnosis not reached due to technical difficulties) and the other had meconium ileus with intestinal obstruction. Non-specific diagnosis in four neonates included aspiration syndrome (2), respiratory distress syndrome (1), and intractable hypoglycaemia (1).

There were 6 class-I findings in 7 neonates after autopsy and are summarized in Table 2. The autopsy of 2 neonates with early onset sepsis confirmed the diagnosis of antibiotic resistant *Citrobacter* septicemia and helped in preventing an outbreak of nosocomial *Citrobacter* septicemia. In the

TABLE 1
Antemortem diagnosis (n = 23)

Diagnosis	Number
Asphyxia neonatorum	4
Meconium aspiration syndrome	2
Septicemia	5
Prematurity	3
Birth trauma	2
Congenital anomalies	2
Hypoxic ischemic encephalopathy	1
Non specific diagnosis	4

TABLE 2
Clinico-pathological correlation in Class I autopsy findings (n = 6)

Clinical diagnosis	No of cases	NICU stay	Autopsy diagnosis
Early onset sepsis	2	4-6 days	<i>Citrobacter</i> septicemia
Early onset sepsis	1	5 days	Kernicterus
Early onset sepsis	1	6 days	Brain abscess
Respiratory distress syndrome	1	18 hours	Viral encephalitis
Aspiration syndrome	1	3 hours	Viral encephalitis
Birth trauma	1	12 hours	Rupture of liver

2 cases with respiratory distress syndrome and aspiration syndrome, the basic diagnosis of viral encephalitis was missed. Lack of facility prevented diagnosis of specific viral etiology. Kernicterus in a full term neonate with features of septicemia was an unsuspected finding. The neonate with multiple brain abscess, diagnosed as a case of *Salmonella havana* meningitis, may have survived if more aggressive therapy with newer antimicrobials had been possible.

There were 8 class-II findings in 10 neonates and are reflected in Table 3. In no instance did a class I or class II finding occur in the same patient. The neonate with an antemortem diagnosis of asphyxia neonatorum was confirmed to have severe pulmonary hypoplasia. This clinical and pathological correlation helped the treating physician in counselling the parents about the exact etiology. Similarly the neonates with aspiration syndrome had, in fact, died of sudden infant death syndrome - a diagnosis possible only after autopsy.

TABLE 3
Clinico-pathological correlation in Class II autopsy findings (n = 8)

Clinical diagnosis	No of cases	NICU stay (days)	Autopsy Diagnosis
Asphyxia neonatorum	1	2	Pulmonary hypoplasia
Aspiration syndrome	1	3	SIDS*
Cyanotic congenital heart disease	1	2	TGV + VSD + PS +
Meconium ileus	1	3	Multiple intestinal atresia
Septicemia	3	6-8	Septicemia
Prematurity	1	5	Patent ductus arteriosus
Respiratory distress syndrome type I	1	3	Hyaline membrane disease
Hypoxic ischemic encephalopathy	1	4	Confirmed on histopathology

*SIDS - Sudden Infant Death Syndrome
+ TGV + VSD + PS - Transposition of Great Vessels; Ventricular Septal Defect; Pulmonary Stenosis.

TABLE 4
Clinico-pathological correlation in Class III autopsy findings (n = 13)

Clinical Diagnosis	No of cases	Class III findings
Prematurity	3	Patent ductus arteriosus Atrial septal defect Intracranial hemorrhage
Birth trauma	5	Fracture humerus Subdural hemorrhage Subgaleal Hemorrhage
Septicemia	5	Acute tubular necrosis Hemorrhagic gastroenteropathy Pulmonary hemorrhage Peritonitis
Asphyxia neonatorum	2	Shock adrenals Hypoxic liver

There were 13 class-III findings in the present study and are presented in Table 4. There was 1 class-IV finding i.e. presence of cephalhematoma, in 4 neonates. This was an incidental finding unrelated to the basic diagnosis.

Discussion

The emotional climate surrounding the event of neonatal death is a highly charged one. The physi-

cian may be tempted to believe that all pertinent pathology has been found. Getting consent for autopsy from a parent in our society is difficult. However by initiating a scientific discussion with the parents, explaining the pros and cons of yet another 'test' and a little bit of firmness does help in obtaining the consent. Autopsy rate of 53% in the present study compared to the recent estimate of 15% [1] is a reflection of the efforts taken in the present study.

The value of postmortem examination of neonates may be even more important than in older children and adults. This is because many neonates die shortly after birth, before diagnosis is clearly established. Craft and Brazy in a study of 71 neonatal autopsies, found that 39% of cases yielded significant new findings [4]. Another large study, at the Postgraduate Institute of Medical Education and Research, Chandigarh (134 neonatal autopsies), the authors summarized the common causes of neonatal mortality. However, the study lacks the objectives of analyzing the correlation between antemortem diagnosis and autopsy diagnosis [5]. The importance of autopsy and the yield of new findings is further highlighted by the study of Nigro et al [6]. In their study of autopsies done in children dying of leukaemia, 49% autopsies yielded significant new diagnoses. Moreover 16% of these new diagnoses were thought to have contributed to the patients death.

In the present study, autopsy demonstrated additional unsuspected class I and class II findings in 6 and 8 cases respectively. In a similar study, Stambouly et al [3] analyzed 50 neonatal autopsies and reported class I and class II findings in 5 and 9 neonates respectively. The class I findings in the present study were directly related to the cause of death, and their antemortem detection may have resulted in a cure or prolonged survival. Postmortem diagnosis of *Citrobacter* septicemia in 2 neonates, helped in control of spread of nosocomial infection. This report on *Citrobacter* septicemia in neonates and its epidemiological study has been reported earlier [7]. *Kernicterus* in a full term neonate with clinical septicemia was a major unsuspected finding. Plevin et al in 1994 in a similar report have analyzed that the primary cause of unconjugated hyperbilirubinemia is due to haemolysis [8]. Another interesting and rare class I

finding in the present study was the neonate with antemortem diagnosis of septicemia confirmed to have multiple brain abscess caused by *Salmonella havana* resistant to exhibited antibiotics. The details have been reported by the authors in a earlier report [9].

The 8 class-II findings in our study not only confirmed antemortem diagnosis but also gave additional details particularly as regards congenital malformations. The case of sudden infant death syndrome proved by autopsy helped in reaching a correct diagnosis and thus dispelling fear from the mind of parents. The additional 13 class-III and 1 class-IV findings would not have made significant contribution to the cause of death. However these findings gave an insight into different pathophysiological changes and the natural course of events in a particular disease. This enables the physician to improve his knowledge and anticipation in subsequent similar clinical situation.

There are limitations to this study. The relatively small number of autopsies performed prevents extrapolating these results to the general population. Since performance of autopsy depends upon the physician requesting for consent, it results in selection bias. However, this review indicates the need for continued emphasis on the autopsy as an important part of medical practice. The autopsy rate of 53% in the present study as

compared to 15% and 26% in other studies [1,6] is very encouraging. Autopsy can raise the clinician's index of suspicion and review the natural course of a disease. The expected benefit is an improvement in medical education and in quality of medical care.

REFERENCES

1. Geller SA. Autopsy. Sci Am 1983; 248 : 124-36.
2. Goldman L, Seyson R, Robbins S, Cohn LH, Bettarann M, Weisberg M. The value of the autopsy in three medical eras. N Engl J Med 1983; 308 : 1000-5.
3. Stambouly JJ, Kahn E, Boxer RA. Correlation between clinical diagnosis and autopsy findings in critically ill children. Paediatrics 1993; 5 : 434-7.
4. Craft H, Brazy JE. Autopsy. High yield in neonatal population. Am J Dis Child 1986; 140 : 1260-2.
5. Joshi VV, Bhakoo ON, Gopalan S, Gupta AN. Primary causes of perinatal mortality - autopsy study. Indian J Med Res 1979; 69 : 963-71.
6. Nigro JF, Gresik MV, Feinbach DJ. Value of the postmortem examination in a paediatric population with leukaemia. J Pediatr 1990; 116 : 350-4.
7. Raghu Raman TS, Singh D, Jayaprakash DG, Krishnamurthy LK, Menon PK. Citrobacter septicemia in neonates. Indian Pediatr 1993; 30 : 377-9.
8. Plevin AA, Enzmann DR, Hann JS, Stevenson DK. Kernicterus in a full term neonate. Paediatrics 1994; 93 : 1003-6.
9. Menon PK, Raghu Raman TS, Rao DVK. Neonatal *Salmonella havana* meningitis. Indian J Microbiol 1994; 37 : 435-8.