Organ Dysfunction in Neonates with Perinatal Asphyxia in a Tertiary Care Hospital of Nepal

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ABSTRACT

Background

Perinatal asphyxia is one of the commonest causes of neonatal mortality and morbidity. Multiple organ dysfunction is an important complication. The adaptive mechanisms triggered are overwhelmed in prolonged or severe asphyxia leading to dysfunction of multiple vital organs.

Objective

To find the prevalence of organ dysfunction among neonates admitted with perinatal asphyxia in Neonatal Intensive Care Unit (NICU) of Bharatpur Hospital.

Method

We conducted a prospective, cross-sectional study in Neonatal Intensive Care Unit of a tertiary hospital from January to December 2023 after obtaining ethical approval from Institutional Review Committee. Neonates admitted to Neonatal Intensive Care Unit with asphyxia were enrolled in the study. The basic information regarding period of gestation, sex, Apgar score, birth weight and birth events were collected. Neonates were investigated and managed as per Neonatal Intensive Care Unit protocol. Enrolled neonates were assessed for central nervous system, renal, respiratory, cardiovascular, gastrointestinal, metabolic and hematologic dysfunction, the number of systems involved and the immediate outcomes.

Result

All 108 enrolled neonates had at least one organ dysfunction. Cardiovascular dysfunction (83.33%) was the most common followed by respiratory dysfunction (79.62%). The Central nervous system, hematologic, renal, gastrointestinal and metabolic dysfunction were seen in 28.70%, 20.37%, 8.33%, 8.33% and 6.48% of neonates respectively. Multiorgan dysfunction was found in 85.19% of neonates. Among the enrolled neonates, 93.52% were discharged, 4.63% left against medical advice while 1.85% died during hospital stay.

Conclusion

Organ dysfunction is seen in all neonates with asphyxia commonly involving cardiovascular and respiratory system. Multiorgan dysfunction is a frequent complication of perinatal asphyxia.

KEY WORDS

Asphyxia, Neonates, Organ dysfunction

INTRODUCTION

Perinatal asphyxia also known as birth asphyxia is defined by World Health Organization as the failure to establish breathing at birth. It accounts for approximately 900,000 deaths per year.[1] Birth or perinatal asphyxia is estimated to occur in approximately 6 per 1000 live births in Nepal.[2] Hypoxic ischemic encephalopathy and multiple organ dysfunction are important complications of perinatal asphyxia.[3]

During birth asphyxia, the blood flow and oxygen to the baby is reduced or absent. This transient insult that occurs before or during the birth of the baby triggers the diving reflex in the baby which shunts the blood from skin and splanchnic circulation and preserves the blood supply to vital organs like brain, heart, and adrenal glands. Significant or prolonged insult results in compromised function across multiple organ system including brain, heart, liver, kidney, gastrointestinal system, lungs and bone marrow causing organ or system dysfunction. Birth asphyxia and multiple organ involvement is associated with poorer outcome.[2-4]

There are fewer studies performed in neonates with perinatal asphyxia who has organ dysfunction in our country. Bharatpur hospital is a tertiary level hospital with Neonatal Intensive Care Unit (NICU) services and large number of deliveries. We aim to estimate the prevalence of organ dysfunction and the multiorgan dysfunction among the neonates with birth asphyxia admitted to Neonatal Intensive care unit of a tertiary care hospital.

METHODS

The study was an observational, cross-sectional study conducted in Neonatal Intensive care unit of Bharatpur Hospital from 01/01/2023 to 30/12/2023 after obtaining ethical approval from the Institutional Review Committee of Bharatpur Hospital (Reference number: 078/79-031).

The sample size was calculated using the formula given below:[5]

$N = z^2XpXq/e^2$

where,

N= sample size required (minimum)

z= 1.96 (confidence interval of 95%)

p= prevalence taken from a study with prevalence of organ dysfunction as 95%.[6]

q= 1-p

e= margin of error (5%)

N= 1.962 X 0.95 X (1-0.95)/0.05 X 0.05

N = 73

A consecutive non-probability method was used for sampling. The study method was explained to the parents or caretakers (when parents were unavailable) and written consent was obtained. Data about period of gestation, sex, birth events, APGAR score, birth weight and the presence of thick meconium were recorded in case proforma. A baseline investigation profile and septic screening was evaluated, which includes Complete blood count, C-reactive protein, Alanine Transaminase (ALT), Urea, Creatinine, Urine microscopy, Arterial blood gas analysis, Chest x-ray and Blood culture, on admission to the NICU. The neonates were followed prospectively up to discharge or death. Daily monitoring of respiratory system with respiratory rate, work of breathing, oxygen saturation and blood gas if required. Cardiovascular system was monitored with Heart rate and blood pressure, and echocardiography if signs of cardiac dysfunction are present. Gastrointestinal system examined to look for abdominal distension (clinician diagnosis), tolerance of feeds and signs of Necrotising enterocolitis (diagnosed based on Modified Bell's staging criteria). Central Nervous System (CNS) monitoring was done with Sarnat and Sarnat staging for Hypoxic ischemic encephalopathy. Urine output was monitored daily, and serum creatinine was repeated on third day of life or as necessary.

The inclusion criteria were babies admitted in our NICU with one or more of the following:

· Five-minute Apgar score < 5

· Metabolic acidosis (base deficit 16 or more) within first hour of birth

· Delayed onset of respiration for five or more minutes

· Need for mechanical ventilation at birth

· Evidence of encephalopathy including altered consciousness and/or seizures

The exclusion criteria were major congenital anomaly and babies requiring < 30 seconds of positive pressure ventilation with no evidence of encephalopathy or acidosis.

The criteria for organ dysfunction were as follows.[3,4,6,7]

CNS dysfunction:

Seizure

Abnormal tone/sensorium

Renal dysfunction

Anuria or Oliguria (< 1 ml/kg/hr) for 24 hours or

more and serum creatinine > 1.1 mg/dl

Anuria of Oliguria for > 36 hours

Serum Urea > 40 mg/dl or Creatinine > 1.4 mg/dl

Raised creatinine > 0.3 mg/dl from baseline

Hematuria and proteinuria > +1 in two successive urine

sample

Respiratory dysfunction

- Oxygen support or Non-invasive ventilation with Fi02 > 40% for ≥ 4 hours after birth
- Ventilator dependent or Hood requirement > 24 hours after birth

Cardiovascular dysfunction

- Serum CPK > 25 IU/L at admission
- Inotrope requirement on over 24 hours
- Heart failure without structural heart disease

Gastrointestinal dysfunction

- Abdominal distension or bleeding
- Necrotizing enterocolitis (NEC)
- ALT >100 U/L at admission

Metabolic dysfunction

- Hypoglycemia (GRBS <40 mg/dl) at admission or during the NICU stay
- Dyselectrolytemia (sodium < 130 mEq/L, potassium > 6 mEq/L, calcium < 7.5 mg/dl) at admission or during NICU stay

Hematologic dysfunction

- Thrombocytopenia (< 150000/mm^3) at admission
- Petechiae/purpura during NICU stay
- Prothrombin time > 20 seconds at admission

Multiorgan dysfunction was defined as neonates having two or more organ dysfunction.[7]

The data were initially recorded in case proforma which was then stored and analyzed using IBM SPSS Statistics version 20 software. Descriptive statistics were used to summarize the results (frequency, mean, percentage and proportions).

RESULTS

Out of 108 enrolled neonates, 65 (60%) were male and 43 (40%) were female (Male : Female = 3:2). One hundred and one babies (93.5%) were inborn and 7 (6.5%) were outborn. Seventy babies (64.8%) were term, 37 (34.2%) were preterm and 1 (1%) was post-term. Sixty-seven babies (62%) were born via normal vaginal delivery, 34 (31.5%) via Cesarean Section and 7 (6.5%) babies were born via vacuum assisted delivery.

Among the neonates with birth asphyxia, 30 (27.8%) have at least one episode of seizure and 15 (13.9) have altered tone and sensorium. Three (2.8%) neonates had oliguria, 6 (5.6%) had raised serum ammonia and 2 (1.85%) had raised creatinine. One hundred five (97.2%) neonates required oxygen supplementation after birth. Among them, 29 (26.9%) required mechanical ventilation. Twenty-two (20.4%) neonates required inotropes for shock. Thrombocytopenia was present in 18 (16.7) neonates (Table1).

Table 1. Common morbidities among neonates with birth asphyxia (n=108)

	n (%)
1. Central Nervous System	
Seizure	30 (27.78)
Abnormal tone/sensorium	15 (13.89)
2. Renal system	
Reduced urine output	3 (2.78)
Raised serum Ammonia	6 (5.56)
Raised serum Creatinine	2 (1.85)
3. Respiratory system	
Oxygen requirement	105 (97.22)
Types of Oxygen support	
Nasal prong	18 (16.67)
Hoodbox	8 (7.4)
Continuous Positive Airway Pressure	19 (17.59)
Non-invasive ventilation (NIPPV)	31 (28.7)
Mechanical ventilation	29 (26.85)
4. Cardiovascular system	
Inotropes required	22 (20.37)
Heart Failure	11 (10.18)
Raised CK-MB	90 (83.33)
5. Gastrointestinal system	
Abdominal Distension	4 (3.7)
GI bleed	3 (2.78)
Necrotising Enterocolitis	1 (0.92)
ALT (>100 U/L)	4 (3.7)
6. Metabolic parameters	
Hypoglycemia	2 (1.85)
Hyponatremia	2 (1.85)
Hyperkalemia	2 (1.85)
Hypocalcemia	2 (1.85)
7. Hematologic parameters	
Thrombocytopenia	18 (16.67)
Prolonged PT	6 (5.56)

In our study, all of the neonates with birth asphyxia showed evidence of at least one organ or system dysfunction. Cardiovascular dysfunction (83.33%) was the most common system involved followed by respiratory dysfunction (79.62%) (Table 2). Sixteen (14.81%) neonates had one organ dysfunction and remaining 92 (85.19%) had multiorgan dysfunction (Table 3).

Among 108 neonates, 2 (1.85%) neonates died during the treatment and 5 (4.63%) neonates discharged against medical advice. The overall mortality rate in babies with asphyxia was 1.85%. The mean duration of hospital stay among the neonates was 5.79 ± 2.13 days.

Table 2. Organ or system dysfunction among enrolled neonates (n=108)

Organ dysfunction	n (%)
Cardiovascular dysfunction	90 (83.33)
Respiratory dysfunction	86 (79.62)
CNS dysfunction	31 (28.70)
Hematologic dysfunction	22 (20.37)
Gastrointestinal dysfunction	9 (8.33)
Renal dysfunction	9 (8.33)
Metabolic dysfunction	7 (6.48)

Table 3. Frequencies of Number of organs involved (n=108)

Number of organs involved	n (%)
1	16 (14.81)
2	50 (46.29)
3	30 (27.78)
4	7 (6.48)
5	2 (1.85)
6	3 (2.78)

DISCUSSIONS

The disruption of blood flow to fetus from placenta initiates various circulatory and non-circulatory mechanisms to preserve vital organs.[8] The major mechanism is redistribution of blood flow to vital organs at the cost of hypoxia and ischemia to other organs. With prolonged and severe asphyxia, the adaptive mechanisms are overwhelmed and there is widespread tissue damage causing multiple organ dysfunction.[7-9]

We had higher proportion of males with birth asphyxia in our study which was similar to other studies done by Pattar et al. and Vemuri et al. in India, and Martin-Ancel et al. in Spain.[3,6,10] In our study, 31.5% neonates were delivered by Cesarean section. This finding is similar to the study done by Pattar et al. and Vemuri et al.[3,6]

All of the neonates with birth asphyxia had at least one organ or system dysfunction in our study which is similar to the study done by Pattar et al., Shah et al., Nguyen et al. and Vemuri et al.[3,4,6,7]

Immature cardiac muscle of newborn is prone to hypoxic cardiomyopathy. Low heart rate and reduced myocardial contractility occur due to poor perfusion, ischemic cardiac injury and acidosis resulting in myocardial dysfunction. In this study, cardiovascular system was the most commonly involved system (80.3%) which was similar to the study done by Vemuri et al.[6] Studies done by Pattar et al. and Martin-Ancel et al. have relatively less proportion of neonates with cardiovascular involvement involving 54.3% and 29% respectively.[3,10] This could be because of different patient characteristics, use of raised CK-MB as cardiac dysfunction criterion and frequent use of point of care echocardiography for cardiac assessment in our study.

Birth asphyxia causes hypoperfusion injury to lung parenchyma. Pulmonary hemorrhage and pulmonary hypertension are also associated complications.[9] The respiratory dysfunction was seen in 79.6% of neonates which is slightly higher than the study done by Pattar et al. with 63.1% of neonates.[3] We have included use of continuous positive airway pressure support for more than 4 hours of life as a criterion of respiratory dysfunction which likely has caused its higher incidence in our study.

CNS dysfunction was found in 28.7% of neonates which is similar to the study by Vemuri et al.[6] In the study done by Pattar et al. all of the neonates had CNS dysfunction.[3] This was because encephalopathy was one of the inclusion criteria among the neonates with asphyxia where apgar score was not available.

Hematologic dysfunction was found in 20.37% of neonates which is similar to the study by Vemuri et al.[6] Only 5.6% of neonates had hematologic dysfunction in the study by Pattar et al.[3] In comparison to their study, we have higher reference for thromobocytopenia which might have caused higher rates of dysfunction in our study. Hypoxia is thought to have direct effect on platelet synthesis resulting in thrombocytopenia.[9]

The renal parenchymal cells are more susceptible to reperfusion injury and they have limited capacity for anerobic respiration causing high risk for renal derangement in neonates with birth asphyxia.[11] Renal dysfunction was seen in 8.3% of cases which is less as compared to the studies by Pattar et al., Nguyen et al. and Vemuri et al.[3,6,7] which might have been influenced by severity of asphyxia and the fluid management in renal dysfunction.

The gastrointestinal system has multiple watershed regions that are prone to asphyxia and hypoxia. Hypoxia and hypoperfusion cause liver dysfunction in neonates.[9,12] In our study, 8.3% of neonates have gastrointestinal dysfunction which is similar in comparison to studies by Pattar et al., Vemuri et al. and Nguyen et al.[3,6,7]

Perinatal stress, excessive glycogenolysis causing decreased glycogen storage, high insulin release and limited capacity of new born in maintaining glucose homeostasis results in hypoglycemia.[13] They also have high serum phosphate level from endogenous breakdown of glycogen and protein. Together with hyperphosphatemia, low calcium intake, bicarbonate therapy and functional hypoparathyroidism causes hypocalcemia in asphyxiated newborns.[14] Increased secretion of ADH in neonates with asphyxia, limited sodium reabsorption capacity and partial resistance to aldosterone contribute to hyponatremia, and potassium level is increased due to metabolic acidosis and acute kidney injury.[15] In our study, we had 6.5% of neonates with metabolic dysfunction.

We found 85.2% neonates have multiorgan dysfunction. This finding is similar to the study done by Pattar et al. who reported multiorgan dysfunction in 80.8% of cases.[3] It is

higher as compared to the study done by Martin-Ancel et al. where 55.6% of neonates have multiorgan dysfunction.[10] This difference could be due to the different patient characteristics as we have included only NICU patients but Martin-Ancel included all neonates.[10] Moreover, we have included hematologic and metabolic dysfunction as criteria of organ dysfunction which could be the reason for increased incidence of multiple organ dysfunction.

There were two mortality (1.85%) in our study. The mortality among asphyxiated neonates were higher in the studies done by Martin-Ancel et al., Pattar et al. and Mohan et al. from 5.6%, 14% to 23.3% mortality respectively.[3,10,16] These could be due to the differences in clinical characteristics and severity of asphyxia among the asphyxiated neonates. We had neonates who were discharged against medical advice that might have affected the mortality rate.

The rate of discharge against medical advice in our study was 4.63%. A study by Vemuri et al. has 13% discharged against medical advice and the survival rate was 87% which was similar to our study.[6]

The limitation of this study is that being a single-center study with limited number of patients, the result cannot be generalized to whole population. A large multicentric study is required for further recommendation.

CONCLUSION

This study showed high incidence of organ dysfunction among neonates with birth asphyxia which reinforces the importance of prevention and appropriate neonatal resuscitation for early management of birth asphyxia. As this is a single-center study with limited number of patients, the result cannot be generalized to whole population. A large multicentric study is required for further recommendation.

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