

Organ dysfunction other than central nervous system in perinatal asphyxia

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Abstract

Introduction: Significant asphyxial insult to the fetus is likely to compromise a number of different organ systems of which the brain, kidneys and myocardium are particularly vulnerable, though bowel, endocrine and pulmonary complications may also occur. However much emphasis is given to central nervous system (CNS) dysfunction while other organs take a backseat.

Objectives: To evaluate the frequency of organ dysfunction other than CNS in perinatal asphyxia and to correlate the organ dysfunction with immediate mortality.

Method: A prospective observational study was done in all asphyxiated newborns, delivered at Pravara Institute of Medical Sciences, Loni, from September 2013 to August 2015. Neonates born before 37 weeks of gestation, or born outside the hospital or with congenital anomalies or with early onset sepsis were excluded from the study. Prior approval was obtained from the institutional ethics committee. A detailed history was taken and examination performed on admission to the neonatal intensive care unit (NICU). The clinical course was followed up to 14 days of birth. Data obtained was recorded. Data analysis was done by descriptive statistics as mean, SD, median, range and percentage. Comparison was done by applying Chi-square test. Significance was assessed at 5% ($p < 0.05$).

Results: During the study period 152 asphyxiated babies, fulfilling the preformed inclusion criteria were admitted in the NICU. The common modes of delivery were normal vaginal (55.2%) and caesarean section (38%). Meconium stained amniotic fluid (35.5%) was the most common perinatal risk factor followed by prolonged second stage of labour (23.7%). The renal system was involved in 64% cases, respiratory system in 45%,

cardiovascular system in 32%, gastrointestinal system in 16%, hepatic system in 05% and the haematological system in 03%. There was an overall mortality rate of 37.5%.

Conclusions: In the present study common organs of involvement other than the CNS were renal (64%), respiratory (45%), cardiovascular (32%) and gastrointestinal (16%). The overall mortality rate was 37.5%. Deaths were higher when 3 or more organs were involved.

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(Key words: Neonates, birth asphyxia, organ dysfunction, mortality)

Introduction

Perinatal asphyxia remains an important cause of neonatal mortality, morbidity and late sequelae especially in a developing country like India. Initially, birth asphyxia was thought to result only in central nervous system (CNS) dysfunction and not much consideration was given to the involvement of other systems as a result of asphyxia. However, it is known now that a significant asphyxial insult to the fetus is likely to compromise a number of different organ systems of which the brain, kidneys and myocardium are particularly vulnerable, though bowel, endocrine and pulmonary complications may also occur¹. Early recognition of infants with multisystem dysfunction after a perinatal asphyxial insult may be beneficial in the management of these infants and may have a bearing on their outcome.

Objectives

To evaluate the frequency of organ dysfunction other than CNS in perinatal asphyxia.

Method

A prospective observational hospital based study was done in all asphyxiated newborns, delivered at Pravara Institute of Medical Sciences, Loni, from September 2013 to August 2015, who had features of birth asphyxia with an Apgar score of ≤ 7 at 5min, or/and umbilical cord arterial pH of < 7.2 at birth, or/and required more than 1 minute of positive pressure ventilation before sustained respiration, or the need for mechanical ventilation at birth. Neonates born before 37 weeks of gestation, or born outside Pravara Institute of Medical Sciences, Loni or with congenital anomalies or with early onset sepsis were excluded


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from the study. Approval from the institutional ethics committee, letter number (PMT/PMIS/RC/2013/17) and written consent was taken from all parents before inclusion of their child in the study.

A detailed history was taken and examination performed at the time of admission to the neonatal intensive care unit (NICU). The clinical course was followed up to 14 days of birth. Data obtained were recorded. Natal history included the mode of delivery and indications for interventions, if any. Complications during and prior to labour were noted. All births were attended and resuscitated by paediatricians following the 2010 neonatal resuscitation protocol of the American Academy of Pediatrics². Postnatal history included details regarding birth asphyxia, resuscitation measures and APGAR scores at 1 and 5 minutes. Gestational age was assessed based on mother's last menstrual period (LMP) and confirmed when necessary by early antenatal ultrasonography (USG). When the LMP was not available and antenatal USG was not done, gestational age was assessed by the Modified Ballard Scoring system³. All biochemical samples were taken on admission. Echocardiography was done at Department of Radiology at Pravara Institute of Medical Sciences, Loni. Daily follow-up of the patient was done and overall progress was monitored till discharge from NICU or death of the baby.

Blood urea, serum creatinine and urine output record (monitored using a plastic collection bag, Minicom) were done in all cases at the time of admission, at 72 hours of age and after one week. Acute renal failure was considered to be present if the urine output was less than 0.5 ml/kg/hour, or the blood urea was more than 40mg/dl, or the serum creatinine was more than 2 SD above the mean value for gestational age which is more than 1.2 mg/dl. For calculating creatinine clearance we used Schwartz formula⁴, Creatinine clearance = $k \times L / Pcr$, where L is length or height of the child in cm, Pcr is plasma creatinine in mg/dl and K is age dependent constant (for preterm 0.33, term 0.45).

Respiratory system was assessed based on the presence of respiratory distress with need for oxygen supplementation for more than 24 hours and/or mechanical ventilation. Assessment of respiratory distress was done by Downes score. Chest x-ray was done in all infants needing oxygen supplementation. Each infant was examined for the presence of a heart murmur, dysrhythmias, cyanosis, increase in respiratory distress with systemic hypotension and signs of shock (hepatomegaly, abnormal peripheral pulses, reduced peripheral pulsation evident by prolonged CRT>3 sec.) that required need of IV inotropes. A

12-lead electrocardiogram (ECG) was done in each asphyxiated neonate within 72 hours of life to look for transient myocardial ischaemia. Infants with grade 1 or 2 ECG changes of were considered to have mild, and those with grades 3 or 4 changes, severe myocardial ischaemia respectively. The grading was done as per criteria defined by Jedeikin et al.⁵. Creatinine kinase-MB isoenzyme levels were estimated at 8 hours and 24 hours of life in all neonates. A value of more than 92.6 U/L at 8 hours and 60 U/L at 24 hours were taken as high. In cases with persistent murmurs and other abnormal findings, an echocardiography was carried out.

Evaluation was done for the presence of gastrointestinal (GI) bleed, abdominal distension, and altered GI aspirate. Enteral feeding was started only after 24 hours after birth in all cases. Modified Bell's criteria were used for necrotizing enterocolitis. Criteria for liver impairment were aspartate transaminase (AST) >100 U/L, alanine transaminase (ALT) >100 U/L, prothrombin time >20 seconds, and/or international normalised ratio (INR) >1.2, measured on postnatal days 1, 3, and 10 in all asphyxiated babies. All infants had platelet counts done. Significant thrombocytopenia was considered to be present when the platelet count was less than 100,000/cu mm. Any evidence of bleeding tendencies like petechiae was noted during the hospital stay. All infants had daily random blood sugar (RBS) estimations. Hypoglycaemia was defined as RBS <45mg%; hyponatremia as serum sodium <130 mg/L; hyperkalaemia as serum potassium >5 meq/L and hypocalcaemia as serum calcium <7.5 mg%. For calculating plasma osmolarity we used the following equation: Calculated osmolarity = $2 Na + Glucose + Urea$ (all in mmol/L). Routine investigations included haemoglobin (Hb)%, total leucocyte count, differential count, platelet count, sepsis screening (C-reactive protein, toxic granules and band cells), blood urea, serum creatinine, serum electrolytes (Na⁺, K⁺, Ca⁺), blood culture and antibiotic sensitivity. Special investigation included x-rays (chest and abdomen), ECG, echocardiography and USG (abdomen and pelvis)

Data analysis was done by descriptive statistics as mean, SD, median, range and percentage. Comparison was done by applying Chi-square test. Significance was assessed at 5% (p<0.05). GraphPadInstat version 3.10 software was used for statistical analysis. Microsoft word and excel were used to generate graphs and tables

Results

Thirteen thousand four hundred and twenty three deliveries were conducted during the study period out of which 12,213 were live births. During this

period 152 asphyxiated babies fulfilling the preformed inclusion criteria were admitted in NICU. Table 1 shows the gender distribution of the neonates with perinatal asphyxia. Table 2 shows the mode of delivery among case of perinatal asphyxia. Table 3 shows the perinatal risk factors in neonates with perinatal asphyxia.

Table 1: Gender-wise distribution of neonates in perinatal asphyxia

Gender	Number (%)
Male	84 (55.3)
Female	68 (44.7)

Table 2: Mode of delivery in cases of perinatal asphyxia

Mode of delivery	Number (%)
Normal vaginal	84 (55.2)
Ventouse	07 (04.9)
Forceps	03 (02.0)
Caesarean section (LSCS)	58 (38.0)
Total	152 (100,0)

Table 3: Perinatal risk factors in perinatal asphyxia

Risk Factor	No. (%)
Meconium stained amniotic fluid	54 (35.5)
Prolonged second stage of labour	36 (23.7)
Pregnancy induced hypertension/eclampsia	13 (08.5)
Cord prolapse	10 (07.7)
Malpresentation	08 (05.2)
Premature rupture of membrane	07 (04.5)
Cord around neck	05 (03.2)
Twin delivery	03 (01.8)
Oligohydramnios	03 (01.8)
Abruptio placentae	03 (01.8)
Antepartum haemorrhage	03 (01.8)
Decreased fetal movements	01 (0.6)
No risk factors	06 (03.9)
Total	152 (100)

The distribution of organ system involvement is shown in Table 4. The distribution of organ dysfunction and outcome is shown in Figure 1. The relationship between the numbers of dysfunctional organs and outcome is shown in Figure 2.

Table 4: Distribution of organ system involvement

Organ involved	Number of cases involved (%)	Number of cases not involved (%)
Renal system	98 (64)	54 (36)
Respiratory system	68 (45)	84 (55)
Cardiovascular system	48 (32)	104 (68)
Gastrointestinal system	24 (16)	128 (84)
Metabolic system	16 (10)	136 (90)
Hepatic system	07 (05)	145 (95)
Haematological system	05 (03)	147 (97)

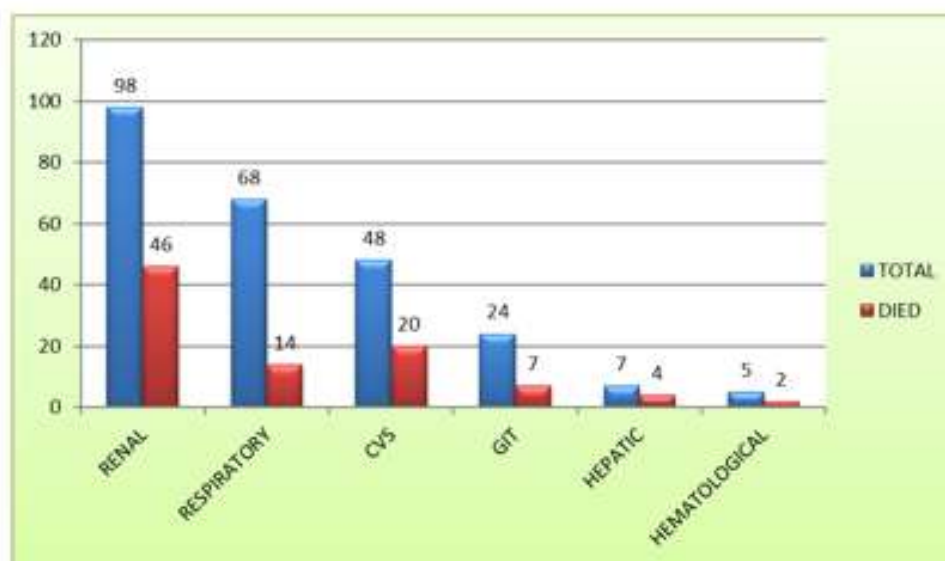


Figure 1: Distribution of organ dysfunction and outcome

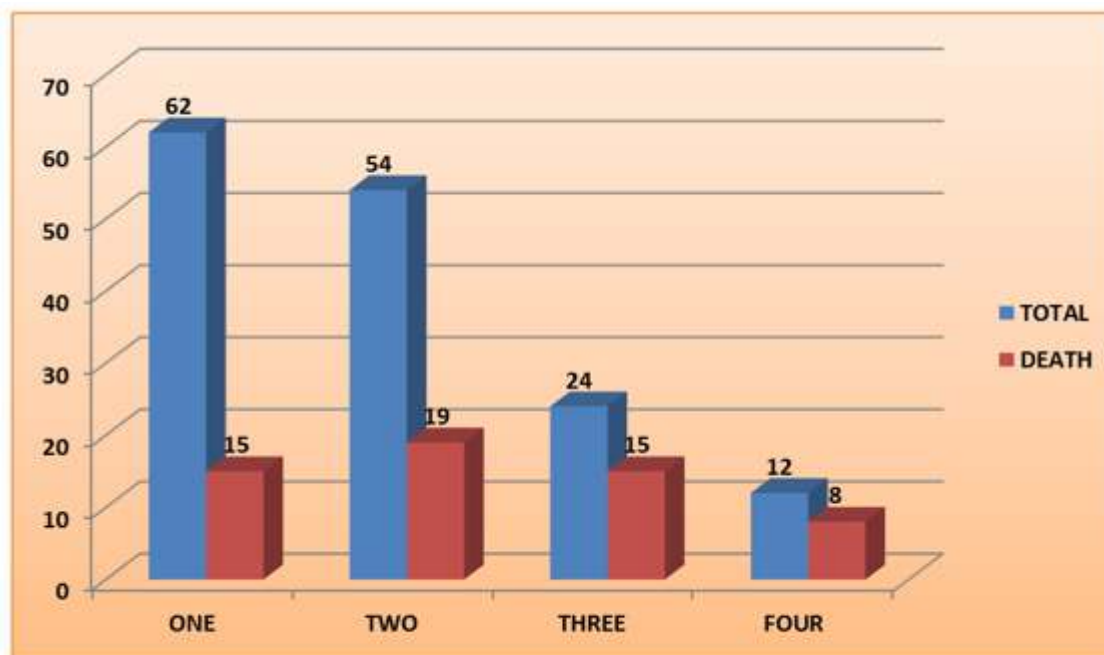


Figure 2: Relationship between the number of dysfunctional organs and outcome

Out of a total of 152 babies studied, 95 survived to hospital discharge and 57 (37%) died. The relationship between organ dysfunction and outcome is shown in Figure 1.

Discussion

The study was undertaken to observe the effects of birth asphyxia on various organ systems of the neonate other than the CNS. One hundred fifty two asphyxiated neonates were followed up for 14 days to note the involvement of the renal system, respiratory system, cardiovascular system, gastrointestinal system, hepatic system, haematological system and the metabolic system.

In the present study, 96% neonates had risk factors for perinatal asphyxia in various forms (Table 3). Ross MG considered the presence of meconium-stained amniotic fluid strong evidence of fetal distress². Shrestha M *et al.* studied the risk factors of hypoxic ischaemic encephalopathy (HIE) and showed that meconium staining of the amniotic fluid was the commonest risk factor (65%)³. In our study, meconium stained amniotic fluid (35.5%) was the most common risk factor in perinatal asphyxia. Bhargava SK *et al* has documented cord prolapse (50%), malpresentation (32%) and fetal distress (26.6%) as major risk factors in perinatal asphyxia⁴. In our study cord prolapse occurred in 07.7% and malpresentation in 0.5%.

In the present study the most commonly affected organ system was the renal system (64%) followed by the respiratory system (45%), the cardiovascular system (32%), the gastrointestinal system (16%), the hepatic system (05%) and the haematological

system (03%). In the study by Shah P *et al.* the renal system was involved in 70%, the respiratory system in 86% and the cardiovascular system in 62%⁵. In the study by Martin-Ancel A, *et al.* the renal system was involved in 42%, the respiratory system in 26%, the cardiovascular system in 29% and the gastrointestinal system in 29%⁶. In the study by Perlman JM *et al*, the renal system was involved in 40%, the respiratory system in 23% and the cardiovascular system in 28%⁷.

An overall mortality rate of 37.5% was observed in the present study. In the study by Shah P *et al.* 62% neonates had adverse outcome including death⁶. A 7% mortality was reported by Goodwin TM, *et al*⁸.

Conclusions

In the present study common organs of involvement other than the CNS were renal (64%), respiratory (45%), cardiovascular (32%) and gastrointestinal (16%). The overall mortality rate was 37.5%. Deaths were higher when 3 or more organs were involved.

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