

The Hypoxic Ischaemic Encephalopathy Score in Predicting Neurodevelopmental Outcomes Among Infants with Birth Asphyxia at the Muhimbili National Hospital, Dar-es-Salaam, Tanzania*

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Summary

Hypoxic Ischemic Encephalopathy (HIE) score may be used to predict neurodevelopment outcome in infants with birth asphyxia. A total of 140 infants who had a 5 min Apgar score of <7 at birth had detailed motor and neurodevelopment assessment. Outcome measures were grouped as normal or abnormal with morbidity (convulsions, abnormal muscle tone and delayed development) or death. The positive predictive value (PPV) for mortality was 42.3% for moderate HIE and 93.8% for severe HIE. For severe HIE the PPV was 100%. Thirteen infants had delayed development, the score had PPV of 63.6% for moderate HIE and 100% for severe HIE. The best correlation with outcome was the peak score of 15 or higher had a PPV of 100%. Specificity was found to be 100% and sensitivity of 14%. The HIE scoring system is a useful predictor of neurodevelopment outcome at 6 months of age in a resource poor setting.

Key words: hypoxic ischemic encephalopathy, scoring system, neonates.

Introduction

Birth asphyxia has been defined as a delay in establishing spontaneous respiration upon delivery of a newborn [1]. Its severity has been related to the degree of depression of the Apgar score [2]. It has also been associated with the presence of electroencephalographic abnormalities, cord blood acidosis and by the occurrence of clinical signs in the infant with post-asphyxial ischaemic injury [3, 4].

Birth Asphyxia is a common problem in developing countries. At the Muhimbili National Hospital,

in Dar-es-Salaam, Tanzania, it accounts for about 10% of all deliveries and 25% of neonatal admissions annually [5, 6].

Several new technologies have become available to determine cerebral damage during perinatal period and predict long-term neurological outcome. These include computer (CT) scanning, magnetic resonance imaging (MRI), cerebral function monitoring, cranial ultrasound scanning and Doppler ultrasound of the middle cerebral artery [20]. These modalities are however not readily available in many neonatal units in developing countries.

The Hypoxic Ischemic Encephalopathy (HIE) score is a clinical tool comprising of a set of clinical signs associated with central nervous system (CNS) dysfunction. It is used to assess status of a child following birth asphyxia. There are various HIE scoring systems [7–10].

In scoring system described below, a score of 0 is normal and a maximum score is 22 which signifies the worst possible status of HIE. Infants scoring 1–10 are considered to have mild HIE, 11–14 have moderate HIE and 15–22 are considered to have severe HIE. This is the modified Sarnat scoring system [7].

The HIE scoring system is very simple and does not need special training. For clinicians working in

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TABLE 1
The HIE scoring chart

Sign	Score			
	0	1	2	3
Tone	Normal	Hyper	Hypo	Flaccid
LOC	Normal	Hyper alert	Lethargic	
Fits	None	Infrequent less than thrice per day	Frequent less than thrice per day	
Posture	Normal	Fisting/cycling	Strong distal flexion	Decerebrate
Moro	Normal/partial	Absent		
Grasp	Normal	Poor	Absent	
Sucking reflex	Normal	Poor	Absent/bites	
Respiration	Normal	Hyperventilation	Brief apnoea	IPPV (apnoea)
Fontanel	Normal	Not full tense	Tense	
Total				

LOC, Level of Consciousness; IPPV, Intermittent Positive Pressure Ventilation.

areas where sophisticated technology is unavailable, this scoring system will be very useful.

This study is therefore assessing the HIE score in our set-up to devise a means of predicting neurodevelopment outcome in babies with birth asphyxia.

Objective

To assess whether HIE scoring is predictive of neurological outcome among infants with birth Asphyxia at 6 months of age.

Methodology

This prospective cohort study was conducted at the Muhimbili National Hospital (MNH) neonatal unit and the high-risk postnatal clinic. MNH is the national referral hospital located in the city of Dar-es-salaam and it is the teaching hospital for the Muhimbili University College of Health Sciences (MUCHS). MNH was selected because it is the only public hospital with a neonatal unit. It has a capacity of 70 beds and admits newborns from the labor ward and referrals from district hospitals as well as from some private hospitals. It has a high-risk postnatal clinic for neonates who were admitted in the neonatal ward for various reasons.

Inclusion criteria

- Full-term babies with low-Apgar score (i.e. a 5min score of ≤ 7) or post-asphyxial symptoms admitted within 24 h of delivery.
- Sick infants with symptoms and signs of HIE (respiratory arrest, apnea, posturing, movement disorder, impaired sucking, swallowing and feeding).

Exclusion criteria

- All infants with obvious congenital malformations.
- Preterm babies.

Sample size estimation

The sample size (N) was calculated using the following formula

$$N = Z_{\alpha}^2 p (100 - p) / \varepsilon^2, \text{ where}$$

- Z_{α} is the standardized normal deviate corresponding to a significant level α ,
- p is the expected prevalence of birth asphyxia and
- ε = margin or bound of error on p .

In this study, the level of significance, α was taken to be 0.05 giving $\alpha=1.96$.

The expected prevalence of birth asphyxia was assumed to be 20%, with the margin of error, ε of 6%. Hence the minimum sample size of 116 babies was obtained.

However on adding 20% loss to follow-up, the sample size was estimated to be 140.

Sampling technique and duration

Simple random selection was done on neonates admitted to the neonatal unit, until the sample size was reached. This study was conducted for 9 months between May 2002 and February 2003. All mothers were consented prior to enrollment.

Data collection techniques and tools

Weight was taken by a seca beam balance to the nearest 10g. The occipital–frontal circumference (OFC) was measured using a non-stretchable measuring tape from the occiput passing just above the eyebrow to the nearest 0.1 cm.

HIE scoring chart

- The chart was filled in detail for seven consecutive days by the investigator (Table 1).
- Infants were classified into according to scoring (an adaptation of the Sarnat and Sarnat categories [20]) whereby neonates scoring 1–10

were classified to have mild HIE, those scoring 11–14 had moderate HIE and those scoring 15–22 were classified to have severe HIE.

- The highest score attained on any of the 7 days (or any day before discharge or death) was used to assess severity of birth asphyxia.

Management was done according to standard protocols of the unit.

- Infants were seen at the high-risk clinic once every month as a routine follow-up for all infants with birth asphyxia. At the clinic a detailed developmental history was taken and mothers were asked about presence of convulsions in their infants.
- Infants who were found to have convulsions were treated accordingly.
- At the age of 6 months Ameal-Tison method of assessment of motor system in under fives was done.
- Assessment of cerebral palsy was performed using the simplified Levene criteria. This included assessment of posture, oropharyngeal reflexes, presence or absence of strabismus, abnormalities in muscle tone, evolutionary reflexes and deep tendon reflexes. A tentative diagnosis of cerebral palsy was reached if the infant scored 4/6 major motor criteria.
- A modified neurodevelopmental assessment using the Griffith mental developmental assessment charts was used to assess the neurodevelopment. This included assessment of locomotor, personal social, hearing and speech, eye and hand co-ordination and performance. Developmental age was recorded in months.
- Abnormal outcome was considered if the infant had abnormal muscle tone, convulsions, developmental age <4 months, cerebral palsy or died. A developmental age of ≥ 5 months (at a chronological age of 6 months) was considered to be normal.

Statistical analysis

Data were analyzed using the EPI INFO 6 statistical program. Assessing the value of the scoring system was done using positive predictive value (PPV), specificity and sensitivity.

The χ^2 -test was generally used to make comparisons, and where the appropriate Fishers exact test was used.

Relative risk was used to compare within groups. A p -value of <0.05 was considered to yield significant differences or associations between groups or variables being compared.

In assessing the correlation between HIE score and OFC at 6 months a scatter plot was used and coefficient of correlation obtained.

Ethical considerations

Ethical clearance was obtained from the MUCHS Higher Degree Research and Publications Committee.

Babies found to have neurodevelopmental disability at discharge from the study were continue to be followed up at the high-risk postnatal clinic. They were later referred to the cerebral palsy clinic of the hospital.

Study limitation

A 20% increase in sample size was included to cater for the envisaged loss to follow-up. We were unable to trace them to their residences due to the limited resources.

Results

A total of 1164 babies were admitted to the neonatal ward during the study period (6 weeks). Of these, 182 (15.6%) had birth asphyxia (defined by a 5 min Apgar score of <7). Of the 140 infants who met the inclusion criteria, 87 (62%) were males and 53 (38%) were females.

Mean birth weight was 2.98 kg (SD \pm 0.47)

Mean OFC at birth was 35.2 cm (SD \pm 2.25)

Of the 140 neonates recruited, 28 neonates died during the neonatal period. Of the 112 who survived, 82 were assessed at 6 months of age. Thirty neonates (21%) were lost to follow-up, the reasons for which are not known. The association between risk of dying and the HIE score is indicated in Table 2.

The association of HIE score and neonatal convulsions is indicated in Table 3.

The association between the HIE score and subsequent convulsions, muscle tone, developmental delay and overall outcome at 6 months have been indicated in Table 4.

In total, 58 (41.7%) of the neonates had convulsions during the early neonatal period. Neonates who scored >10 had a risk of developing convulsions. The risk of having convulsions was 3 times higher among infants with moderate HIE relative to those with mild HIE. Among infants with severe HIE, the risk was more than twice compared to infants with mild HIE. The associations were found to be statistically significant ($p < 0.001$ by Fisher exact test). The 95% confidence interval (CI) estimates of the respective risk ratios (RR) are as shown in the Table 3.

Infants with mild HIE were taken as standard in the calculation of sensitivity, specificity, positive and negative predictive values.

The scoring system was found to be very specific (with specificity ranging from 85.1% to 100%) in predicting abnormal outcome but the sensitivity was found to be low in all the categories of outcome except for neonatal mortality (88.3%).

TABLE 2
Association between HIE Score and the risk of dying during the early neonatal period

HIES	Died n (%)	Survived n (%)	Total	RR (95% CI)	P-value
1-10	2 (2.0)	96 (98.0)	98	1	
11-14	11 (44.0)	15 (56.0)	26	20 (4.9, 87.8)	<0.001*
15+	15 (93.8)	1 (6.3)	16	46 (11.6, 82.0)	<0.001*
Total	28 (20)	112 (80)	140		

Score of 15 and above had a sensitivity of 88.3%, specificity of 99% and a PPV of 93.8% for mortality.

*Fisher exact test.

TABLE 3
Association between HIES and neonatal convulsions

HIES	Neonatal Present n (%)	Convulsions Absent n (%)	Total	RR (95%CI)	P
1-10	25 (25.5)	73 (74.5)	98	1	
11-14	22 (88.8)	4 (12.0)	26	3.3 (2.8, 4.8)	<0.001*
15+	11 (68.8)	5 (31.3)	16	2.7 (1.7, 4.3)	<0.001
Total	58 (41.7)	81 (58.3)	140		

Score of 15 and above had a sensitivity of 30.6%, specificity of 93.6% and a PPV of 68.8% for convulsions.

*Fisher Exact test

TABLE 4
Association between HIES and convulsions, muscle tone, developmental delay, cerebral palsy and overall outcome by 6 months of age

Convulsions	Present n (%)	Absent n (%)	Total	RR (95%CI)	p
1-10	5 (7.1)	65 (92.9)	70	1	
11-14	7 (63.6)	4 (36.4)	11	8.9(3.4, 23.2)	<0.001*
15+	1 (100)	0	1	14 (6.0, 32.6)	0.08**
Total	13 (16.7)	69 (83.3)	82		
Muscle tone					
	Normal	Abnormal			
1-10	57 (81.4)	13 (18.3)	70	1	
11-14	3 (27.5)	8 (72.7)	11	3.9 (2.1, 7.2)	<0.001*
15+	1 (100)	0	1	-	
Total	61 (74)	21 (26)	82		
Developmental delay	Delayed	Normal			
1-10	5 (7.7)	65 (92.3)	70	1	-
11-14	7 (63.6)	4 (36.4)	11	8.9 (3.4, 23.2)	<0.001*
15+	1 (100)	0	1	14 (6.0, 32.6)	0.08**
Total	13 (16.7)	64 (83.3)	82		
Cerebral palsy	Present	Absent			
1-10	2 (2.9)	68 (97.1)	70	1	-
11-14	4 (36.4)	7 (63.6)	11	12 (2.6, 61.4)	0.002*
15+	1 (100)	0	1	35 (8.9, 130)	0.04**
Total	7 (8.5)	75 (91.5)	82		
Overall outcome	Good	Poor			
0-10	57 (81.4)	13 (18.6)	70	1	-
11-14	1 (9.1)	10 (90.9)	11	4.9 (2.9, 8.8)	<0.001*
15+	0	1 (100)	1	5.4 (3.3, 8.8)	=0.19**
Total	58 (70.7)	24 (29.3)	82		

*Fisher exact test used.

**Statistically not significant, since the number is very small. The explanation is biological plausible.

Discussion

HIE is a term commonly used to describe the neurological syndromes that occur following perinatal asphyxia and was originally described by Amiel-Tison in 1969 [11].

Early diagnosis of cerebral palsy which results from HIE is difficult except for the severe cases. It is important to predict the neurological outcome early so that necessary rehabilitative measures can be instituted. In many cases, however, early diagnosis is extremely difficult, and on occasion, impossible [12].

HIE scoring systems have been used in various studies. Portman *et al.* [12] developed a score that predicts early morbidity and mortality. While others

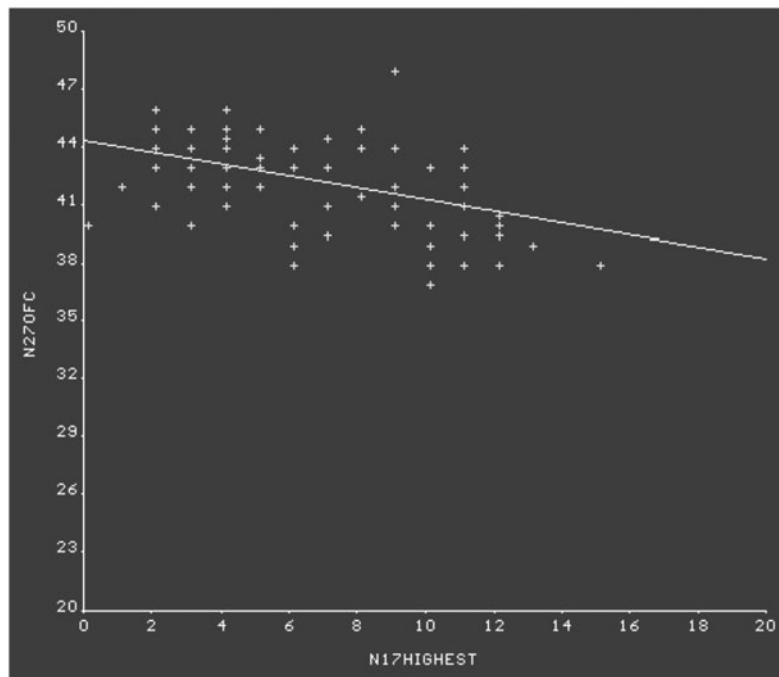


FIG. 1. Association between HIE score and head circumference at 6 months. Figure 1 shows that the head circumference decreases with increasing HIE score. There is an inverse correlation between HIE score and head circumference at 6 months of age. The coefficient of correlation was $r = 0.78$ (neg).

have developed a score that has been related with long-term outcome [9]. The most widely used classification of HIE is that of Sarnat and Sarnat [7], and utilizes the EEG and other laboratory parameters that may not be available in a neonatal unit in the developing country. Our study use the modified Sarnat scoring which has been validated by Thompson *et al.* and has more clinical approach, with numeric value, and fewer items [8].

In the present study, we found that the HIE score was highly specific in detecting early neonatal mortality (within 7 days of life) among neonates who had moderate and severe HIE (specificity 86.9% and 99%, respectively). The sensitivity of the scoring system to detect an infant who may die during the early neonatal period was 88.3%. The risk of dying during the neonatal period increased with increasing HIE score. Other studies have shown a similar finding that severely asphyxiated infants have a high mortality within the first 72 h of life [13, 14].

Neonates with moderate HIE in this study also had a high-mortality rate. The reasons for this are not clear, but it may be due to lack of facilities for close monitoring in the neonatal unit at the MNH. Levene *et al.* [15] compared Apgar score and post-asphyxial encephalopathy in predicting adverse outcome, whereby it was demonstrated that infants with

moderate or severe encephalopathy were at a much greater risk of death or severe handicap, the risk increasing with severity of encephalopathy. In a retrospective study of 227 infants by Thornberg *et al.* [16], infants with severe HIE either died or developed neurological damage. Half of the infants with moderate and all infants with mild HIE were reported to be normal at 18 months of age. These findings are similar to the previous studies and this scoring system can be used to predict neurodevelopment outcome [15, 16].

Fifty-eight (41.7%) neonates had convulsions during the first week of life. Convulsions were found in all categories of HIE. In this study, the risk of having convulsions was about 3 times higher in moderate HIE relative to mild HIE, while for severe HIE the risk was 2.7. This lower risk is not biological plausible, and could be due to the over sedation of high-risk neonates, or due to the very small number in statistical analysis for meaningful measure.

A study by Finner *et al.* [17] to assess factors affecting outcome of HIE in term infants found that factors which significantly correlated with outcome included the Sarnat stage and the occurrence of intractable seizures. It was found that there was no association between 1 or 5 min Apgar score, need for ventilation, the EEG, the occurrence of seizures and

the subsequent outcome. This study agrees with the above study that neurodevelopment outcome in neonates who had HIE is associated with the Sarnat staging of encephalopathy and it is speculated that presence of seizures is a risk for neurodevelopment abnormality. In another study, a detailed neurodevelopment follow-up was conducted on 167 infants with a diagnosis of HIE. In that study, neonatal convulsions were associated with an increased number of handicapped children [18]. Thus neonates who had convulsions in this study group are at an increased risk of neurodevelopment disability and they need to be followed up more closely.

At 6 months of age, 82 infants were evaluated for neurodevelopment outcome. Neurodevelopment abnormalities detected during the 6 months follow-up were convulsions, abnormal muscle tone, delayed developmental age and cerebral palsy. Of the 82 infants assessed, 13 (16.7%) had convulsions by 6 months of age. The scoring system had very low sensitivity (16.7% for severe HIE) in detecting neonates that may have convulsions.

However, the scoring system was found to be highly specific (specificity 100% for severe HIE) in detecting neonates who may not have convulsions by 6 months. The PPVs to predict convulsions were found to be 63.6% for moderate HIE and 100% for severe HIE. These figures mean that the score could detect neonates who may have convulsions at 6 months of age with 100% accuracy for severe HIE. Hence, this scoring system can be used to predict infants who may have or not have convulsions as early as 6 months of age.

Sixty percent of those in the moderate post-asphyxial group and all of those in the severe group had delayed development at 6 months. A similar finding was obtained in a study by Thompson *et al.* [8] whereby the HIE was found to be negatively correlated with the general quotient obtained from the Griffiths mental developmental assessments. These findings suggest that HIE correlated with severity of brain damage and therefore with delayed milestones. In our study, we may also speculate that presence of convulsions in an infant who had perinatal asphyxia is a risk factor for delayed development since all the infants who had convulsions also had delayed development.

In this study, the HIE score was found to be highly specific in detecting infants who may have delayed development (specificity 93.8% and 100% for moderate and severe HIE, respectively). However the sensitivity was low (8% and 17% for moderate and severe HIE, respectively). Thus the HIE scoring that was used in this study is highly predictive of delay in development and can be used safely while counseling parent/caretakers of affected neonates.

Twenty-one (26%) out of the 82 of the infants assessed at 6 months of age had abnormal muscle tone. The risk of having abnormal muscle tone

increased with increasing HIE score. One infant with severe HIE had normal muscle tone. This was an unexpected finding because normally there is more neurological damage in severe HIE than in other forms hence more disability is expected. The presence of normal muscle tone in this child cannot be explained. All but one infant with abnormal muscle tone had hypertonia. This reflects that HIE mainly resulted in cerebral lesions in this group of infants [18]. Infants with abnormal tone were referred for physiotherapy to avoid contractures and obtain normal posture. Abnormalities of tone have been shown to be an important predictor of severity of handicap [19]. Toh [20] found that out of 35 infants with post-asphyxial HIE, 23 had severe adverse outcome. Of them, 13 died and, 10 survived with major neurological sequel: 8 had spastic quadriplegia, 1 had spastic quadriplegia and choreoathetosis. The relation of higher incidence of muscle tone abnormalities with corresponding higher HIE scores in this study is in agreement with the studies cited above.

Seven (8.5%) infants were found to have cerebral palsy. The risk of having cerebral palsy was proportional to HIE score. The score was found to have a predictive value of 100% for cerebral palsy.

Although the criteria we used to identify cerebral palsy are most reliable in children who are 1 year and older, nonetheless, at 6 months of age 8.5% of the children had obvious signs of cerebral palsy. It is known that cerebral palsy may not be accurately diagnosed until 3–4 years of age [20]. Thus, it is possible that some infants who were found to be normal during the 6-month assessment may develop cerebral palsy. A small number of infants had only two or three major motor features using the criteria in this study developing cerebral palsy. Among the infants who had cerebral palsy, four were found to be blind and one was deaf and blind. These children were also seen by the ophthalmology and otorhinolaryngology specialists who confirmed the diagnosis and are assisting in management.

A study by Aggarwal *et al.* [21] assessed 40 neonates with clinical signs suggestive of HIE. They found that neonates with Stage 1 encephalopathy (mild HIE) were all normal at 1 year. Twenty-nine had Stage 2 encephalopathy (moderate HIE), 15 were normal, 14 showed delayed development and 4 had cerebral palsy. The neonate with Stage 3 encephalopathy (severe HIE) had hypotonic cerebral palsy with blindness [22]. Thornberg *et al.* [16] studied 292 term infants with Apgar score <7 at 5 min. A total of 0.2 per 1000 live births developed neurological disability related to birth asphyxia. The disabilities were dyskinetic, tetraplegic, spastic diplegic, cerebral palsy and mild neuromotor dysfunction. This study agrees with the previous studies in that the more severe the HIE the worst the neurodevelopmental disability.

In this study, a total of 23 infants had microcephaly (14 boys and 9 girls). HIE score was found to

be negatively correlate with OFC meaning the the higher the HIE score attained the smaller the OFC at 6 months age (Figure 1). Similar findings have been obtained by other researchers. In a study to predict neurological outcome using proton spectroscopy in asphyxiated infants, Roth *et al.* [23] found that the severity of asphyxia was inversely proportional to the velocity of increase in OFC in centimeter per year. A retrospective case control study by Mercuri *et al.* was conducted to establish a relationship between head growth in the first year of life with the pattern of injury by neonatal MRI in infants with HIE. These were related to the neurodevelopmental outcome. It was found that suboptimal head growth predicted abnormal neurodevelopment with a sensitivity of 79% and specificity of 78%, compared with the presence of microcephaly at 1 year of age that had a sensitivity of 65% and specificity of 73% [24].

Thus, children in this study who were found to have microcephaly need close follow-up to as they may be at risk of mental retardation later in life [24].

Conclusions

- The HIE scoring system used in this study was highly predictive of neonatal outcome in terms of morbidity and mortality.
- Neurodevelopmental abnormalities observed at 6 months of age were convulsions, abnormal muscle tone, delayed developmental age and cerebral palsy. These abnormalities were highly correlated to the HIE score.
- HIE score was found to be correlated with OFC at 6 months of age. It was found that the higher the HIE score, the smaller the OFC.

Recommendations

- The HIE scoring system should be used for all infants with birth asphyxia so as to enable the clinician to identify infants that may be at high risk of neurodevelopmental abnormality.
- HIE score can be used as an early tool by clinicians to counsel parents/caretakers on neurodevelopmental outcome of their infants.

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