



Delayed development in newborns with hypoxic ischemic encephalopathy stage-2.

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ABSTRACT... Objective: To determine the frequency of delayed development in newborns with hypoxic ischemic encephalopathy (HIE) stage 2 presenting to Nishtar Hospital Multan. **Study Design:** Descriptive Case Series. **Setting:** Department of Pediatrics, The Children's Hospital and The Institute of Child Health, Multan. **Period:** August 2019 to February 2020. **Material & Methods:** Children with birth asphyxia (HIE stage 2) admitted in NICU were registered. The basic demographic information including name, age, sex, address and telephone number was recorded in a specifically designed proforma. Children were followed up at 3 months and developmental milestones were recorded in the proforma. **Results:** Mean age of newborns was 17.15 ± 15.95 hours and mean weight was 2.88 ± 0.28 kg. There were 55 male newborns (67.9%) and 26 female newborn babies (32.1%). Male to female ratio was 2.1:1. Frequency of delayed development of the beabies in our study was 34.6% while 53 babies (65.4%) had normal development assessed through milestones achieved at 3 months. Milestones achieved at 3 months were; head control in 54 newborns (66.7%), lifts head and chest above couch in prone position in 50 newborns (61.7%), head above line of body on ventral suspension in 55 newborns (67.9%), follows light through an arc of 180 degrees/defensive blink in 21 newborns (25.9%), turns to nearby voice in 38 newborns (46.9%), happy response to mother's face when feeding in 63 newborns (77.8%). **Conclusion:** Frequency of delayed development of the newborns with stage-2 HIE in our study was high.

Key words: Birth Asphyxia, Delayed Development, Hypoxic Ischemic Encephalopathy.

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INTRODUCTION

The term "birth asphyxia" has been used for newborns who are born flat with delayed onset of breathing, bradycardia, impaired muscle tone as well as reflexes while fetal hypoxia remains the most likely cause.¹ Last few decades have seen major improvements in fetal and neonatal care, yet, perinatal asphyxia or hypoxic ischemic encephalopathy (HIE) is still a serious health issue. With prematurity and infections, HIE is noted to be one of the leading causes of neonatal mortality.^{2,3}

HIE is described in terms of clinical as well as laboratory findings of acute or sub acute brain injury because of asphyxia that progress into hypoxia and acidosis. The exact underlying cause and timing of brain injury is not always clear. Sub-optimal intrapartum obstetric care is labelled as

one of the most important risk factor for HIE.^{4,5}

In comparison to developed countries, developing countries report much higher figures of incidence of HIE whereas exact numbers are not available. Worldwide, HIE related neonatal mortality varies from 0.7-1.2 million per year while as many survive with long term neurological sequelae.⁶ It is estimated that 15 to 20% of newborns with HIE die in between neonatal period whereas 30% of the survivors suffer from neurodevelopmental abnormalities.⁷ In Pakistan, HIE is considered to be one of the most frequent reasons for neonatal admissions.⁸ Local data about HIE related morbidity reveals that most causes are preventable.⁹

HIE related neural damage affecting cognitive development among infants impair the capacity

to learn, talk, read, calculate, memorize, conceptualise, organize, pay attention, interact socially and behave appropriately. Other problems like poor coordination, scholastic backwardness, certain learning disability, very short attention span, behavioural issue or hyperactivity might appear later. This study was planned to determine the frequency of delayed development in newborns with hypoxic ischemic encephalopathy stage 2.

MATERIAL & METHODS

This descriptive case series study was carried out in Department of Pediatrics, The Children's Hospital and The Institute of Child Health, Multan from August 2019 to February 2020.

Sample size was determined according to formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

where; confidence level=95%, $p=30\%$,⁷ and margin of error (d)=0.10; so the sample size is $n=81$ patients.

Non probability purposive sampling technique was used.

Inclusion Criteria

1. Full-term neonates by history \geq 37 wks of gestation confirmed through record (clinically assessed by the presence of 1 crease on sole, nipple size more than 5mm, ear margin folded completely)
2. History of delayed cry for more than 5 minutes.
3. Hypoxic ischemic encephalopathy stage 2

Exclusion Criteria

1. Stage 1 & 3 encephalopathy.
2. Congenital brain malformations (e.g., hydrocephalus).
3. LBW (<2.5 kg) & preterm babies (<37 wks of gestation)
4. Baby of eclamptic mother delivered under general anesthesia.
5. Multiple congenital anomalies (e.g., down syndrome, turner syndrome, Edward syndrome, patau syndrome)

Birth Asphyxia was defined as delayed cry >5 minutes at birth (by a note from duty doctor for delayed cry received from labour room).

Hypoxic ischemic Encephalopathy Stage 2 was defined as when 2 or more of the following are present: 1.Hypotonia ----sluggish passive limb movements assessed by the clinician. 2.Seizures---tonic (increased resistance on examination)/clonic (jerky) body movements. 3.Miosis----pupil size less than 3mm. 4.Absent Moro reflex: Absence of any one or more component will be labeled as absent moro reflex. a. Spreading out of arm b. Unspreading the arm c. crying, along with history of delayed cry > 5 min.

Delayed development was defined if milestones (3 or more out of 6) were not achieved at 3 months of age. Developmental Milestones appropriate for 3 months of age are: 1. Head control 2. Lifts head and chest above couch in prone position 3. Head well above the line of body on ventral suspension 4. Follows light through an arc of 180 degrees/defensive blink 5. Turns to nearby voice 6. Happy response to mother's face when feeding

Permission from ethical review committee was taken. Informed consent was taken from the parents for inclusion in the study. The basic demographic information including name, age, sex, address and telephone number was recorded in a specifically designed proforma. Children were followed up at 3 months and developmental milestones were recorded in the proforma. Assessment was done under the supervision of consultant (5 years post graduate experience). The child was labeled as having delayed development if 3 or more out of 6 were absent at 3 months of age. This information was noted on the specially designed proforma.

Data were entered in the computer and analyzed by using statistical software SPSS-20. Mean and standard deviation was calculated for age and weight. Frequencies and percentages were calculated for gender and developmental delay. Stratification was done with regard to age, weight and gender of child to see the effects on outcome. Chi-square test was applied to see the difference.

P-value ≤ 0.05 was taken as significant.

RESULTS

Present study was conducted on 81 newborns presenting with hypoxic ischemic encephalopathy stage 2 within first two days of life. Mean age of newborns was 17.15 ± 15.95 hours and mean weight was 2.88 ± 0.28 kg.

When age was rounded off to nearest hour, there were 60 newborns (74.1%) between 1–24 hours and 21 newborns (25.9%) between 25–48 hours. There were 55 male newborns (67.9%) and 26 female newborn babies (32.1%) as shown in Table-VIII. Male to female ratio was 2.1:1.

Milestones achieved at 3 months were; head control in 54 newborns (66.7%), lifts head and chest above couch in prone position in 50 newborns (61.7%), head above line of body on ventral suspension in 55 newborns (67.9%), follows light through an arc of 180 degrees/defensive blink in 21 newborns (25.9%), turns to nearby voice in 38 newborns (46.9%), happy response to mother's face when feeding in 63 newborns (77.8%) as shown in Table-I.

Frequency of delayed development of the babies in our study was 34.6% while 53 babies (65.4%)

had normal development assessed through milestones achieved at 3 months.

Table-II shows that out of the total 60 newborns of 1–24 hours, 25 newborns had delayed development while 35 had not. Out of 21 newborns of 25–48 hours, 3 newborns had delayed development while 18 had not. Age at presentation had no significant effect on occurrence of delayed development ($p=0.712$).

Table-II shows that out of the total 55 male newborns, 20 newborns had delayed development while 35 had not. Out of total 26 female newborn babies 8 had delayed development while 18 had not. There was no significant difference between male and female newborns regarding delayed development ($p=0.621$).

Table-II shows that out of the total 55 newborns having weight 2.5–2.9 kg, 18 had delayed development while 37 had not. Out of the total 20 newborns having weight 3.0–3.4 kg, 9 had delayed development while 11 had not, and out of total 6 newborns having weight 3.5–3.9 kg, 1 had delayed development and 5 had not. There was no significant difference among different weight groups regarding delayed development ($p=0.722$).

Milestone Achieved	No. of Newborns	Percentage (%)
Head control	54	66.7
Lifts head and chest above couch in prone position	50	61.7
Head above line of body on ventral suspension	55	67.9
Follows light through an arc of 180 degrees/defensive blink	21	25.9
Turns to nearby voice	38	46.9
Happy response to mother's face when feeding	63	77.8

Table-I. Milestone achieved at three months in newborns with hypoxic ischemic encephalopathy (n=81)

Note: Milestones are overlapping because most of newborns achieved > 1 milestone.

Study Variables	Delayed Development		P-Value
	Yes (n=28)	No (n=53)	
Age (in hours)	1 — 24	25 (89.3%)	0.712
	25 — 48	3 (10.7%)	
Gender	Male	20 (71.4%)	0.621
	Female	8 (28.6%)	
Weight (in kg)	2.5 — 2.9	18 (64.3%)	0.722
	3.0 — 3.4	9 (32.1%)	
	3.5 — 3.9	1 (3.4%)	

Table-II. Age distribution of newborns with hypoxic ischemic encephalopathy stage-2 in relation to outcome (n=81)

DISCUSSION

Outcomes of the survivors of mild or severe HIE are predictable, yet, outcome of moderate (stage-2) HIE is uncertain but these children are more prone to have neurological disabilities as well as academic failure.^{10,11} Development delay is a condition where infant or children is unable to attain developmental milestones with reference to 1 or more major streams like motor, perceptual, speech, cognition and behavior.¹²

In the present study, 34.6% of the study participants having stage-2 HIE were found to have developmental delays. A local study from Lahore by Malik TS followed up and assessed 150 children of birth asphyxia till 6 months of age for neurodevelopmental status.¹³ The researchers concluded that stages of HIE are strongly linked with outcomes in the asphyxiated neonates. Behera A et al from India¹⁴ noted 100% of the infants with stage-3 HIE to have neurodevelopmental abnormalities while very similar to the present study, 34.4% of the neonates with stage-2 HIE were having neurodevelopmental abnormalities. Another recent study from India evaluating neurodevelopmental outcomes in preterm infants with HIE, noted 100% of the study participants to have morbidity with moderate disability while all stage-3 HIE infants had neurological abnormalities.¹⁵ Three to 5 months of age seems like an ideal time to start intervention aiming improved long term outcomes.

Memon S et al evaluated early neurological outcomes (72 hours) among newborns with clinical signs of HIE.¹⁶ They noted 53.3% of the neonates to be normal while 31.6% had neurological abnormalities and 15% died. Qureshi AM et al¹⁷ noted 55.1% of the neonates with stage-2 HIE to have fits, again depicting major chunk of the children with stage-2 HIE to have neurological abnormalities. Samatha S from India found 37.8% of the neonates to have neurodevelopmental delay at 1 year period.¹⁸

Allan WC¹⁹ found 26% of the infants with moderate HIE to have worst or severe adverse outcomes. Bohr L et al²⁰ in their literature review spanning 30 years, found neurodevelopmental outcomes

to be closely related to severity of HIE in the newborns.

Birth asphyxia is termed preventable considering its impact on morbidity and mortality in the newborns. Period of labour and delivery along with prenatal and intranatal factors plays vital roles in the development of birth asphyxia. Improvement in antenatal screening and delivery by trained professional can certainly prevent large number of newborns developing birth asphyxia.^{21,22}

Our study had few limitations as well. As it was a hospital based study, sample size was small. The results of this study cannot be generalized as follow up was comparatively shorter (3 months) which is quite early to detect neurodevelopmental delays.

CONCLUSION

Frequency of delayed development of the babies in our study with stage-2 HIE was high. There was no association of age, gender and weight of newborns with regards to delayed development).

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

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Maria Saleem	Methodology, Literature review.	
3	Asim Khurshid	Study concept, Supervision, Proof reading.	