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Original Research Article

Short-Term Outcome Among Full-Term Neonates with Moderate/Severe Hypoxic-Ischemic Encephalopathy Admitted in Neonatal Intensive Care Unit in A Tertiary Care Hospital in Rawalpindi

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Abstract: *Hypoxic-ischemic encephalopathy (HIE) is a major contributor to neonatal morbidity and mortality, particularly in low- and middle-income countries.* ***Objective:*** *To determine the short-term clinical outcomes among full-term neonates with moderate to severe HIE admitted to the Neonatal Intensive Care Unit (NICU) of a tertiary care hospital.* ***Methods:*** *This cross-sectional study was conducted over six months from October 2024 to March 2025. at the Department of Paediatrics and Child Health, Benazir Bhutto Hospital, Rawalpindi. A total of 155 full-term neonates diagnosed with moderate or severe HIE were enrolled using convenience sampling. Data were collected through clinical assessments and medical records using a structured proforma.* ***Results:*** *Among 155 neonates, 57.4% had moderate HIE and 42.6% had severe HIE. Overall mortality was 14.2%, significantly higher in severe HIE cases (27.3%) compared to moderate (4.5%) (p<0.001). Mechanical ventilation was required in 38.1% of neonates, more frequently in severe HIE (62.1%) than moderate (20.2%) (p<0.001). Seizures occurred in 29.7% of cases, significantly higher in the severe group (48.5%) versus moderate (15.7%) (p<0.001). PPV was needed in 72.3% of cases, with no significant difference between groups. Apgar score ≤4 and birth weight <2.5 kg were associated with significantly poorer outcomes.* ***Conclusion:*** *It is concluded that severity of HIE is directly associated with adverse short-term outcomes, including mortality, mechanical ventilation, and seizure occurrence. Early identification of high-risk neonates through Apgar scores and birth weight assessment, alongside appropriate NICU support, is essential for improving neonatal prognosis in resource-limited settings.*

Keywords: Hypoxic-Ischemic Encephalopathy, Neonates, Mortality, Seizures, Mechanical Ventilation, NICU, Outcomes

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Introduction

Hypoxic-ischemic encephalopathy (HIE) is the primary cause of death and neuro disability in newborns affecting an estimated 1.5–2.0/1000 births (1). The etiology of neonatal encephalopathy (NE) disorder includes several conditions, e.g., hypoxia, congenital malformation, neurological/or metabolic causes, trauma, and infection. Antepartum or intrapartum hypoxic-ischemic events, e.g., perinatal asphyxia or birth asphyxia, refer to an insult accompanied by decreased oxygen delivery to the fetal brain before or during birth (2). When hypoxia is the cause of neonatal encephalopathy (NE) and is followed by encephalopathy signs during the first few hours after birth, a clinical syndrome known as hypoxic-ischemic encephalopathy (HIE) has been described, which is a subgroup of NE (3). Variables related to HIE short-term outcomes include HIE severity, mortality, requirement for positive pressure ventilation at birth, mechanical ventilation, and seizure for moderate and severe (clinically significant HIE); moreover, on the 7th day of admission, the lack of nutritive suckling reflex and need for respiratory support of any form: supplemental oxygen and non-invasive or invasive respiratory support. Seizure load in HIE is associated with more severe brain damage and worse neurodevelopmental outcomes, and this may be independent of HIE severity (4,5). Additionally, studies have shown that TH for HIE lowers and lessens the overall burden of seizures, leading some to believe that seizures worsen the underlying brain damage and are perhaps one of the processes by which TH protects the brain (6). Parents of babies with HIE-related seizures experience higher mental health issues, including feelings of worry and sadness (7). Hypoxic ischemic encephalopathy (HIE) is a leading cause of death and neurologic morbidity in term newborns (8). Neonatal mortality accounts for up to 44% of under-five mortality globally, with 99% occurring in poor and middle-income countries (9). Intrapartum hypoxia and subsequent Hypoxic Ischemic Encephalopathy (HIE) are prevalent causes of potentially preventable infant brain damage and death (10). Birth asphyxia and its sequelae are the third most prevalent cause of infant death, accounting for 26.2% of all cases (11). Hypoxic-ischemic encephalopathy (HIE) is a serious condition that can occur in newborns, resulting from oxygen deprivation and reduced blood flow to the brain. The severity of HIE is typically classified into three stages: mild, moderate, and severe, with the outcomes varying accordingly. The incidence of mortality and the requirement for interventions like positive pressure ventilation (PPV), mechanical ventilation, and the occurrence of seizures in moderate and severe HIE varies as follows: the mortality rate for moderate/severe HIE is 11.3%. Neonates with moderate HIE may require PPV initially after birth due to respiratory distress or apnea. In severe cases, neonates often require PPV immediately after birth due to severe respiratory compromise or apnea. The incidence for the requirement of PPV is 70.2%. Seizures are relatively common in moderate HIE, with reported incidence rates ranging from 26.6%. The incidence of the requirement of mechanical ventilation is 36.3% (12). National studies are scarce on HIE. Unfortunately, the prevalence and consequences of HIE are poorly reported in most impoverished countries. Understanding and addressing these factors are crucial in providing the best possible care for neonates with moderate/severe HIE, aiming to optimize short-term outcomes.
To determine the short-term outcome among full-term neonates with moderate/severe hypoxic-ischemic encephalopathy.

Methodology

This cross-sectional study was conducted in the Department of Paediatrics and Child Health, Benazir Bhutto Hospital, Rawalpindi from October

2024 to March 2025. A convenience sampling technique was employed to recruit eligible participants. The sample size was calculated using the WHO sample size calculator, assuming a population proportion of 11.3%, with a 95% confidence level and an absolute precision of 5%. The minimum required sample size was determined to be 155 neonates.

Inclusion Criteria: Term newborns delivered at ≥37 completed weeks of gestation. Full-term neonates diagnosed with moderate or severe HIE admitted to the Neonatal Intensive Care Unit (NICU). **Exclusion Criteria**: Infants with major congenital malformations or insufficient clinical data. Preterm neonates and those with congenital anomalies or other non-HIE-related conditions.

Neonates meeting the inclusion criteria were enrolled upon admission to the NICU. The diagnosis of HIE was confirmed through clinical evaluation and standardized neurological assessments, including Sarnat and Sarnat staging. Medical records were reviewed to extract demographic data, birth history, Apgar scores, and other relevant clinical findings. Prospective monitoring was carried out for each neonate to assess key short-term outcomes, including mortality, requirement for positive pressure ventilation (PPV), mechanical ventilation, and occurrence and management of seizures. Follow-up continued until discharge or up to 28 days of life. All findings were documented using a structured proforma. To minimize confounding and selection bias, strict adherence to the exclusion criteria was ensured.

Data were analyzed using SPSS version 27. Descriptive statistics including means, medians, and standard deviations were calculated for continuous variables such as birth weight, gestational age, and Apgar scores. Frequencies and percentages were used for categorical variables such as HIE severity and clinical outcomes (mortality, PPV, mechanical ventilation, seizures). Effect modifiers such as age, gender, birth weight, and gestational age were assessed using post-stratified chi-square tests. A p-value ≤ 0.05 was considered statistically significant.

Results

Data were collected from 155 patients, with a mean gestational age of 38.5 ± 1.2 weeks and an average birth weight of 2.95 ± 0.48 kg. The majority were male (59.4%), while females accounted for 40.6% of the sample. The mean Apgar score at 5 minutes was relatively low at 4.3 ± 1.6, reflecting compromised neonatal condition at birth. Based on Sarnat staging, 57.4% of neonates were classified with moderate HIE, whereas 42.6% had severe HIE, indicating a substantial proportion of high-risk cases.

Table 1: Demographic and Clinical Characteristics of the Study Population (n = 155)

Variable	Value
Mean gestational age	38.5 ± 1.2 weeks
Mean birth weight	2.95 ± 0.48 kg
Male gender	92 (59.4%)
Female gender	63 (40.6%)
Mean Apgar score (5 min)	4.3 ± 1.6
Moderate HIE	89 (57.4%)
Severe HIE	66 (42.6%)

Mortality rates were nearly identical, with 14.1% in males and 14.3% in females (*p = 0.97*). The need for positive pressure ventilation (PPV) at birth was also similar—72.8% in males and 71.4% in females (*p = 0.86*). Mechanical ventilation was required in 39.1% of male neonates and 36.5% of females (*p = 0.74*), while seizures occurred in 31.5% of males and 27.0% of females (*p = 0.54*).

Table 2: Stratified Analysis of Short-Term Outcomes by Gender

Outcome	Male (n=92)	Female (n=63)	p-value
Mortality	13 (14.1%)	9 (14.3%)	0.97
Required PPV at birth	67 (72.8%)	45 (71.4%)	0.86
Required mechanical ventilation	36 (39.1%)	23 (36.5%)	0.74
Experienced seizures during NICU stay	29 (31.5%)	17 (27.0%)	0.54

Overall mortality was 14.2%, with a much higher rate observed in the severe HIE group (27.3%) compared to the moderate group (4.5%) (*p < 0.001*). The need for mechanical ventilation was also significantly greater in severe cases (62.1%) than in moderate cases (20.2%) (*p < 0.001*). Seizure occurrence followed a similar trend, affecting 48.5% of those with severe HIE versus 15.7% in moderate cases (*p < 0.001*). While the requirement for positive pressure ventilation (PPV) was high across both groups, the difference was not statistically significant (*p = 0.08*).

Table 3: Short-Term Clinical Outcomes Among Full-Term Neonates with Moderate and Severe HIE (n = 155)

Outcome	Total (n=155)	Moderate HIE (n=89)	Severe HIE (n=66)	p-value
Mortality	22 (14.2%)	4 (4.5%)	18 (27.3%)	<0.001
Required PPV at birth	112 (72.3%)	60 (67.4%)	52 (78.8%)	0.08
Required mechanical ventilation	59 (38.1%)	18 (20.2%)	41 (62.1%)	<0.001
Experienced seizures during NICU stay	46 (29.7%)	14 (15.7%)	32 (48.5%)	<0.001

Neonates weighing less than 2.5 kg had a notably higher mortality rate (23.9%) compared to those with a birth weight ≥ 2.5 kg (10.1%), with the difference being statistically significant (*p = 0.03*). Similarly, mechanical ventilation was required in 54.3% of low birth weight neonates versus 31.2% of those with normal birth weight (*p = 0.008*), and seizures were more frequent in the low birth weight group (41.3% vs. 24.8%, *p = 0.04*). Although the need for positive pressure ventilation was higher among low birth weight infants (80.4%), this did not reach statistical significance (*p = 0.14*).

Table 4: Short-Term Outcomes Stratified by Birth Weight

Outcome	< 2.5 kg (n=46)	≥ 2.5 kg (n=109)	p-value
Mortality	11 (23.9%)	11 (10.1%)	0.03
Required PPV at birth	37 (80.4%)	75 (68.8%)	0.14
Required mechanical ventilation	25 (54.3%)	34 (31.2%)	0.008
Experienced seizures during NICU stay	19 (41.3%)	27 (24.8%)	0.04

Discussion

This study evaluated the short-term outcomes of full-term neonates diagnosed with moderate to severe hypoxic-ischemic encephalopathy (HIE) admitted to a tertiary NICU. The findings underscore the significant burden of early morbidity and mortality associated with HIE, particularly in neonates classified as having severe disease (13). Mortality in this cohort was 14.2%, aligning with previously reported rates in LMICs, where therapeutic hypothermia (TH) and specialized neurocritical care may be inconsistently available (14). As expected, the mortality was significantly higher among neonates with severe HIE (27.3%) compared to those with moderate HIE (4.5%) ($p < 0.001$), highlighting the prognostic value of Sarnat staging at admission. The requirement for positive pressure ventilation (PPV) at birth was high (72.3%), with no statistically significant difference between the moderate and severe HIE groups ($p = 0.08$), suggesting that while PPV is a common initial intervention, its need alone may not be a specific predictor of outcome severity (15). In contrast, the need for mechanical ventilation was significantly higher in severe HIE cases (62.1%) compared to moderate cases (20.2%) ($p < 0.001$), emphasizing the extent of respiratory failure and central nervous system depression in more advanced disease. Seizures were observed in 29.7% of neonates, with a significantly higher incidence among those with severe HIE (48.5%) than moderate HIE (15.7%) ($p < 0.001$). This supports the growing evidence that seizure burden correlates with both HIE severity and long-term neurodevelopmental risk (16). Studies such as those by Aker et al. (2020) have demonstrated that seizure frequency may independently predict poor outcomes, further justifying its inclusion as a key monitoring parameter. Stratified analyses revealed no significant gender-based differences in outcomes, echoing previous findings that biological sex may not substantially influence HIE prognosis (17). However, lower Apgar scores (≤4 at 5 minutes) and low birth weight (<2.5 kg) were strongly associated with worse outcomes, including higher rates of mortality, seizures, and need for mechanical ventilation. These findings suggest that these early life metrics are valuable adjuncts for risk stratification and resource prioritization in the NICU (18). The present findings align with previous multicenter studies such as HELIX, which highlighted not only the severity-dependent nature of HIE outcomes but also the resource gaps in low-income countries contributing to adverse prognoses. Despite improvements in neonatal care, the high burden of preventable complications underscores the need for widespread implementation of neonatal resuscitation protocols, early neurological assessment, and access to therapeutic hypothermia where feasible.

Conclusion

It is concluded that hypoxic-ischemic encephalopathy (HIE) in full-term neonates, particularly in its moderate and severe forms, is associated with significant short-term morbidity and mortality. The severity of HIE strongly correlates with adverse outcomes such as increased mortality, greater need for mechanical ventilation, and higher incidence of seizures. Neonates with severe HIE demonstrated markedly poorer outcomes compared to those with moderate HIE. Low Apgar scores and low birth weight were found to be independent predictors of worse clinical outcomes, emphasizing their utility in early risk stratification. These findings highlight the urgent need for timely identification, effective resuscitation, and comprehensive neonatal intensive care support.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-BBRR-082-24)

Consent for publication

Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

HZM (Resident)
Review of Literature, Data entry, Data analysis, and drafting article. Manuscript drafting, Study Design,
MM (Research Associate)
Conception of Study, Development of Research Methodology Design
KS (Resident)
Study Design, manuscript review, critical input.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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