Multi Organ Dysfunction in Term Neonates with Perinatal Asphyxia

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Abstract

Introduction: Multiorgan dysfunction (MOD) is one of the four consensus based criteria for the diagnosis of intrapartum asphyxia. The theoretical concept behind MOD is the diving reflex -conservation of blood flow to vital organs at the cost of non-vital organs. The objective of this study was to assess the patterns of involvement of each major organ/system in term asphyxiated neonates. **Material and Methods:** This was a hospital based prospective study. Sixty term neonates who had suffered perinatal asphyxia were assessed for central nervous system, kidney, cardiovascular system, gastrointestinal system and liver dysfunction. **Results:** Out of 60 eligible neonates, 57 (95%) had evidence of at least one organ dysfunction. Cardiovascular system involvement (95%) was most common, followed by renal system (37%), hepatic system (22%), central nervous system and hematological system (20% each) and finally, gastrointestinal tract (8%). **Conclusion:** MOD is frequently associated with perinatal asphyxia with cardiovascular system being the most commonly affected.

Key words: Perinatal asphyxia; Multi-organ dysfunction; Term neonates.

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Introduction

Perinatal asphyxia refers to a condition during the first and second stage of labor in which impaired gas exchange leads to fetal hypoxemia and hypercarbia[1]. Obstetric and pediatric associations have opined that dysfunction of organs other than the central nervous system is a common feature of perinatal asphyxia.[2] The phenomenon of multi organ dysfunction (MOD) is due to asphyxia induced diving reflex that leads to shunting of blood from non-vital organs like skin to vital organs like heart, adrenals and brain to protect these organs from hypoxic-ischemic (HI) injury.

The presence of MOD in every neonate with neonatal asphyxia has been questioned by some authors[3]. Human and animal studies have demonstrated differences in the involvement of the various organs which would suggest an inconsistency in the activation of diving reflex. The objective of the study was to assess the frequency and pattern of involvement of each major organ system and combination of organs in infants with post-asphyxial encephalopathy.

Material and Methods

This is a prospective study carried out on 60 asphyxiated term neonates who were admitted on their first day of life to the neonatal intensive care unit (NICU) of a tertiary care hospital in Pune over a period of two years from September 2012 to September 2014.

Inclusion criteria:

- Term neonates born intramural requiring resuscitation (bag and mask ventilation for 30 sec and above) and admitted to NICU.
- Term neonates born outside with history of not having cried after birth, having required resuscitation and referred within 24 hours of life.

Exclusion criteria:

- Neonates with congenital malformations.
- Preterm neonates (less than 37 weeks gestational age).

Collection of data:

- Detailed birth history including all major events, resuscitation details, other neonatal and maternal data were recorded.
- Gestational age was assessed by last menstrual period and new Ballard score.
- All babies were thoroughly examined at the time of admission and each baby was followed up till discharge with special emphasis on the affected organ system.
- Basic investigations for evaluation of MOD were done as per NICU protocol.

Criteria for organ dysfunction:

- *Central nervous system involvement*: Detailed neurological examination was done and features of CNS involvement like seizures, abnormal tone and altered sensorium were noted. Clinical classification of neurological status for HIE staging was done by modified Sarnat and Sarnat's staging. Ultrasonography (USG) of brain was done within 48 hours of admission. Magnetic Resonance Imaging (MRI) of brain and electroencephalogram (EEG) were done before discharge for babies who were HIE stage II or more.
- *Renal involvement:* Anuria or oliguria (urine output < 1 ml/kg/hr) persisting for 24 hours or more after a volume challenge test [20 ml/kg of normal saline (NS) bolus] and diuretic challenge [Furosemide (@4 mg/kg)], and/or blood urea > 40 mg/dl, and/or serum creatinine > 1 mg/dl, and/or rise in serum creatinine > 0.3 mg/dl.
- *Cardiovascular system involvement:* Hypotension (mean BP < 40 mm Hg) treated with inotropes and/or serum CPK–MB more than 25 IU/l.
- *Hepatic involvement:* Serum SGPT more than 60 IU/l at 24 hours of life.
- *Gastro-intestinal tract:* RT aspirates more than 30 % of total intake in last 6 hours.
- *Hematological involvement:* NRBC count of more than 10 per 100 WBC.

Microsoft Excel 2007 and Microsoft Windows 2007 were used for analysis. Percentage of involvement of individual organs was calculated.

Results

From September 2012 through September 2014, 60 babies met the eligibility criteria. Data enabling the evaluation of all six organ systems was collected. Seven babies were excluded from the study. Four were referred after 24 hours of life, one had congenital malformation and resuscitation details were unavailable for two babies.

Table 1: Showing the basic perinatal characteristics of all the babies.

Perinatal Characteristics	Total (n = 60)
Gender	
Male	37 (62%)
Female	23 (38%)
Gestational age (wk)	38.4 ± 1.14*
Birth weight (g)	2720 ± 350*
Maternal age (years)	
15 – 19	6 (10%)
20 – 24	29 (48%)
25 – 29	19 (32%)
30 – 34	6 (10%)
≥ 35	0 (0%)
Parity of mother	
Primipara	26 (43%)
Multipara	34 (57%)
Mode of delivery	
NVD	28 (47%)
LSCS	26 (43%)
Vaccum	6 (10%)
Place of delivery	
Inborn	38 (63%)
Outborn	22 (37%)
Meconium stained liquor	24 (40%)
Ventilatory requirement	
Ventilated	33 (55%)
Non-ventilated	27 (45%)

* Data were expressed as mean ± SD (range).

Out of 60 babies, 57 (95%) babies had evidence of at least one organ dysfunction. Cardiovascular, renal, hepatic, central nervous system, hematological and gastro-intestinal tract dysfunction was present in 57 (95%), 22 (37%), 13 (22%), 12 (20%), 12 (20%) and 8 (13%) babies respectively as illustrated in Table 2.

Table 2: Perinatal characteristics, pattern of organ involvement and outcome among babies with encephalopathy and without encephalopathy

Features	No encephalopathy (n = 48)		HIE (n = 12)	
	Number	Percentage (%)	Number	Percentage (%)
Sex				
Male	28	58.33	9	75
Female	20	41.66	3	25
Parity of mother				
Primipara	21	43.75	5	41.66
Multipara	27	56.25	7	58.33
Place of delivery				
Inborn	34	70.83	4	33.33
Outborn	14	29.16	8	66.66
Mode of delivery				
NVD	22	45.83	6	50
LSCS	22	45.83	4	33.33
Vaccum	4	8.33	2	16.66
Meconium Stained Liquor				
Present	18	37.5	6	50
Absent	28	58.33	5	41.66
Not known	2	4.16	1	8.33
Organ System Involvement				
Renal	14	29.16	8	66.66
GIT	7	14.58	1	8.33
Liver	7	14.58	6	50
CVS	45	93.75	12	100
Hematological System	10	20.83	2	16.66
Ventilator Requirement				
Ventilated	22	45.83	11	91.66
Non-ventilated	26	54.16	1	8.33
Outcome				
Survival	43	89.5	9	75
Death	0	0	0	0
DAMA	5	10.41	3	25

Discussion

As in our study, a high male to female ratio was also observed in studies conducted by Martin-Ancel et al[3], Mohammed LH et al[4], Lin MH et al[5], Shireen N et al[6] and Dalal EA et al[7]. These results concur with Futrakul et al found a statistically significant relationship between HIE and male gender[8]. Our study revealed a greater incidence of asphyxia in infants born to multiparous mothers as opposed to primi mothers in studies conducted by Dalal EA et al[7] and Shireen N et al[6]. Incidence of meconium stained liquor in our study was 40%. Martin-Ancel et al[3] and Dalal EA et al[7] reported meconium stained liquor in 42% and 42.2% babies respectively.

The pattern of organ involvement in our study has been illustrated in Table 2. Martin-Ancel et al found CNS, renal and cardiac involvement in 72%, 42.1% and 29% infants respectively[3]. The variability in the reported incidence of MOD may be explained by differences in the inclusion criteria for studies, definition of MOD and sample size of encephalopathic babies in our study.

Encephalopathy with seizures was present in 20% babies. Lin MH et al reported clinical seizures

in 11.5% of term asphyxiated infants[5]. Five out of seven babies who underwent neuroimaging showed changes consistent with HIE. Neurosonography was normal in 29 (60%) babies without encephalopathy. Abnormalities detected included cerebral edema and bilateral germinal matrix hemorrhage. Noman F et al documented a normal ultrasound study of brain in 80% term neonates[9]. EEGs done in nine babies revealed evidence of multifocal epileptiform discharges over various areas of the brain in six babies. Ajay Kumar et al[10] studied clinic-etiological and EEG profile of 90 babies with seizures, demonstrated asphyxia as the cause for seizures in 40 babies and an abnormal EEG in 8(20%) babies.

Twenty (33%) babies had raised serum creatinine of which two also had raised blood urea. We observed oliguria in only 5(8%) babies which improved after giving an intravenous normal saline bolus. Three babies showed rising serum creatinine but two of them showed a rise by 0.1 mg/dl which was considered insignificant. Serum creatinine levels showed a decreasing trend with subsequent normalization in all except one baby who developed non-oliguric acute kidney injury. The involvement of kidneys in 67% of cases in this cohort was comparable to the reported incidence in representative studies by Shah P et al[11] (70%) and Mohammed LH et al[4](63.5%) reflecting the severity of asphyxia although we chose the middle of the spectrum of published definitions and our sample size was small. Anomalies like hydronephrosis, pelvi-ureteric junction obstruction and adrenal hemorrhage were found on abdominal sonography in 14% infants. Gupta BD et al demonstrated abnormalities on renal sonography in 6.6% cases in form of increased size, altered echo texture and loss of corticomedullary differentiation[12].

GIT involvement was found in 13% neonates and had feed intolerance. Martin-Ancel el al reported an incidence of 21% taking into account various features like presence of gastric residuals, vomiting, abdominal distension or tenderness and gastrointestinal bleeding[3].

Hepatic in involvement was observed in 22% babies with 50% involvement among those with HIE and 14% among those without encephalopathy. Shah P et al[11], Mohammed LH et al[4] and Tarcan A et al [13] demonstrated elevated liver enzymes at any time during the first week of life in 85%, 35.1% and 39% infants with HIE. Lin MH et al concluded that there was no significant difference in the elevation of liver enzymes in babies with both mild and severe asphyxia[5].

Five (8.33%) babies had clinically appreciable murmurs. Hypotension was observed in 11 (18%) babies and all of them required inotropic support for maintaining blood pressures within normal range. Serum CPK – MB was elevated in 57 (95%) babies. Functional 2D Echo showed structural abnormalities (patent ductus arteriosus, ventricular septal defect and patent foramen ovale) and functional defects like tricuspid regurgitation in 13 (22%) babies. The high percentage of cardiovascular system involvement in our study is possibly due to inclusion of serum CPK–MB as one of the criteria which is a sensitive marker of heart involvement. Primhak et al studied serial electrocardiogram and CK–MB in term infants and found that CK–MB was associated with myocardial injury in asphyxiated infants[14]. However, Omokhodion et al concluded that specificity of CK–MB as a marker of myocardial injury in asphyxiated newborns is possible but remains uncertain[15].

Our study showed hematological involvement in 14 (23%) babies. Colaco SM also reported high NRBC count in 47% babies[16].

Our study showed a survival rate of 87%. Eight (13%) babies had taken discharge against medical advice. Among them, three had HIE and were on inotropic support. All of them had involvement of two or more organ systems. Lin MH[5], Shireen N et al[6], Khatoon[17] and Etuk[18] also demonstrated mortality rates of 9.8%, 16%, 25.4% and 20.8% in their respective studies.

Conclusion

Cardiovascular system involvement was most common, followed by renal, hepatic, central nervous, renal systems and lastly, the gastrointestinal tract. Babies with and without encephalopathy both showed highest incidence of cardiovascular system involvement. Survival rate was good.

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