Clinical Profile and Neurobehaviour at Discharge of Term Neonates with Perinatal Asphyxia - A Prospective Observational Study

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ABSTRACT

Introduction: Perinatal asphyxia is a major cause of neonatal mortality and morbidity in developing nations. The study aims to evaluate the clinical profile and outcome at discharge of term asphyxiated newborns in an Indian tertiary care center.

Material and methods: This is a prospective observational study of 120 term asphyxiated neonates admitted in NICU of an Indian tertiary care center. Maternal risk factors associated with birth asphyxia were recorded. Babies were treated as per the standard treatment protocol for birth asphyxia. Neurological assessment at discharge was done by clinical examination, Amiel-Teison tone assessment and neuroimaging.

Results: Of 120 asphyxiated infants, 82 infants were delivered via normal vaginal delivery while 22 were extracted by LSCS and 16 babies by forceps/vaccum delivery. The most common associated maternal risk factor was meconium stained amniotic fluid. 51 infants developed mild HIE, 66 moderate HIE and 3 severe HIE. Acute Kidney Injury was diagnosed in 19 infants with moderate to severe HIE. Among 69 infants with moderate to severe HIE, 52 developed seizures which were controlled in 42 infants within 2 days. Among infants with moderate to severe HIE, 53 infants were on direct breast feeds, 54 infants had normal neurobehavior and 48 infants had normal neuroimaging at discharge. The mean duration of hospital stay was 8 days. The overall mortality rate was 1.6%.

Conclusions: Early identification of maternal risk factor, timely obstetric intervention and optimum neonatal care will improve the outcome of perinatal asphyxia. Even majority of infants with moderate to severe HIE had normal neurobehavior and were on oral feeds at discharge.

Keywords: Perinatal asphyxia; Newborn; Neurobehavior.

INTRODUCTION

Perinatal asphyxia is an important cause of early neonatal death and stillbirth. The major difficulty in collecting accurate epidemiological data on perinatal asphyxia is the lack of a common definition of the condition.World Health Organization (WHO) defines birth asphyxia as failure to initiate and sustain breathing at birth. According to latest estimates by World Health Organization, approximately 4 million babies die each year before they reach the age of one month. Ninety-eight percent of these neonatal deaths take place in the developing countries. Perinatal asphyxia and birth injuries together contribute to almost 29% of these deaths.[1]

Failure to initiate and sustain breathing immediately after delivery has been associated with hypoxic-ischemic injury to the central nervous system and the clinical manifestations of this injury have been termed as Hypoxic Ischemic Encephalopathy (HIE). HIEis of concern in an asphyxiated neonate because it can lead to serious long-term neuro-motor sequelae among survivors. So the way in which an asphyxiated baby is managed at birth determines the immediate morbidity and quality of life among survivors.

MATERIAL AND METHODS

The present study was a prospective observational study conducted in neonates with perinatal asphyxia delivered at Cheluvamba hospital attached to Mysore Medical College and Research Institute, Mysore, India from November 2011 to February 2012. A minimum sample size calculation of 120 infants with perinatal asphyxia was done with the incidence of perinatal asphyxia of 2/100 live births at our institution at a 0.05 significance level and a power of 80%. The formula used was $n=z^2pq/d^2$ where z=1.96, p=0.02,
q=1-p, d=0.05.

Neonates were enrolled after informed consent from parents. The study was approved by the Institutional Ethical Committee. The infants were enrolled when following inclusion criteria were met:

1) A sentinel hypoxic event occurring immediately before or during labour.
2) Failure to initiate breath at birth or APGAR score < 7 at one minute (National Neonatal and Perinatal Database –NNPD definition).
3) Need for resuscitation at birth (positive pressure ventilation or chest compression).
4) Early onset of features of hypoxic ischemic encephalopathy.
5) Exclusion of other etiologies.

Preterm infants, infants whose mothers received pethidine or phenobarbitone which might cause depression in baby and neonates with any obvious external congenital malformations were excluded from the study.

As soon as the baby was admitted to NICU, the details were entered in a predesigned proforma. This included history regarding antenatal risk factors for perinatal asphyxia like age of mother, history of pregnancy induced hypertension, anemia, bleeding, infection and systemic disease. Intrapartum factors like mode of delivery, history of prolonged rupture of membrane, meconium stained amniotic fluid, malpresentation and cord prolapse were also entered. The examination findings including vitals and detailed anthropometry were recorded and a complete neurological examination and other systemic examination were done.

The neonates were treated according to the routine NICU

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protocol for perinatal asphyxia.

Clinical assessments included assessment of the neurologic status twice daily during the stay, Sarnat and Sarnat stage of HIE (Stage I, Stage II or Stage III),the type of respiratory support needed, the presence of seizures, involvement of multiorgan dysfunction, the time for establishment of full oral feedings through sucking, and neurologic examination at discharge.

Neurobehavior assessment before discharge included ability to suck well at breast, swallow without choking, wake up in 2-3 hours for feeds, spontaneous movement of all limbs, sleep for 2-3 hours after feeds and quality of cry.

STATISTICAL METHODS

All the statistical methods (descriptive statistics, chi square/ contingency coefficient analysis, independent samples t test) were carried out through the SPSS for windows (version 16.0). The p value <0.05 was taken as statistically significant.

RESULTS

Male to female ratio was 1.8:1. 81 infants were born out of normal vaginal delivery, 22 LSCS and 16 by assisted delivery (forceps/ vaccum extraction). The mean age of mothers was 21 years out of which 90 were primiparous. The most common risk factors associated with perinatal asphyxia were meconium stained amniotic fluid in 56 infants, prelabour rupture of membrane in 27, prolonged labour in 20 and cord around neck in 9 infants. Other risk factors included pregnancy induced hypertension, pre-eclampsia, birth injuries, oligamnios, maternal febrile illness, maternal systemic diseases and antepartum hemorrhage. 51 infants had one minute APGAR score 4-6 and 69 infants had score 1-3 at one min. 40 infants required bag and mask ventilation during resuscitation, 79 infants required endotracheal intubation and positive pressure ventilation and one required chest compression.

Among 120 infants, 114 were appropriate weight for gestation age, 7 were small for gestation age and 1 was large for gestation age. 51 infants had features of HIE stage 1, 66 HIE stage 11, and 3 infants HIE stage 111 (Table-1).

On systemic examination, abnormal respiratory system examination including tachypnoea, grunting, intercostal and subcostal retractions was present in 12 infants. Abnormal cardiovascular examination including prolonged capillary refilling time, weak peripheral pulses, compensated or decompensated shock was present in 14 infants.

Laboratory investigations included mean total count 10589±2793, Neutrophils 58.41±9.15, Lymphocyes 34.46±10.50, Monocytes 4.06 ±1.49. C-Reactive Protein positive (more than 10mg/dl) in 47, Band Neutrophil Ratio positive (more than 0.2) in 36, Growth in Blood Culture for 23.

12 infants had hypoglycemia (RBS < 40mg/dl), 6 had hyperglycemia (RBS > 180mg/dl), 19 had hyponatremia (serum sodium <135meq/L), 1 Hypernatremia (serum sodium >145meq/L), 6 Hyperkalemia (serum potassium >4.5meq/L) and 17 elevated creatinine (serum creatinine > 1 mg/dl).

Of 69 infants with moderate to severe encephalopathy, 11 developed shock requiring ionotropes with a mean 2 days for recovery from shock. Oxygen supplementation need was present for 13 and ventilation need for 3 infants. 52 infants developed seizure during NICU stay of which 44 infants seizure got controlled with one antiepileptic drug. Mean duration of seizure control was 1 day. Seizure was controlled within 2 days in 42 infants.

Acute kidney injury was present in 19 infants, oliguria for 13, polyuriafor 5. Duration of recovery from kidney injury was 3 days. The mean duration to start tube feeding was 3 days, palladai feeds 4 days and direct breast feeds 6 days.

At discharge 54 infants of 69 with moderate to severe encephalopathy had normal neurological examination, 54 had normal Amiel – Tison angle, 48 had normal neuroimaging. 53 of 69 infants were on direct breast feeding at discharge.

The mean duration of hospital stay was 8 days. 2 infants with severe encephalopathy expired with an overall mortality rate of 1.6% (Table-2).

DISCUSSION

The incidence of perinatal asphyxia in our institution was found 2%. Out of 120 infants included in the study, the mortality rate was 1.6%. It is estimated that around 23% of all newborn deaths are caused by birth asphyxia, with a large proportion of stillbirths.[1]

Following improvements in primary and obstetric care in most industrialized countries incidence of birth asphyxia has reduced significantly and less than 0.1% newborn infants die from birth asphyxia. In developing countries, rates of birth asphyxia are several folds higher. However, accurate epidemiological

Baseline features	Number (percentage)
1.male:female	1.8:1
2. Mean age of mothers (years)	21
3.Primipara	90 (75)
4.Mode of delivery	
a)Normal vaginal	82(67.5)
b)Cesarean section	22 (18)
c)Assisted vaginal	16 (13)
5.Major risk factors	
a) Meconium stained amniotic fluid	56 (46)
b)Premature rupture of membranes	27 (22)
c) Prolonged labour	20 (17)
d) Others (cord around the neck,pregnancy induced hypertension and antepartum hemorrhage)	22 (18)
6. Weight for gestational age	
a)Appropriate for gestation	114 (95)
b)Small for gestation	5 (4)
c) Large for gestation	1 (0.08)
7.Physiological variables at birth	
a)Non-invasive BP(mm Hg)	45.6±3.22
b)Heart rate (per min)	147±14.5
c)Respiratory rate(per min)	46±8
d) oxygen saturation (percentage)	96.6± 3.40
8. Methods of resuscitation	
a)Bag and Mask ventilation	40 (33)
b)Intubation and positive pressure ventilation	79(66)
c)Intubation,positive pressure ventilation and chest compression	1 (0.8)
9.Sarnat and Sarnat HIE staging	
Mild (HIE stage 1)	51(42)
Moderate (HIE stage 11)	66 (55)
Severe (HIE stage 111)	3(2.5)

Table-1: Baseline features of infants with perinatal asphyxia.

	Number (percentage)
1. Laboratory Parameters	
a) Total count (cells/cu mm)	10589±2793
b) C-Reactive Protein positive(>10mg/L)	47 (39)
c) Band Neutrophil Ratio positive (>0.2%)	36 (30)
d) Blood culture growth	23 (19)
e) Hypoglycemia	12 (10)
f) Hyponatremia	19 (16)
g) Elevated creatinine	17 (14)
2. Clinical profiles	
a) Shock requiring ionotropes	11 (9)
b) Respiratory supports	16 (13)
c) Convulsions	52 (43)
d) Seizure control with one antiepileptic drug	44 (37)
e) Seizure control within two days	42 (35)
f) Acute Kidney Injury	19 (16)
g) Oliguria	13 (11)
h) Normal neurobehavior at discharge among moderate-severe HIE	54 (78)
i) Normal AmielTison angle at discharge among moderate-severe HIE	54 (78)
j) On direct breast feed at discharge among moderate-severe HIE	53 (77)
k) Normal neuroimaging among moderate-severe HIE	48 (69)
l) Mean duration of hospital stay (days)	8

Table-2: Laboratory parameters, clinical profile and outcome at discharge of infants with perinatal asphyxia

data are lacking, and the exact burden of severe neurological disability in developing countries is unknown. According to the World Health Organization, between four and nine million newborns develop birth asphyxia each year. Of those, an estimated 1.2 million die and at least the same number develop severe consequences, such as epilepsy, cerebral palsy, and developmental delay.[2]

The most common risk factors associated with perinatal asphyxiawere meconium stained amniotic fluid, prelabour rupture of membrane, prolonged labour and cord around neck in our study. Chandra et al had similarly correlated prolonged labour, pregnancy induced hypertension and antepartum hemorrhage with asphyxia.[3] Singh et al had found the association of one or more high maternal- fetal risk factors and birth asphyxia.[4]

The study done by Lalsclottir et al[5] in Iceland found 50% of the women of asphyxiated babies had meconium stain amniotic fluidcompared with 42% in our study.

These findings emphasizes that good perinatal care is the major determinant factor in prevention of asphyxia.

In our study asphyxia was defined and classified based on a sentinel hypoxic event, failure to initiate breath at birth or APGAR score < 7 at one minute, need for resuscitation at birth (positive pressure ventilation or chest compression), features of hypoxic ischemic encephalopathy and exclusion of other etiologies.Classification of asphyxia was done based on APGAR score at one minute or 5 minute by Babu BVA et al[6], Kriti Mohan et al[7] and BC Yelamali et al.[8] While pH in addition to APGAR score and need for resuscitation was used by Siva Saranappa et al in 2015.[9] Due to resource limitations in a public health facility, pH could not be used to assess the metabolic status in our study.

In our study 42% of infants had features of HIE Stage 1, 55% stage 11 and 2.5 % stage 111. In study byKriti Mohan et al[7] in term neonates maximum number of neonates had features of stage II (54%) while 31% and 14% had stage I and III features respectively. While, Sarnat and Sarnat[10] found that 33% neonates were in stage I, 50% in stage II while 28% had progressed to stage III.

16% infants were reported to have Acute Kidney Injury and 10% had oliguria in our study.6% infants reported to haveAcute Kidney Injury in study by Kriti Mohan et al.[7] Jayshree et al[15] reported 16% Acute Kidney Injury incidence. Finer et al observed oliguria in 25% cases.[14] This again emphasizes that renal system is one of the most commonly affected system in asphyxia and warrants monitoring of renal parameters.

Of total 120 infants, 43% developed seizure during NICU stay. Of 69 infants with moderate to severe HIE 75% had convulsions. Convulsions werereported for 46% by Kriti et al.[7] Finer et al[14] observed convulsion in 68% of cases.

Cardiovascular complication such as hypotension were present and have been observed by other workers including Babu BVA[6], Dongol et al[11] and Bashir et al.[12]

At discharge 78% infants with moderate to severe encephalopathy had normal neurobehavior and normal Amiel – Tison angle. 69% infants had normal Neuroimaging. 76% of infantsinfants with moderate to severe encephalopathy were on direct breast feeding and had a good sucking reflex at discharge. Overall 42% cases were recovered without apparent sequelae and 26% had neurological sequelae in study of Babu BVA.[6] As reported by other authors recovery rate was higher in Stage-I and Stage-II compared to Stage-III.[11-13]

CONCLUSION

Even in this 21stcentury, perinatal asphyxia is a major cause of neonatal mortality and future neurological disability in an infant born in any developing nation. Accurate estimation of incidence and any data regarding asphyxia is still difficult due to controversies in definitions and criteria. This is of paramount importance as with accurate data specific areas where management needs to concentrate can be ascertained. Optimal perinatal care forms the cornerstone of success in the management limiting mortality and serious morbidities. Even in resource limited settings, majority of infants can be discharged with normal neurobehavior. Further studies need to be done to extrapolate whether the long term outcome is also promising.

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