***Original Research Article***

 **Clinical and biochemical correlation in Perinatal Asphyxia and its association with short term outcome**

**ABSTRACT**

**Background:** Perinatal asphyxia is a leading cause of neonatal morbidity and mortality worldwide. According to the [World Health Organization](https://iris.who.int/bitstream/handle/10665/330587/WH-1997-Mar-Apr-p28-30-eng.pdf?sequence=1&isAllowed=y), in developing countries, 3% of all infants (3.6 million) experience moderate to severe birth asphyxia, Among these, approximately 23%, or 840,000, die while a comparable number suffer from long – term neurological disabilities**.**

**Methods:** This hospital – based, retrospective, study included term neonates with perinatal asphyxia admitted in Neonatal Intensive Care Unit of Dhulikhel hospital from 1st January 2021 till 31st December 2022. The data was collected from the maternal and neonatal hospital records and then entered on SPSS 25.0 for analysis after obtaining the ethical approval from the Institutional Review Committee.

**Results:** Out of the total 123 term neonates enrolled, a male preponderance of 66.7% was observed. Based on HIE staging, 23.6% were HIE stage I, 69.1% were HIE stage II and 7.3% were HIE stage III. Seizures were present in 74.8% neonates; majority were of subtle type. Among the neonates enrolled, 9.75% expired. Hyponatremia, hyperkalemia, hypocalcemia, and hypoglycemia were some common biochemical changes noted. Seizures, respiratory distress, bradycardia, and hypothermia were found to be significantly associated with increasing severity of HIE (P<.05). There was also statistically significant difference in the outcome of babies depending upon the severity of HIE.

**Conclusion:** Hypoxic – ischemic neonates with seizures, respiratory distress, advanced resuscitation needs, and electrolyte imbalances were more likely to have severe disease. Early detection and correction of biochemical abnormalities are crucial. Prompt resuscitation and metabolic support can reduce mortality and long-term sequelae.

**Keywords:** Perinatal asphyxia, neonates, Hyponatremia, hyperkalemia

**INTRODUCTION**

Perinatal asphyxia (PA) is a condition occurring during the first and second stages of labor, characterized by impaired gas exchange leading to fetal acidosis, hypoxemia, and hypercarbia. It is diagnosed by evidence of fetal acidosis in umbilical arterial blood.1 Globally, PA ranks among the top twenty causes of death across all age groups and remains a major contributor to neonatal morbidity and mortality. Each year, approximately four million neonates experience significant oxygen deprivation during birth, with about 20 per 1,000 deliveries requiring resuscitation and showing biochemical or clinical signs of PA.2In developed countries with advanced obstetric and neonatal care, PA is a relatively rare complication affecting roughly 1.5% of live births, with an inverse relationship to gestational age and birth weight.1 However, in developing countries like Nepal PA remains one of the leading causes of neonatal morbidity and mortality. The reported prevalence of PA in Nepal varies across studies, ranging from 9.3% to 25%.3-5

All organ systems can be affected by PA, potentially resulting in multiorgan dysfunction. However, hypoxic injury to the brain is of greatest concern, as it is the least likely to recover fully and often results in permanent neurological damage.6 Hypoxic Ischemic Encephalopathy (HIE) resulting from PA is the leading cause of acquired brain injury in the perinatal period which can lead to neonatal death or long – term neurological sequelae.7 The greatest burden of HIE lies in low – and middle – income countries (LMICs), where its incidence is estimated to be 10 – 20 times higher than in high – income countries.8 In high – income settings, the incidence ranges from 1 to 8 per 1,000 live births, while in LMICs, it may be as high as 26 per 1,000 live births.9

PA triggers a shift to anaerobic metabolism, resulting in decreased production of adenosine triphosphate (ATP), impaired function of ion pumps, and the accumulation of intracellular sodium, chloride, water, and calcium, along with increased extracellular potassium. This electrolyte imbalance negatively impacts the prognosis of asphyxiated neonates.1,10 In addition to the central nervous system (CNS), the kidneys are particularly vulnerable to hypoxic injury. PA can cause ischemia in the proximal tubules, leading to acute tubular necrosis (ATN) and acute renal failure (ARF), often evidenced by elevated serum urea and creatinine levels. Careful management of body temperature, electrolytes, blood glucose levels, and adequate oxygenation is essential in reducing the severity of ischemic damage.11

The prognosis and severity of symptoms in neonates with PA largely depend on the presence of risk factors and the quality of clinical management. With timely recognition and appropriate intervention, many cases of asphyxia can be anticipated or even prevented particularly when maternal and fetal risk factors are identified and addressed.12 Early detection of multiorgan dysfunction in PA is critical, as it enables intensive monitoring and targeted management, thereby improving neonatal outcomes. Hence, the present study was conducted to identify the risk factors, clinical and biochemical correlation in perinatal asphyxia and its effect on short term outcome in term neonates.

**METHODOLOGY**

This hospital – based, retrospective study included term neonates with perinatal asphyxia admitted in the Neonatal Intensive Care Unit (NICU) of Dhulikhel hospital, Kathmandu University Hospital, Dhulikhel, Kavre, Nepal from 1st January 2021 till 31st December 2022. Ethical approval was obtained from the Institutional review board of Kathmandu University School of Medical Sciences (KUSMS – IRC) with approval number 232/23. A purposive sampling method was used where medical records of term neonates admitted with a diagnosis of PA during the study period were reviewed. Data were extracted from institutional maternal and neonatal medical records. The study included both qualitative and quantitative data. To ensure confidentiality, all data were identifiable by the subject’s case number, which was recorded on the forms. Standardized pre – designed data collection proforma were used to record all data.

The inclusion criteria consisted of term neonates (gestational age ≥ 37 weeks as assessed by the Modified Ballard Score) diagnosed with PA and admitted to the NICU of Dhulikhel Hospital during the study period, with complete medical records available for review. PA was defined as neonates with no spontaneous breathing at birth and requiring assisted ventilation for more than 1 minute or neonates with APGAR score of less than 3 at 1 minute of life or less than 7 at 5 minutes of life. Preterm (gestational age < 37 weeks as assessed by the Modified Ballard Score), neonates born by caesarean section with general anesthesia and mother on sedatives (anticonvulsants, opioids) and neonates with congenital malformations and suspected inborn errors of metabolism were excluded from the study.

Detailed history, examination findings and information of all the neonates with PA including social demography, risk factors, comorbid conditions and relevant investigations were obtained from the institutional records and filled in the predesigned proforma. Detailed history regarding type and place of delivery, type of resuscitation required, any complication before/during delivery, onset and duration of seizure, and findings of clinical examination, with special reference to the central nervous system was noted. Clinical findings during the treatment in the hospital until discharge or death was recorded. Neurological findings like seizure, feeding problems, or neurological deficits were recorded. The biochemical parameters included hemoglobin, total leukocyte and differential counts and platelet count. blood glucose, calcium, sodium, potassium, lactate dehydrogenase (LDH), urea, creatinine and arterial blood gas monitoring. HIE classification was done using Sarnat and Sarnat classification of HIE. Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0. Descriptive statistics such as frequency and percentage were calculated. Inferential statistics, including the Chi – square test and Fisher’s exact test, were used to assess associations. A P–value of less than .05 was considered statistically significant.

**RESULT**

The clinical profile of neonates with perinatal asphyxia are presented in Table 1. A total of 123 term neonates with PA fulfilling the inclusion criteria were included in this study, with a male preponderance of 82 (66.7%), yielding a male-to-female ratio of 2:1. Most of the neonates, 72 (58.5%) were born via vaginal delivery and majority 95 (77.2%) were inborn (born at Dhulikhel hospital). Maximum, 84 (68.3%) of them presented at < 1 hours of life followed by 20 (16.3%) presenting at 1 – 6 hours of life. Term and post – term neonates constituted 102 (82.9%) and 21 (17.1%) cases, respectively and the birth weight of most of the neonates 87 (70.7%) enrolled was between 2500 – 3500 gram. Delayed cry was present in 85 (69.1%) of the neonates and advanced neonatal resuscitation was required in 59 (48%).

According to HIE staging, 29 (23.6%) were HIE stage I, 85 (69.1%) were HIE stage II and 9 (7.3%) belonged to HIE stage III. Seizures were present in 92 (74.8%) neonates; majority were of subtle type 53 (75.6%). Among most of the asphyxiated neonates, in 70 (76%) the onset of seizure was within 24 hours of life and maximum 83 (90.2%) had multiple episodes of seizure. 81 (65.85%) of the neonates required polytherapy (more than one antiepileptic). Bradycardia, hypothermia, respiratory distress, hypotonia and hypertonia were noted in 33 (26.8%), 32 (26%), 55 (44.7%), 29 (23.6%) and 17 (13.8%) neonates, respectively. Inotropes and mechanical ventilation were required in 61 (49.6%) and 49 (39.8%) asphyxiated neonates, respectively. Out of the 123 asphyxiated neonates enrolled 111 (90.24%%) survived and were discharged while 12 (9.75%) expired.

**Table 1: Clinical profile of neonates with perinatal asphyxia**

|  |  |  |  |
| --- | --- | --- | --- |
| **Clinical details** | **Categories** | **Frequency (n)** | **Percentage (%)** |
| **Gender** | Male | 82 | 66.7 |
| Female | 41 | 33.3 |
| **Mode of delivery** | Vaginal delivery | 72 | 58.5 |
| Caesarean section | 47 | 38.2 |
| Instrumental delivery | 4 | 3.3 |
| **Delivery place** | Inborn | 95 | 77.2 |
| Outborn | 28 | 22.8 |
| **Age at clinical presentation** | < 1 hour of life | 84 | 68.3 |
| 1 – 6 hours of life | 20 | 16.3 |
| 7 – 24 hours of life | 16 | 13 |
| >24 hours of life | 3 | 2.4 |
| **Gestational age** | Term (37 – 42 weeks) | 102 | 82.9 |
| Post term (> 42 weeks) | 21 | 17.1 |
| **Birth weight (gram)** | < 2500 | 23 | 18.7 |
| 2500 – 3500  | 87 | 70.7 |
| >3500 | 13 | 10.6 |
| **APGAR score at 1 minute** | <3 | 37 | 30.08 |
| >3 | 82 | 66.67 |
| Not documented | 4 | 3.25 |
| **APGAR score at 5 minutes** | <5 | 32 | 26.02 |
| >5 | 87 | 70.73 |
| Not documented | 4 | 3.25 |
| **Delayed cry** | Present | 85 | 69.1 |
| Absent | 38 | 30.9 |
| **Advanced neonatal resuscitation** | Required | 59 | 48 |
| Not required | 64 | 52 |
| **HIE staging** | Stage I | 29 | 23.6 |
| Stage II | 85 | 69.1 |
| Stage III | 9 | 7.3 |
| **Seizure** | Present | 92 | 74.8 |
| Absent | 31 | 25.2 |
| **Onset of seizure** | < 24 hrs | 70 | 76 |
| >24 hours | 22 | 24 |
| **Seizure episode** | Single  | 9 | 9.8 |
| Multiple | 83 | 90.2 |
| **Type of seizure** | Subtle | 53 | 57.6 |
| Tonic | 14 | 15.2 |
| Clonic | 2 | 2.17 |
| Focal | 10 | 10.9 |
| Generalized | 9 | 9.8 |
| Mixed | 4 | 4.34 |
| **Antiepileptics required** | Monotherapy | 14 | 11.38 |
| Polytherapy | 81 | 65.85 |
| None | 28 | 22.76 |
| **Heart rate at birth** | Normal | 90 | 73.2 |
| Bradycardia | 33 | 26.8 |
| **Hypothermia** | Present  | 32 | 26 |
| Absent | 91 | 74 |
| **Respiratory distress** | Present | 55 | 44.7 |
| Absent | 68 | 55.3 |
| **Tone** | Normal | 77 | 62.6 |
| Hypotonic | 29 | 23.6 |
| Hypertonic | 17 | 13.8 |
| **Inotropes required** | Yes | 61 | 49.6 |
| No | 62 | 50.4 |
| **Mechanical ventilation** | Yes | 49 | 39.8 |
| No | 74 | 60.2 |
| **Outcome** | Discharged | 111 | 90.24 |
| Expired | 12 | 9.75 |

As shown in Figure 1, the most common maternal risk factor among asphyxiated neonates was meconium-stained liquor, observed in 47 neonates (38.2%), followed by cord around the neck in 22 neonates (17.9%). Prolonged second stage of labor and maternal hypertension were each present in 20 neonates (16.3%). Malpresentation was noted in 14 neonates (11.8%), while premature rupture of membranes (PROM > 18 hours) was observed in 10 neonates (8.1%).

**Figure 1: Risk factors associated with perinatal asphyxia**

The biochemical profile of neonates with perinatal asphyxia is summarized in Table 2. The most frequently observed abnormalities included hypocalcemia in 45 neonates (36.6%), hyponatremia in 24 (19.5%), acidosis (pH < 7.15) in 22 (17.9%), hyperkalemia in 18 (14.6%), and hypoglycemia in 17 (13.8%). Increased levels of urea, serum creatinine and LDH were found in 12 (9.8%), 15 (12.2%) and 82 (66.7%) of the neonates, respectively. Among the asphyxiated neonates, leukocytosis was seen in 30 (24.4%), thrombocytopenia in 28 (22.8%) and anemia in 25 (20.3%),

**Table 2: Biochemical profile of neonates with perinatal asphyxia**

|  |  |  |  |
| --- | --- | --- | --- |
| **Biochemical details** | **Category** | **Frequency (n)** | **Percentage (%)** |
| **pH** | <7.15 | 22 | 17.9 |
| >7.15 | 101 | 82.1 |
| **Serum Sodium****(135 – 145 mEq/L)** | Normal | 95 | 77.2 |
| Hypernatremia  | 4 | 3.3 |
| Hyponatremia | 24 | 19.5 |
| **Serum Potassium****(3.5 – 5.5 mEq/L)** | Normal | 93 | 75.6 |
| Hyperkalemia | 18 | 14.6 |
| Hypokalemia | 12 | 9.8 |
| **Serum Calcium****(8.6 – 10.2 mg/dl)** | Normal | 78 | 63.4 |
| Hypocalcemia | 45 | 36.6 |
| **Urea****(10 – 45 mg/dl)** | Normal | 111 | 90.2 |
| Increased | 12 | 9.8 |
| **Serum creatinine****(0.4 – 1.1 mg/dl)** | Normal | 108 | 87.8 |
| Increased  | 15 | 12.2 |
| **LDH****(170 – 580 U/L)** | Normal  | 41 | 33.3 |
| Increased | 82 | 66.7 |
| **Blood sugar****(40 – 90 mg/dl)** | Normal | 99 | 80.5 |
| Hyperglycemia | 7 | 5.7 |
| Hypoglycemia | 17 | 13.8 |
| **Hemoglobin****(14 – 22 gm/dl)** | Normal | 94 | 76.4 |
| Increased | 4 | 3.3 |
| Decreased | 25 | 20.3 |
| **Total leukocyte count****(4000 – 11000/cumm)** | Normal | 85 | 69.1 |
| Leukocytosis | 30 | 24.4 |
| Leukopenia | 8 | 6.5 |
| **Platelets****(150000 – 400000/cumm)** | Normal | 92 | 74.8 |
| Thrombocytosis | 3 | 2.4 |
| Thrombocytopenia | 28 | 22.8 |

Various clinical and biochemical parameters were analyzed in relation to HIE and observations are shown in Table 3 and 4. Gender of neonates, mode of delivery, place of delivery, age at clinical presentation, gestational age and birth weight were not found to be statistically significant in association with HIE. While, seizures (P<.001), respiratory distress (P=.037), bradycardia (P<.001), hypothermia (P=.015) and change in tone (P<.001) were found to be statistically significant in relation to increasing severity of HIE. Similiarly, APGAR score at 1 minute and 5 minutes, need of advanced neonatal resuscitation, requirement of inotropes and mehanical ventilation were all highly statistically significant (P<.001) in relation to HIE, all more prevalent in cases with HIE stage II and III. There was also statistically significant difference in the outcome of asphyxiated neonates with increasing severity of HIE (P=.009).

**Table 3: Clinical profile of neonates and their correlation with HIE**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Clinical details** | **Category** | **HIE** **stage I** | **HIE** **stage II** | **HIE** **stage III** | **P value** |
| **Gender** | Male | 19 | 59 | 4 | .316 |
| Female | 10 | 26 | 5 |
| **Mode of delivery** | Vaginal delivery | 18 | 48 | 6 | .944 |
| Caesarean section | 10 | 34 | 3 |
| Instrumental delivery | 1 | 3 | 0 |
| **Place of delivery** | Inborn | 25 | 65 | 5 | .142 |
| Out born | 4 | 20 | 4 |
| **Age at clinical presentation** | < 1 hour of life | 21 | 57 | 6 | .403 |
| 1 – 6 hours of life | 6 | 14 | 0 |
| 7 – 24 hours of life | 2 | 11 | 3 |
| >24 hours of life | 0 | 3 | 0 |
| **Gestational age** | Term (37 – 42 weeks) | 24 | 72 | 6 | .320 |
| Post term (> 42 weeks) | 5 | 13 | 3 |
| **Birth weight (gram)** | < 2500 | 5 | 15 | 3 | .380 |
| 2500 – 3500  | 22 | 61 | 4 |
| >3500 | 2 | 9 | 2 |
| **APGAR score at 1 minute** | <3 | 1 | 29 | 7 | <.001 |
| >3 | 28 | 53 | 1 |
| No documentation | 0 | 3 | 1 |
| **APGAR score at 5 minutes** | <5 | 0 | 25 | 7 | <.001 |
| >5 | 29 | 57 | 1 |
| No documentation | 0 | 3 | 1 |
| **Delayed cry** | Present | 28 | 52 | 5 | <.001 |
| Absent | 1 | 33 | 4 |
| **Advanced neonatal resuscitation** | Required | 4 | 48 | 7 | <.001 |
| Not required | 25 | 37 | 2 |
| **Seizure** | Present | 1 | 82 | 9 | <.001 |
| Absent | 28 | 3 | 0 |
| **Onset of seizure** | <24 hours | 0 | 62 | 8 | <.001 |
| >24 hours | 1 | 20 | 1 |
| **Seizure episode** | Single  | 0 | 8 | 1 | <.001 |
| Multiple | 1 | 74 | 8 |
| **Type of seizure** | Subtle | 1 | 48 | 4 | <.001 |
| Tonic | 0 | 12 | 2 |
| Clonic | 0 | 2 | 0 |
| Focal | 0 | 8 | 2 |
| Generalized | 0 | 8 | 1 |
| Mixed | 0 | 4 | 0 |
| **Antiepileptics required** | Monotherapy | 2 | 11 | 1 | <.001 |
| Polytherapy | 1 | 72 | 8 |
| None | 26 | 2 | 0 |
| **Heart rate** | Normal | 29 | 57 | 4 | <.001 |
| Bradycardia | 0 | 28 | 5 |
| **Hypothermia** | Present  | 26 | 61 | 4 | .015 |
| Absent | 3 | 24 | 5 |
| **Respiratory distress** | Present | 19 | 33 | 3 | .037 |
| Absent | 10 | 52 | 6 |
| **Tone** | Normal | 28 | 48 | 1 | <.001 |
| Hypotonic | 1 | 21 | 7 |
| Hypertonic | 0 | 16 | 1 |
| **Inotropes required** | Yes | 3 | 50 | 8 | <.001 |
| No | 26 | 35 | 1 |
| **Mechanical ventilation** | Yes | 1 | 39 | 9 | <.001 |
| No | 28 | 46 | 0 |
| **Outcome** | Discharged | 29 | 77 | 5 | .009 |
| Expired | 0 | 8 | 4 |

Note: *P < .05 considered statistically significant.*

Of various biochemical tests, pH (P<.001), serum sodium level (P=.025), serum potassium level (P<.001), serum calcium level (P<.001), blood urea (P=.039), serum creatinine (P=.035), serum LDH (P<.001), total leukocyte count (P=.008) and platelet count (P=.030) were the parameters which differed significantly with severity of HIE as demonstrated in Table 4.

**Table 4: Biochemical profile of neonates and their correlation with HIE**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Biochemical details** | **Category** | **HIE****stage I** | **HIE****stage II** | **HIE****stage III** | **P value** |
| **pH** | <7.15 | 0 | 16 | 6 | <.001 |
| >7.15 | 29 | 69 | 3 |
| **Serum Sodium****(135 – 145 mEq/L)** | Normal | 27 | 64 | 4 | .025 |
| Hypernatremia  | 0 | 3 | 1 |
| Hyponatremia | 2 | 18 | 4 |
| **Serum Potassium****(3.5 – 5.5 mEq/L)** | Normal | 26 | 66 | 1 | <.001 |
| Hyperkalemia | 2 | 13 | 3 |
| Hypokalemia | 1 | 6 | 5 |
| **Serum Calcium****(8.6 – 10.2 mg/dl)** | Normal | 26 | 51 | 1 | <.001 |
| Hypocalcemia | 3 | 34 | 8 |
| **Urea****(10 – 45 mg/dl)** | Normal | 28 | 77 | 6 | .039 |
| Increased | 1 | 8 | 3 |
| **Serum creatinine****(0.4 – 1.1 mg/dl)** | Normal | 29 | 72 | 7 | .035 |
| Increased  | 0 | 13 | 2 |
| **LDH****(170 – 580 U/L)** | Normal  | 28 | 13 | 0 | <.001 |
| Increased | 1 | 72 | 9 |
| **Blood sugar****(40 – 90 mg/dl)** | Normal | 23 | 71 | 5 | .124 |
| Hyperglycemia | 3 | 3 | 1 |
| Hypoglycemia | 3 | 11 | 3 |
| **Hemoglobin****(14 – 22 gm/dl)** | Normal | 22 | 67 | 5 | .059 |
| Polycythemia | 3 | 1 | 0 |
| Anemia | 4 | 17 | 4 |
| **Total leukocyte count****(4000 – 11000/cumm)** | Normal | 24 | 59 | 2 | .008 |
| Leukocytosis | 3 | 21 | 6 |
| Leukopenia | 2 | 5 | 1 |
| **Platelets****(150000 – 400000/cumm)** | Normal | 24 | 64 | 4 | .030 |
| Thrombocytosis | 2 | 1 | 0 |
| Thrombocytopenia | 3 | 20 | 5 |

Note: *P < .05 considered statistically significant.*

**DISCUSSION**

PA is multifactorial, including obstetric risk factors like – maternal age, antenatal care, maternal comorbidities, primiparity, maternal fever, prolonged second stage of labor, rupture of membrane, and place of delivery.12-14 Likewise neonatal related factors such as male gender, prematurity, low birth weight, and delayed presentation are all recognized to be associated with a poorer prognosis for survival in cases of PA.2,15 Even in the present study, male preponderance of 82 (66.7%) was noted, yielding a male-to-female ratio of 2:1. This is in accordance to various studies done in Nepal, India, Pakistan, Nigeria and Ethiopia.13,14,16-18 In contrast to these studies a study done by Saeed et al in Pakistan showed a female preponderance among asphyxiated newborns.19

In the current study, the mode of delivery, place of delivery, age at clinical presentation, gestational age and birth weight did not show a statistically significant corelation with the degree of severity of HIE. This was in contrast with other studies done by Uleanya et al in Nigeria, Niaz et al in Pakistan, Alfaifi et al in Sudan and Ajibo et al in Ethiopia where caesarean section, outborn neonates, delayed age of presentation, prematurity and low birth were found to be associated with poor prognosis and survival in asphyxiated neonates.14,18,20,21 These factors likely contribute to worse outcomes in asphyxiated neonates due to delayed resuscitative efforts, immature organ systems, inadequate physiological reserves, and failure to timely therapeutic interventions.

Most prevalent maternal risk factors identified in this study were meconium stained liquor, cord around the neck, prolonged second stage of labor, hypertension, malpresentation, and premature rupture of membrane (PROM > 18 hours). Similar results were also documented in several studies done in India, Pakistan and Nigeria.11-13,18,22 Maternal factors have been associated with an increased risk of birth asphyxia. These conditions can impair oxygen delivery to the fetus, increasing the likelihood of hypoxic events during labor and delivery. Early screening and effective management of these maternal conditions are critical steps in reducing the incidence and severity of birth asphyxia and improving neonatal outcomes.

Among the neonates enrolled in the present study, 29 (23.6%) were HIE stage I, 85 (69.1%) were HIE stage II and 9 (7.3%) belonged to HIE stage III. A poorer outcome was noted in neonates with HIE stage II and III. Clinical parameters like low APGAR score at 1 minute and 5 minutes, delayed cry, need of advanced neonatal resuscitation, presence of bradycardia, hypothermia, respiratory distress, seizures, early onset of seizure (< 24 hours of life), multiple episodes of seizure, polytherapy requirement for control of seizures, requirement of inotropes and need of mechanical ventilation showed a statistically significant corelation with the degree of severity of HIE indicating a poorer outcome and prognosis. These findings were similar to various studies done in Nepal, India, Nigeria and West Indies.11,15,22-24 Increase in morbidity and mortality occurred in stages II and III of HIE, showing that once severe hypoxia occurs, treatment cannot be very effective, so more attention needs to be paid on early assessment and intervention, during which intervention might be efficacious in reducing severity of brain damage.

In the present study, alterations in pH, serum sodium level, serum potassium level, serum calcium level, blood urea, serum creatinine, serum LDH, total leukocyte count and platelet count were found to have significant corelation with the degree of severity of HIE. These findings are comparable with other studies done in Nepal, India and Pakistan.11,13,24-26 In this study, cases of hyponatremia, hypocalcemia, and hyperkalemia increased with the severity of HIE, indicating a strong correlation between electrolyte imbalances and disease progression, which may lead to seizures and various metabolic abnormalities. Calcium, functioning as a crucial second messenger, plays an essential role in activating numerous cofactors involved in enzymatic processes and muscle contraction. Therefore, early diagnosis and appropriate management of fluid and electrolyte disturbances are vital for improving outcomes and preventing complications in neonates with HIE.

**Limitations**

Since this is a retrospective study, there is a possibility of information bias due to incomplete recorded data. Additionally, being a single – center study, the findings may not be generalizable to the broader population. Therefore, the observed clinical and biochemical profile of perinatal asphyxia among term neonates in this study may not fully represent the patterns seen in other regions or healthcare settings.

**CONCLUSION**

Perinatal asphyxia is one of the leading causes of neonatal mortality, with consequences that extend beyond death. It often results in severe hypoxic – ischemic organ damage, leading to long – term physical, cognitive, and social impairments in affected newborns. In our study, hypoxic – ischemic neonates with multiple episodes of seizures, respiratory distress, need for advanced resuscitation, biochemical derrangements including dyselectrolytemia were more likely to present with increasing severity of disease, highlighting the importance of monitoring and correcting electrolyte imbalances early. Many of the risk factors for PA are preventable through appropriate antenatal care and timely, active management during labor. Furthermore, effective neonatal resuscitation combined with the prompt correction of biochemical derrangements can significantly contribute to reducing neonatal mortality and minimizing long – term neurological sequelae.

**Ethical approval**

The study was approved by the Institutional review board of Kathmandu University School of Medical Sciences (KUSMS – IRC) with approval number 232/23.

**COMPETING INTERESTS**

Authors have declared that no competing interests exist.

**DISCLAIMER (ARTIFICIAL INTELLIGENCE)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) have been used during the writing or editing of this manuscript.

**REFERENCES**

1. Hansen, A. R., & Soul, J. S. (2017). Perinatal Asphyxia and Hypoxic – Ischemic Encephalopathy. In E. C. Eichenwald, A. R. Hansen, C. R. Martin & A. R. Stark (Eds.), Cloherty and Stark’s Manual of Neonatal Care (8th ed., pp. 791-811). Lippincott Williams & Wilkins, a Wolters Kluwer business.
2. Getaneh, F. B., Sebsbie, G., Adimasu, M., Misganaw, N. M., Jember, D. A., Mihretie, D. B., et al. (2022) Survival and predictors of asphyxia among neonates admitted in neonatal intensive care units of public hospitals of Addis Ababa, Ethiopia, 2021: a retrospective follow-up study. BMC Pediatrics, 22, 262.

<https://doi.org/10.1186/s12887-022-03238-w>

1. Shakya, A., Shrestha, D., Shakya, H., Shah, S. C., & Dhakal, A. K. (2015). Clinical profile and outcome of neonates admitted to the Neonatal Care Unit at a teaching hospital in Lalitpur, Nepal. Journal of Kathmandu Medical College, 3(4), 144–148. <https://jkmc.com.np/ojs3/index.php/journal/article/view/707>
2. Dongol, S., Singh, J., Shrestha, S., & Shakya, A. (2010). Clinical Profile of Birth Asphyxia in Dhulikhel Hospital: A Retrospective Study. Journal of Nepal Paediatric Society, 30(3), 141–146.

<https://doi.org/10.3126/jnps.v30i3.3916>

1. Gupta, S. K., Sarmah, B. K., Tiwari, D., Shakya, A., & Khatiwada, D. (2014). Clinical Profile of Neonates with Perinatal Asphyxia in a Tertiary Care Hospital of Central Nepal. *Journal of Nepal Medical Association*, *52*(196), 1005–1009.

<https://doi.org/10.31729/jnma.2802>

1. Imam, AB. AH., & El–Sayed, R.M. (2021). Early biochemical predictors of hypoxic ischemic encephalopathy after perinatal asphyxia. Al-Azhar Journal of Pediatrics, 24(3), 2248-2266.

doi: 10.21608/azjp.2021.210116

1. Ouwehand, S., Smidt, L. C. A., Dudink, J., Benders, M. J. N. L., de Vries, L. S., Groenendaal, F., et al. (2020). Predictors of Outcomes in Hypoxic-Ischemic Encephalopathy following Hypothermia: A Meta-Analysis. Neonatology, 117(4), 411–427. <https://doi.org/10.1159/000505519>
2. Aker, K., Thomas, N., Adde, L., Koshy, B., Martinez-Biarge, M., Nakken, I., et al. (2022). Prediction of outcome from MRI and general movements assessment after hypoxic-ischaemic encephalopathy in low-income and middle-income countries: data from a randomised controlled trial. Archives of disease in childhood. *Fetal and neonatal edition*, *107*(1), 32–38.

<https://doi.org/10.1136/archdischild-2020-321309>

1. Thomas, C. W., & Merhar, S. L. (2020). Hypoxic – Ischemic Encephalopathy. In R. M. Kliegman, J. W. S. Geme, N. J. Blum, S. S. Shah, R. C. Tasker & K. M. Wilson (Eds.), Nelson Textbook of Pediatrics (21st ed., pp. 3944-3959). Elsevier.
2. Basu, P., Som, S., Das, H., & Choudhuri, N. (2010). Electrolyte status in birth asphyxia. Indian journal of pediatrics, *77*(3), 259–262.

<https://doi.org/10.1007/s12098-010-0034-0>

1. Acharya, A., Swain, B., Pradhan, S., Jena, P. K., Mohakud, N. K., Swain, A., et al. (2020). Clinico-Biochemical Correlation in Birth Asphyxia and Its Effects on Outcome. Cureus, 12(11), e11407.

<https://doi.org/10.7759/cureus.11407>

1. Adebami, O. J. (2015). Maternal and fetal determinants of mortality in babies with birth asphyxia at Osogbo, Southwestern Nigeria. Global Advanced Research Journal of Medicine and Medical Science, 4(6), 270-276.
2. Amritanshu, K., Banerjee, D., Pathak, A., Smriti, S., & Kumar, V. (2014). Clinical profile and short-term outcome of hypoxic ischemic encephalopathy among birth asphyxiated babies in Katihar Medical College Hospital. Journal of Clinical Neonatology, 3(4), 195. <https://doi.org/10.4103/2249-4847.144749>
3. Uleanya, N. D., Aniwada, E. C., Ekwochi, U., & Uleanya, N. D. (2019). Short term outcome and predictors of survival among birth asphyxiated babies at a tertiary academic hospital in Enugu, South East, Nigeria. African health sciences, 19(1), 1554–1562. <https://doi.org/10.4314/ahs.v19i1.29>
4. Ogunkunle, T. O., Odiachi, H., Chuma, J. R., Bello, S. O., & Imam, A. (2020). Postnatal Outcomes and Risk Factors for In-Hospital Mortality among Asphyxiated Newborns in a Low-Resource Hospital Setting: Experience from North-Central Nigeria. Annals of Global Health, 86(1), 63.

<https://doi.org/10.5334/aogh.2884>

1. Manandhar, S. R., & Basnet, R. (2019). Prevalence of Perinatal Asphyxia in Neonates at a Tertiary Care Hospital: A Descriptive Cross-sectional Study. JNMA, 57(219), 287–292. <https://doi.org/10.31729/jnma.4550>
2. Tibebu, N. S., Emiru, T. D., Tiruneh, C. M., Getu, B. D., Abate, M. W., Nigat, A. B., et al. (2022). Magnitude of birth asphyxia and its associated factors among live birth in north Central Ethiopia 2021: an institutional-based cross-sectional study. BMC pediatrics, 22(1), 425.

<https://doi.org/10.1186/s12887-022-03500-1>

1. Niaz, H., Jalil, J., Khan, Q. U. Z., Basheer, F., Akhtar, S., & Hamid, N. (2021). Clinical Profile and Short term outcome of Hypoxic Ischemic Encephalopathy among birth asphyxiated babies in a tertiary care hospital. Pakistan Armed Forces Medical Journal, 71(1), 24-28.

<https://doi.org/10.51253/pafmj.v71i1.3847>

1. Saeed, T., Zulfiqar, R., Afzal, M. A., Raja, T. M., & Zahoor ul Haq, M. (2012). Outcome of Asphyxiated Term Newborns in Relation to the Time of Referral to a Tertiary Care Hospital. Journal of Rawalpindi Medical College, 16, 34-36.
2. Alfaifi, J., Ahmed, M. A., Almutairi, G. S., Alhumaidi, N. H., AlHabardi, N., & Adam, I. (2025). Prevalence of perinatal asphyxia and its associated factors among live birth in Khartoum, Sudan: a hospital-based cross-sectional study. BMC pediatrics, *25*(1), 150. <https://doi.org/10.1186/s12887-025-05499-7>
3. Ajibo, B. D., Wolka, E., Aseffa, A., Nugusu, M. A., Adem, A. O., Mamo, M., et al. (2022). Determinants of low fifth minute Apgar score among newborns delivered by cesarean section at Wolaita Sodo University Comprehensive Specialized Hospital, Southern Ethiopia: an unmatched case control study. BMC pregnancy and childbirth, 22(1), 665. <https://doi.org/10.1186/s12884-022-04999-z>
4. Yadav, N., & Damke, S. (2017). Study of risk factors in children with birth asphyxia. International Journal of Contemporary Pediatrics, 4(2), 518–526. <https://doi.org/10.18203/2349-3291.ijcp20170701>
5. Trotman, H., & Garbutt, A. (2011). Predictors of outcome of neonates with hypoxic ischaemic encephalopathy admitted to the neonatal unit of the University Hospital of the West Indies. Journal of tropical pediatrics, 57(1), 40–44. <https://doi.org/10.1093/tropej/fmq040>
6. Shah, G. S., Agrawal, J., Mishra, O. P., & Chalise, S. (2013). Clinico-Biochemical Profile of Neonates with Birth Asphyxia in Eastern Nepal. Journal of Nepal Paediatric Society, 32(3), 206–209.

<https://doi.org/10.3126/jnps.v32i3.7626>

1. Tirupathi, K., Swarnkar, K., & Vagha, J. (2016). Study of risk factors of neonatal thrombocytopenia. International Journal of Contemporary Pediatrics, 4(1), 191–196. <https://doi.org/10.18203/2349-3291.ijcp20164603>
2. Samad, N., Farooq, S., Hafeez, K., Maryam, M., & Rafi, M. A. (2016). Analysis of Consequences of Birth Asphyxia in Infants: A Regional Study in Southern Punjab, Pakistan. Journal of the College of Physicians and Surgeons--Pakistan : JCPSP, 26(12), 950–953.