THE HYPOXIC ISCHAEMIC ENCEPHALOPATHY SCORE IN PREDICTING NEURODEVELOPMENTAL OUTCOME IN INFANTS WITH BIRTH ASPHYXIA AT THE MUHIMBILI NATIONAL HOSPITAL.

By

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A dissertation submitted in partial fulfillment of the Degree of Master of Medicine (Paediatrics and Child Health) of the University of Dar es Salaam.

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March 2003.

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the University of Dar es Salaam a dissertation entitled: *The Hypoxic ischaemic encephalopathy score in predicting neurodevelopmental outcome in infants with birth asphyxia at the Muhimbili National Hospital,* in partial fulfillment of the requirements for the Degree of Master of Medicine (Paediatrics and Child Health).

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DECLARATION

AND

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I, Sekela David Mwakyusa, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature .....

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Many thanks go to my husband Victor for his prayers and support.

DEDICATION

To my parents, whose guidance and support has made me who I am today.

To my daughter Nicole and my son David-James.

To my beloved husband Victor.

ABSTRACT:

Background: Hypoxic ischaemic encephalopathy (HIE) is known to be associated with significant morbidity and mortality in the full term infant. It is evident from some studies that HIE in the long-term produces a spectrum of neurological disabilities and impairments. This study aimed at assessing the value of the HIE scoring system in predicting early neurodevelopmental outcome of the infants who suffered birth asphyxia.

Objective: To assess the value of the HIE score in predicting neurodevelopmental outcome in infants with birth asphyxia at six months of age.

Study design: Prospective cohort study.

A numeric scoring system for the assessment of HIE during the neonatal period was tested for seven days (or any number of days before discharge or death). The highest score attained at any of these days was used to assess severity of birth asphyxia.

Materials and methods: One hundred and forty infants with a five minute Apgar score of <7 were studied. Eighty-two infants were evaluated at six months of age by taking a history from the mother about development and presence of convulsions. Amiel-Tison method of assessment of motor systems was used to assess the motor function. A modified neurodevelopmental assessment using the Griffith mental developmental charts was used to assess

neurodevelopment at six months. Thirty infants (21%) of the survivors were lost to follow-up.

Outcome measures: Normal development, delayed development, morbidity (convulsions, abnormal muscle tone, cerebral palsy) or death.

Results: Twenty- eight (20%) of the infants died during the neonatal period while 112 (80%) survived. The RR of dying during the neonatal period was 20 for moderate HIE and 46 for severe HIE. The PPV for mortality was 42.3% for moderate HIE and 93.8% for severe HIE. NPV was 98% in both categories. Fifty-eight (70.7%) of the infants were normal at six months of age while 24 (29.3%) had a poor outcome. Of those who had abnormality some had more than one finding. The risk of poor outcome increased with increasing HIE score.

Neurodevelopmental abnormalities detected during the six months follow-up were convulsions (17%), abnormal muscle tone (21%), delayed developmental age (17%) and cerebral palsy (8.5%).

The HIE score had low sensitivity but it was highly specific in detecting the neurodevelopmental abnormalities. The positive and negative predictive values were found to be high. Twenty-three infants (14 boys and 9 girls) had microcephaly by six months of age. HIE score was found to be negatively correlated with the occipital frontal

circumference (OFC) i.e. the higher the HIE score attained the smaller the OFC.

Conclusion and recommendations:

The HIE scoring system used in this study was highly predictive of neonatal outcome in terms of morbidity and mortality.

Neurodevelopmental abnormalities observed at six 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 six months of age. It was found that the higher the HIE score, the smaller the OFC.

It is recommended that 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.

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ABBREVIATIONS

CT scan - Computed tomography scan

EEG - Electroencephalogram

HIE - Hypoxic ischaemic encephalopathy

HIES - Hypoxic ischaemic encephalopathy score

ICU - Intensive care unit

LOC - Level of consciousness

MRI - Magnetic resonance imaging

MUCHS -Muhimbili University College of Health Sciences

MNH -Muhimbili National Hospital

OFC -Occipital frontal circumference.

NPV - Negative predictive value

PPV - Positive predictive value

RR - Relative risk

WORKING DEFINITIONS

Abnormal muscle tone	-	Hypotonia, Hypertonia
Normal development	-	Developmental age equal to or more than five months
Delayed development	-	Developmental age equal to or less than four months.

1.0 INTRODUCTION AND LITERATURE REVIEW

1.1.0 BIRTH ASPHYXIA

1.1.1 Definition

Birth asphyxia has been defined as a delay in establishing spontaneous respiration upon delivery of a newborn.[1] It causes impaired gas exchange leading to progressive hypoxaemia and hypercapnoea with significant metabolic acidosis.[2] Its severity has been related to the degree of depression of the Apgar score[3,4] or by the presence of cord blood acidosis.[4] It has also been associated with the presence of electroencephalographic abnormalities and, finally, by the occurrence of clinical signs in the infant with post- asphyxial hypoxic ischaemic injury.[5] The severity of such encephalopathy should correlate with the degree or duration of asphyxia.[5]

1.1.2 Epidemiology

Perinatal asphyxia remains a major cause of mortality and neurodevelopmental disability in full term infants. It has remained a common problem in the developing world with high attendant mortality.[6,7] Incidence has ranged from 9.4/1000 in Kuwait[8] to 26.5/1000 in Nigeria [7] with mortality rates ranging from 1.1/1000 in Kuwait [8] and 18.7% in Nigeria.[7] These rates are higher than what is

seen in the more affluent societies or developed countries with incidence between 2.9 to 9.0/1000.[3,4,9,10]

Among 3886 babies delivered in the New Maternity unit of Muhimbili Medical Centre within a three months period in 1992, it was found that 404 (10.4%) were asphyxiated.[11] Birth asphyxia was found to be the second commonest cause of morbidity in neonates admitted at the Muhimbili Medical Centre accounting for 25% of all admitted neonates. It also accounted for 26.4% of all neonatal deaths, being the commonest cause of death.[11] Msemo GRL, conducted a study at the same centre in 1990 and reported the incidence of birth asphyxia to be 40.5 per 1000 live births.[12]

1.1.3 Assessment of birth asphyxia

The severity of asphyxia is widely assessed by the Apgar score (Apgar 1953). This scoring system was devised by Virginia Apgar in 1952 as a method to assess the well being of a newborn at one and five minutes. It only gives an estimate of severity of asphyxia but not the duration.[13] Apgar score is a practical method of systematically assessing the newborn infant immediately after birth to help identify infants requiring resuscitation for hypoxic acidosis. It does not predict neonatal mortality or subsequent cerebral palsy. Indeed the score is normal in most patients who subsequently develop cerebral

palsy, and the incidence of cerebral palsy is very low among infants with Apgar score of 0-3 at five minutes.[14]

Apgar score at one minute may be used to indicate the need for active resuscitative measures while the five-minute score appears to correlate better with neurological status at one year.

When Virginia Apgar introduced the score, she had intended to apply it to the infants' condition at delivery and how smoothly the transition from fetal to newborn life is made.[1] The Apgar score best accomplishes assessment of the newborn in the delivery room and in settings in which laboratory tests, radiographs and prolonged observation are impossible. Immediate and repeated Apgar score provides a rapid but dependable measurement of the physiologic status of the newborn.[1]

The value of the Apgar score has become controversial because of attempts to use it as a predictor of neurological development of the infant, a use for which it was never intended.[4,15] For example the use of Apgar score to identify birth asphyxia is a misapplication, since conditions such as congenital anomalies, preterm birth and administration of some drugs such as pethidine to the mother can result in low scores that are not reflective of asphyxia.[16]

In developing countries like Tanzania newborns are often brought to the neonatal unit from within the hospital or from other hospitals with clear clinical evidence of asphyxia. However, Apgar scores are

not well documented or when documented, they do not tally with the condition of the child.[1]

Neonates with Apgar score of 7 at 1 minute and 10 at five minutes have demonstrated a very low risk of developing long-term abnormalities. The score range of 0 at 1 minute and 3 at five minutes is significant because of the higher mortality and CNS morbidity among infants in this range than infants with scores of 4 at 1 minute and 6 at five minutes or 7 at 1 minute and 10 at five minutes.[13]

Although the Apgar scoring system has stood the test of time, the manner in which it is done in a busy labour ward in a developing country may have some deficiencies. For this reason it is important to have an alternative scoring system which will enable clinicians to identify neonates with intrapartum asphyxia and be able to prognosticate.

More recently, there has been an increasing concern regarding the usefulness of the Apgar score for the immediate assessment of neonates. Repeated observations have shown that low Apgar scores, umbilical acidaemia, fetal heart rate abnormalities and meconium stained liquor are insensitive in predicting death or neurodevelopmental sequel.[4, 17]

Levene et al assessed two methods of diagnosing intrapartum asphyxia for their ability to identify infants with good or poor

prognosis.[18] They compared the predictive value of low Apgar score at 10 minutes with that of post asphyxial encephalopathy. The likelihood of handicap (sensitivity) was predicted with almost complete accuracy (96%) in moderate or severe encephalopathy, compared with only 43% in a low 10 minute Apgar score.[18] This study concluded that post-asphyxial encephalopathy was better than Apgar score in predicting an adverse outcome.

The value of the Apgar score for the evaluation of very premature infants has been questioned. Because some components of the Apgar score such as reflex irritability, muscle tone and respiratory effort are affected by the maturity of the infant, premature infants are inevitably assigned lower Apgar scores than infants born at term.[19]

1.1.4 Postnatal symptoms of asphyxia

Symptoms of birth asphyxia vary with the degree of severity. It is not certain why some babies exhibit multi-organ involvement while others have only one or two organ systems involved.[1] The main clinical features are generally in agreement worldwide and these tally with the minimal criteria for an asphyxial syndrome. This includes the exhibition of alterations in the state of consiousness and abnormalities of muscle tone.[1,5,7,20] Some specific effects of birth asphyxia by organ system include:

In the heart; severe or prolonged asphyxia may result in hypoxic cardiomyopathy that may present with hypotension, poor myocardial contractility, cardiomegaly and heart failure.

In the kidneys; decreased blood flow during an asphyxial event causes acute tubular or cortical necrosis with features of haematuria, proteinuria and oliguria. However this is usually self-limited.[1, 21]

In the gastrointestinal tract; birth asphyxia is usually associated with poor intestinal motility and ileus. The hypoxia also predisposes to secondary bacterial invasion and the development of necrotising enterocolitis.

In the blood; hypoxia from birth asphyxia depresses bone marrow and initiates intravascular coagulopathy, which results in thrombocytopenia, prolonged prothrombin time and partial thromboplastin time and clinical evidence of bleeding

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The brain usually bears the most damage in perinatal asphyxia; the mechanism of injury is demonstrated in section 2.2 below.

2.0 HYPOXIC ISCHAEMIC ENCEPHALOPATHY

2.1 Definition

Hypoxic ischaemic encephalopathy (HIE) is a term commonly used to describe the neurological syndromes that occurs following perinatal asphyxia. It is usually caused by severe birth asphyxia with secondary cerebral ischaemia.[22]

It is an important cause of permanent damage to the central nervous system which may result in neonatal death or manifest later as cerebral palsy or mental deficiency.[23] It has long been known that survivors of HIE are at an increased risk of neurological handicap.[24,25]

HIE was originally described by Amiel-Tison in 1969.[26] There have been numerous studies describing HIE since then.[7, 27]

2.2 Pathophysiology

The neonatal brain can be deprived of oxygen by two major pathogenetic mechanisms, i.e. hypoxaemia-diminished amount of oxygen in the blood supply or ischaemia-diminished amount of blood perfusing the tissue. In the latter condition, the cerebrum of the newborn is subjected not only to hypoxia but also to ischaemia and hypercarbia from failure of spontaneous respiration.[1] This results in age specific neuropathology whereby term babies usually develop neuronal necrosis of the cortex and parasagital ischaemic injury. Preterm babies may develop periventricular leukomalacia (PVL), intraventricular haemorrhage (IVH) and status marmorata of the basal ganglia and thalamus.[28] These infants often have foetal distress with asphyxia and metabolic acidosis at birth. However, some infants may appear normal for several hours after birth.[19]

2.3 Clinical features

When full-term neonates suffer asphyxia during labour or delivery, some may develop HIE with outcomes ranging from complete recovery to death.[29] While adverse outcome does not occur in the absence of HIE, it may be difficult to correctly stage the HIE, such that prognostic discrimination can be maximized.[29, 30]

HIE can be classified into mild, moderate and severe. In mild HIE the infant is hyperalert, has uninhibited reflexes and sympathetic over activity. Moderate HIE is associated with lethargy-stupor, hypotonia, suppressed primitive reflexes and seizures. In severe HIE, there may be coma, flaccid tone, suppressed brain stem function, seizures and increased intracranial pressure.[13]

The major neurological concomitants are readily predicted from the topography of the lesions.[13] Thus mental retardation, seizure disorders and motor deficits are related to cerebral lesions. The lesion of the basal ganglia (status marmorata) is associated with striking extrapyramidal signs especially choreoathetosis and rigidity.[13] The onset of extrapyramidal abnormalities is not apparent until after the age of one year and often much later.[13] The neurological sequel of periventricular leukomalacia (PVL) probably includes the most

important motor deficit observed in prematurely born infants, i.e., spastic diplegia affecting the lower limbs more than upper limbs.[13] Early diagnosis of cerebral palsy and its associated defects is imperative so that we can institute therapy and rehabilitative measures to these children. In severe cases the diagnosis is easily made even in the early weeks of life e.g. in spastic tetraplegia with severe generalized spasticity and gross mental retardation.[31] In many cases, however, early diagnosis is extremely difficult, and on occasion, impossible.[32]

Recently, new technologies have become available to determine cerebral damage more accurately and earlier in the perinatal course. 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 especially in the developing countries.

The HIE scoring system has been shown to be a better indicator in predicting neurodevelopmental outcome in children with birth asphyxia.[27]

2.4 The HIE score

The 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. [20,27,32,33]

HIE scoring systems have been used in various studies. Portman et al developed a score that predicts early morbidity and mortality.[32] Another author developed a score that has been related with long-term outcome.[33] The most widely used classification of HIE is that of Sarnat and Sarnat [20], which groups affected infants into one of three categories: mild, moderate and severe. The decision whether the infant falls into moderate or severe category is at times difficult and the outcome of the infants in the moderate group is variable.[27] This scoring system utilizes the EEG and other laboratory parameters that may not be available in a neonatal unit in the developing country. Thompson et al put together a scoring system that is numeric with fewer items.[27] It is based on the scoring system by Sarnat and Sarnat but is much simpler. The score consists of clinical assessment of nine signs namely level of consciousness, posture, tone, reflexes (Moro, sucking, grasp), seizures, respiration and state of the anterior fontanel.

Each sign is scored from 0 to 3 and the total HIE score for each day is documented. The higher the score the more severely affected is the

infant. The maximum possible score on any one-day is 22. The score is equally applicable in ventilated infants, but it cannot be used in a paralyzed infant.

Components of the HIE score are:

- Tone

  The tone progresses from normal and slightly increased peripheral tone in the mildly affected infant. The more severely affected infant is generally hypotonic or completely flaccid.

- Level of consciousness (LOC)

  The mildly affected infant has a normal LOC or is hyper alert and staring. There may be normal or decreased spontaneous movement and exaggerated responses to minimal stimuli. The more seve·ely affected infant progresses through lethargy to complete unresponsiveness.

- Fits (clinically apparent seizures)

  The score increases with increasing frequency of seizures.

- Posture

  In this study an intermediate score of 1 is given to the neonate who has mild to moderate HIE. The neonate may show intermittent bicycling movements of the limbs together with fisting (thumbs flexed, adducted and opposed across the palms).

- Primitive reflexes: Moro, palmar grasp and sucking reflex

  These reflexes are normal in the mildly affected infant, poor or partial in moderate HIE and absent in severe HIE.

- Respiratory pattern

  In mild HIE the infant breathes normally or hyperventilates. More severely affected infants have episodes of apnoea and may require ventilation.

- Fontanel tension.

  The severely affected infant may have a full or tense (bulging) fontanel.

The HIE score that has been adapted in the MNH neonatal ward is shown in the following table;

Sign	Score			
	0	1	2	3
Tone	Normal	Hyper	Hypo	Flaccid
LOC	Normal	Hyper alert	Lethargic	
Fits	None	Infrequent (<3/d)	Frequent (>3/d)	
Posture	Normal	Fisting/cycling	Strong distal flexion	Decerebrate
Moro	Normal/partial	Absent		
Grasp	Normal	Poor	Absent	
Suck	Normal	Poor	Absent/bites	
Respiration	Normal	Hyperventilation	Brief apnoea	IPPV (apnoea)
Fontanel	Normal	Full not tense	Tense	
Total				

According to this scoring system, 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.

Thompson et al found that this scoring system was highly predictive of outcome, the best correlation with outcome being the peak score.[27] The study showed that a peak score of 15 or higher had a positive predictive value of 92% and a negative predictive value of 82% for abnormal developmental outcome with sensitivity of 71% and specificity of 92%.[27] They suggested that for clinicians working in areas where sophisticated technology is unavailable, this scoring system will be useful for assessing and prognosticating neurodevelopmental outcome in infants with HIE.

Boo NY et al studied early cranial ultrasound changes as predictors of outcome during the first year of life in term infants with perinatal asphyxia.[34] He found that early cranial ultrasound changes although common in asphyxiated infants, were not significant predictors of adverse outcome.

Hallioglu et al studied 57 infants admitted to the neonatal ICU to find widely available, inexpensive parameters for early identification or prediction of cerebral palsy in infants who will have severe adverse outcome defined as death or major neurological deficit. Denver developmental screening test II (DDST II), occurrence of seizures and cranial ultrasound findings were analyzed in the first five days of life. The DDST II at six months of age yielded a very high predictive accuracy (sensitivity 100%, specificity 95%).[35]

Another assessment method is the 20-item behavioral neurological assessment (NBNA) used in predicting prognosis of asphyxiated newborns that was studied by Bao et al.[36] The result showed that in predicting prognosis, the sensitivity and specificity of NBNA score at 7 days after birth were 88.9% and 82.6% and at 12-14 days, 84.6% and 97.4% respectively. He concluded that its value in predicting prognosis is superior to Sarnat classification, cranial CT scan and B mode ultrasound.

The favourable development of the foetus is connected with the sufficient oxygen requirement. The brain of the foetus is extraordinarily sensitive to the disorders of oxygen supply. During infancy the growth of the head reflects normality of brain development. Microcephaly (defined as head circumference as measured around the glabella and the occipital protuberance that is more than 3 standard deviations below the mean for age, sex, race and gestation) generally suggests impaired development of the brain. It may be caused by a small brain (microencephally) and the two terms are used interchangeably.

The growth of the skull parallels in part with the rapid growth of the brain during fetal life. At birth the mean head circumference is 35.5 (SD± 1.2) centimeters. There is a 5 cm increment during the first three months after birth and an additional 6 cm increment during the later part of the first year of life. Birth asphyxia and subsequently

HIE is known to cause brain damage leading to neuronal loss hence a small brain.

3.0 RATIONALE

HIE is a common condition, the estimated prevalence at the Muhimbili National Hospital (MNH) being about 20%. Early recognition of birth asphyxia and correct resuscitation measures are essential. Long term follow up for possible neurodevelopmental sequelae is necessary so that rehabilitative measures may be instituted when neurological disability is identified.

Apgar score is widely used as a means of assessing newborns immediately after birth but it does not predict neonatal mortality or subsequent cerebral palsy.

The HIE scoring system is very simple and does not need special training. For clinicians working in areas where sophisticated technology is unavailable, this scoring system will be very useful.

No study has been done in our set up to devise a means of predicting neurodevelopment outcome in babies with birth asphyxia.

This study aims at assessing the value of the HIE scoring system in early assessment and identification of infants at risk of long-term neurodevelopmental sequel.

4.0 HYPOTHESIS

The hypoxic ischaemic encephalopathy score does not correlate with neurodevelopmental outcome.

5.0 OBJECTIVES

5.1 Broad objective

To assess the value of the HIE scoring system in predicting neurodevelopmental outcome at six months of age.

5.2 Specific objectives

1. To determine the newborn outcome according to the severity of birth asphyxia by HIE score.
2. To determine the neurodevelopmental disabilities seen at six months of age in relation to the HIE score.
3. To correlate the HIE score and occipital frontal circumference (OFC) at six months of age.

6.0 METHODOLOGY

6.1 Study design

This was a prospective cohort study.

6.2 Study area

The 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 government hospital having a neonatal unit in Dar es Salaam. The unit has a capacity of 70 beds. It admits newborns from the hospital labour ward and babies referred from district hospitals as well as from some private hospitals. A few patients are referred from other regions in the country.

High-risk postnatal clinics provide follow up services for neonates who were admitted in the neonatal ward for various reasons. Neonates from outside the hospital who do not have indications for admission to the neonatal unit are also seen at this clinic.

6.3 Study population

All live born babies with birth asphyxia delivered in the hospital labour ward during the study period and babies transferred from peripheral hospitals with birth asphyxia.

6.3.1 Inclusion criteria

- Full term babies with low Apgar score (i.e. a five minute score of less or equal to 7). The Apgar scoring was done by the midwives at time of delivery and it was not standardized.
- Sick infants with symptoms and signs of HIE (respiratory arrest, apnea, posturing, movement disorder, impaired sucking, swallowing, feeding).

6.3.2 Exclusion criteria

- All infants with obvious congenital malformations
- Preterm babies
- Babies with birth asphyxia transferred from other hospitals after the first day of life.

6.4 Sample size estimation

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

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

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

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

- 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.

6.5 Sampling technique

The purpose and advantages of the study were written on a piece of paper and read to or given to the mother to read. After informed written consent was obtained from mothers, neonates were selected. Selection of the first case was by convenience and henceforth all neonates who met the inclusion criteria were enrolled daily until the sample size was reached.

6.6 Duration of the study

The study took nine months between May 2002 and February 2003. This included two months of recruitment (May to July) up to follow up at six months of age of all the study subjects (November 2002 to January 2003).

6.7 Data collection techniques and tools

6.7.1 Anthropometric measurements of the infant were recorded in a structured questionnaire. These included birth weight, sex, OFC and length (Appendix A).

Weight

Weight was taken by a seca beam balance to the nearest 10g,with the infant completely naked during measurement.

OFC

A non-stretchable measuring tape from the occiput passing just above the eyebrow was used to measure the OFC to the nearest 0.1 cm.

6.7.2 HIE scoring chart

- This was filled in detail for seven consecutive days by the investigator (Appendix B).
- Infants were classified into Sarnat and Sarnat categories [20], whereby neonates scoring 1-10 were considered to have mild HIE, score 11-14 had moderate HIE and those scoring 15-22 were considered to have severe HIE.
- The highest score attained on any of the seven days (or any day before discharge or death) was used to assess severity of birth asphyxia.

Management of the cases was done according to standard protocols of the unit.

6.8 Follow-up

- 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 occurrence of convulsions in their infants.
- Infants who were found to have convulsions were given phenobarbitone. One infant had uncontrolled seizures and was given carbamazepine.

6.8.1 Clinical examination

- Clinical examination including OFC, weight and muscle tone assessment was done on every visit.

6.8.2 At six months

- Ameil-Tison method of assessment of motor system in under fives was done (appendix C).
- Assessment of cerebral palsy was performed using the Malcolm Levene (Poster) criteria (appendix D). This involves 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 out of the six major motor criteria.

- A modified neurodevelopmental assessment using the Griffith mental developmental assessment charts was used to assess the neurodevelopment (Appendix E). This includes assessment of locomotor, personal social, hearing and speech, eye and hand co-ordination and performance. Developmental age was recorded in months.
- Outcome was considered to be normal if the infant did not show any sign of neurodevelopmental deficit. Abnormal outcome was considered if the infant had abnormal muscle tone, was getting convulsions, had developmental age below four months, had cerebral palsy or died. A developmental age of equal to or more than five months was considered to be normal.

6.6 Statistical analysis

Data were entered, cleaned and analyzed using the EPI INFO 6 computer program. Assessing the value of the scoring system was done using positive predictive value, negative predictive value, specificity and sensitivity.

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

Relative risk was used to assess the risk of one group of children to develop a certain complication (e.g. neonatal seizures, death, cerebral palsy).

P value of <0.05 was considered to yield statistically significant differences or associations between groups or variables being compared.

In exploring the correlation between HIE score and occipital frontal circumference at six months a scatter plot was used.

6.7 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 will continue to be followed up at the high-risk postnatal clinic. They will later be handed over to the already existing cerebral palsy clinic.

6.8 Study limitations

The main limitation was the mothers who did not bring back their babies for follow-up. The reasons are not known. We were unable to trace them to their residences due to the limited budget that could not suffice transportation.

7.0 RESULTS

One thousand one hundred and sixty four babies were admitted to the neonatal ward during the study period (6 weeks). Of these 182 had birth asphyxia (defined by a five minute Apgar score of less than 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 ± 0.47)

Mean OFC at birth was 35.2 cm (SD ± 2.25)

Of the 140 neonates recruited, outcome of 110 (79%) neonates was known. Twenty-eight neonates died during the neonatal period and 112 survived. Of those who survived, 82 were assessed at six months of age. Thirty neonates (21%) were lost to follow-up the reasons for which are not known.

Table 1:Association between HIES 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		

*- Fisher exact test

Twenty-eight (20%) of the studied neonates died within the first week of life and 112 neonates (80%)survived.

The relative risk (RR) of dying increased with an increasing HIES, the association was found to be statistically significant (P < 0.001).

Table 2: Association between HIES and neonatal convulsions.

	Neonatal	convulsions			
HIES	Present n (%)	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		

In total, 58 (41.7%) of the neonates had convulsions during the early neonatal period. Neonates who scored more than one 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% CI estimates of the respective risk ratios are as shown in the table.

Table 3: Association between HIES and convulsions by six months of age.

HIES	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		

*- Fisher exact test

About 17% of the infants had convulsions by six months of age with the risk of convulsions increasing with increasing HIE score.

The RR of having convulsions by six months of age was 9 times higher in infants who had moderate HIE than those with mild HIE. The difference was statistically significant (P<0.001).

Infants who had severe HIE had 14 times higher risk of having convulsions by six months of age compared to those with mild HIE. However, the difference was not statistically significant (P =0.08)

Table 4: Association between HIES and Muscle tone at six months of age.

HIES	Normal n (%)	Abnormal n(%)	Total	RR (95% CI)	P
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		

*- Fisher exact test

Twenty-one (26%) of the infants that were seen at six months had abnormal muscle tone. The risk of having an abnormal muscle tone was about four times higher in infants with moderate HIE compared to those with mild HIE. The associations were found to be statistically significant (P<0.001). One infant who had severe HIE was found to have normal muscle tone.

Table 5: Association between HIES and developmental age at six months.

HIES	Delayed n (%)	Normal n (%)	Total	RR(95% CI)	P
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		

*- Fisher exact test

Thirteen (17%) of the infants had delayed development at six months of age.

The risk of infants with moderate HIE to have delayed development was 9 times higher relative to those with mild HIE. The associations were found to be statistically significant (P <0.001).

Whereas the RR of infants with severe HIE to have delayed development was 14 times more compared to infants with mild HIE. However, the difference was not statistically significant (P=0.08).

Table 6: Association between HIE score and Cerebral palsy at six months of age.

HIES	Present n (%)	Absent n (%)	Total	RR (95% CI)	P
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		

*- Fisher exact test

From this table, 7 (8.5%) infants had cerebral palsy at six months of age. The risk of developing cerebral palsy increased with increasing HIE score. The associations were found to be statistically significant for both moderate and severe HIE ($P < 0.05$).

Table 7: Association between HIES and overall outcome at six months of age.

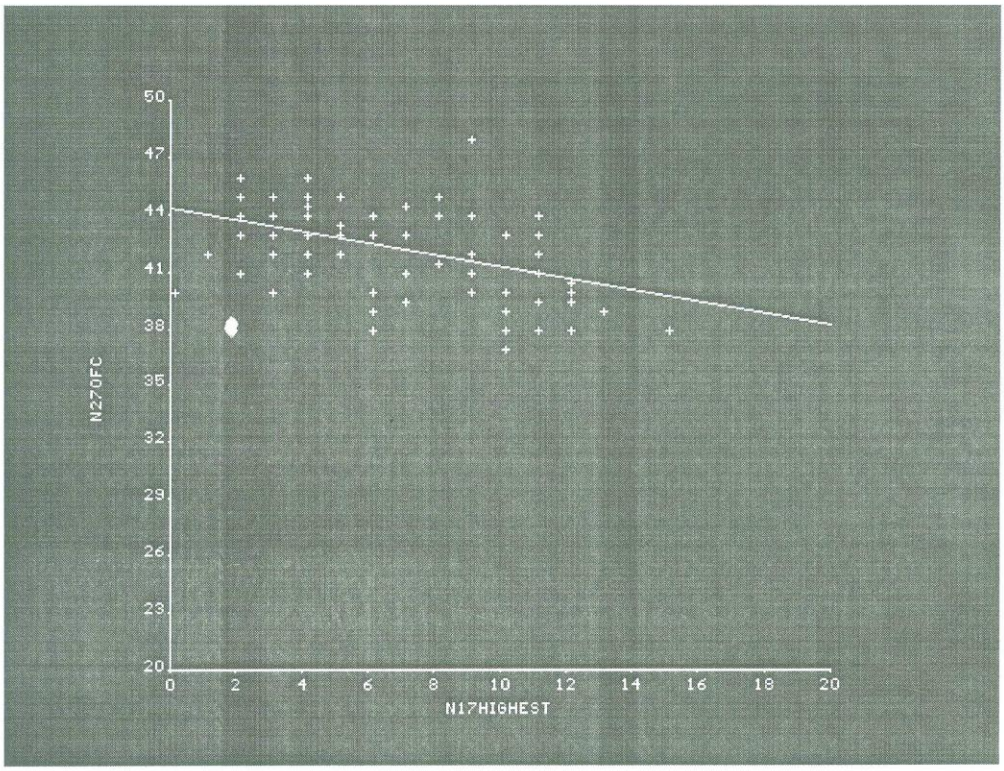
HIES	Good n(%)	Poor n (%)	Total	RR (95%CI)	P
0-10	57 (81.4)	13 (18.6)	70	1	-
11-14	1 (9.1)	10 (90.9)	11	4.9 (2.9,8.8)	<0.001*
15+	0	1 (100)	1	5.4 (3.3,8.8)	=0.19*
Total	58 (70.7)	24 (29.3)	82		

*- Fisher exact test

From this table, 58 (70.7%) of the infants had a good outcome while 24 (29.3%) had a poor outcome.

The risk of poor outcome increased with increasing HIES. The association was found to be statistically significant for moderate HIE (P<0.001) but not significant for severe HIE (P= 0.19).

Figure 1: Association between HIE score and head circumference at six months age.



The graph shows a significant negative relationship between head circumference at six months of age and the HIE score. The higher the HIE score the smaller the head circumference.

Table 8: Using the HIE score as a validity test for poor infant outcome.

	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)
Neonatal	**Mortality**			
Score				
11-14	42.3	98	84.6	86.5
15+	93.8	98	88.3	99
Convulsions				
11-14	84.9	74.5	46.8	94.8
15+	68.8	74.5	30.6	93.6
Six months				
Convulsions				
11-14	63.6	92.9	58.3	94.2
15+	100	92.9	16.7	100
Developmental Age				
11-14	63.6	92.3	58	93.8
15+	100	92.3	17	100
Cerebral palsy				
11-14	36.4	97.1	66.7	90.7
15+	100	97.1	33.3	100
Muscle tone				
11-14	72.7	81.7	38.1	95.1
15+	97	82.9	38.1	98.3
Overall outcome				
11-14	90.9	81.4	7.1	85.1
15+	100	81.4	7.1	100

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

From this table, 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%).

The positive predictive values were high for severe HIE whereas the negative predictive values were high in both categories.

8.0 DISCUSSION

Hypoxic ischaemic encephalopathy is known to be associated with significant morbidity and mortality in the full term infant. This study aimed at assessing the value of the HIE scoring system in predicting early outcome of the infants who suffered birth asphyxia.

Of the 140 neonates recruited, outcome of 110 (79%) neonates was known. Twenty-eight neonates died during the neonatal period and 112 survived. Of those who survived 82 were assessed at six months of age. Thirty neonates (21%) were lost to follow-up the reasons for which are not known.

In this study, it was found that HIE score was highly specific in detecting early neonatal mortality 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%. Thus this study has shown that this HIE scoring system can be used to predict infants who may die with great accuracy because its validity is high.

The risk of dying during the neonatal period increased with increasing HIE score. This study also revealed that majority of neonates with HIE die within the first week of life. Other studies have shown a similar finding that severely asphyxiated infants have a high mortality within the first 72 hours of life.[6,18]

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 Muhimbili National Hospital. In another study that compared Apgar score and post asphyxial encephalopathy in predicting adverse outcome, 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.[18] In a retrospective study of 227 infants by Thornberg et al, 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.[37] Thus findings from this study are similar to the previous studies[18, 37] and this scoring system can be used to predict neurodevelopmental outcome since all the studies cited show the risk of adverse outcome increasing with increasing HIE score.

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 whereby for severe HIE the risk was 2.7. This could be due to the fact that neonates with severe HIE were most of the time heavily sedated and convulsions alone may not reflect severe neurological damage.

A study by Finer et al to assess factors affecting outcome of HIE in term infants found that factors that significantly correlated with outcome included the Sarnat stage and the occurrence of intractable seizures.[38] It was found that there was no association between one or five minute Apgar score, need for ventilation, the EEG, the occurrence of seizures and the subsequent outcome. The findings of this study are similar to the findings in the study by Finer et al. It has been shown that neurodevelopmental outcome in neonates who had HIE is associated with the Sarnat staging of encephalopathy. It is speculated in that study that presence of seizures is a risk for neurodevelopmental abnormality. In another study, a detailed neurodevelopmental 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.[39] Thus neonates who had convulsions in this study group are at an increased risk of neurodevelopmental disability and they need to be followed up more closely.

At six months of age, 82 infants were evaluated for neurodevelopmental outcome. Neurodevelopmental abnormalities detected during the six 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 six 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 six months. The positive predictive values to predict convulsions were found to be 63.6% for moderate HIE and 100% for severe HIE. Negative predictive value was 92.9% in both categories. This means that the score could detect neonates who may have convulsions by at six months of age with 100% accuracy for severe HIE. Hence this scoring system can be used to predict infants who may have or may not have convulsions as early as six months of age.

The same proportion of infants who had convulsions was found to have delayed development on assessment at six months. The relative risk of having a delayed development increased with increasing HIE score. A similar finding was obtained in a study by Thomson et al whereby the HIE was found to be negatively correlated with the general quotient as obtained from the Griffths mental developmental charts.[27] These findings suggest that the more the brain damage form HIE, the more likely is the infant to have delayed development. It may also be speculated 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 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 six 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 suggests that HIE mainly resulted in cerebral lesions in this group of infants.[13] Infants with abnormal tone were referred for physiotherapy to avoid contractures and to facilitate normal posture. Abnormalities of tone have been shown to be an important predictor of severity of handicap.[40] Toh found that out of 35 infants with post asphyxial HIE, 23 had severe adverse outcome.[17] Thirteen died and ten survived with

major neurological sequelae: eight had spastic quadriplegia, one had spastic quadriplegia and choreoathetosis. The association of higher incidence of muscle tone abnormalities with corresponding higher HIE scores in this study is in agreement with the 2 studies cited above.

Seven (8.5%) infants were found to have cerebral palsy by using the Poster criteria (Appendix D). The risk of having cerebral palsy increased with increasing HIE score. The score was found to have a predictive value for cerebral palsy of 100% for severe HIE and negative predictive value of 97.1%. This shows that the scoring system was highly accurate in detecting infants who may and those who may not have cerebral palsy.

Although the Poster criteria are most reliable in children who are one year and older, nonetheless, at six months of age 8.5% of the children in this study already had obvious signs of cerebral palsy. It is known that cerebral palsy may not be accurately diagnosed until 3 to 4 years of age.[17] Thus it is possible that some infants who were found to be normal during the six months assessment may develop cerebral palsy. A small number of infants had two or three major motor features in the Poster criteria. These infants need close follow-up as they are at a high risk of having cerebral palsy later on. Of 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 otorhinolaryngiology specialists who confirmed the diagnosis and are assisting in management.

A study by Aggarwal et al assessed 40 neonates with clinical signs suggestive of HIE. They found that neonates with stage one encephalopathy 'mild HIE) were all normal at one year. Twenty-nine had stage 2 encephalopathy (moderate HIE) 15 were normal and 14 showed delayed development and 4 had cerebral palsy. The neonate with stage 3 encephalopathy (severe HIE) had hypotonic cerebral palsy with blindness.[24] Thornberg et al studied 292 term infants with Apgar score <7 at five minutes. 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 r euromotor dysfunction.[37] This study agrees with the previous studies in that the more severe the HIE the worst the neurodevelopmental disability.

Overall outcome was also assessed and the infants were classified as having a good or poor outcome. The infant was said to have a good outcome when he/she was well without any neurological disability. Poor outcome was considered if the infant had convulsions, abnormal muscle tone, de'ayed developmental age or cerebral palsy whether isolated or in combination. Fifty-eight (70.7%) infants were found to

be normal and 23 (29.3%) had a poor outcome. The positive predictive values for poor outcome was 90.9% for moderate HIE and 100% for severe HIE and negative predictive value was 81.4%. This signifies that outcome can be predicted in infants with moderate HIE with 90.9% and 100% accuracy in moderate and severe HIE respectively. The negative predictive value of the scoring system was 81.4%, implying that good outcome can be predicted in infants who had birth asphyxia by 81.4%. In term infants with documented HIE at birth, major neurodevelopmental dysfunction depend more on the stage of HIE than other perinatal or social factors.[39] Thus from this study the HIE score was found to be highly useful in predicting outcome.

Microcephaly is defined as a head circumference that is more than two standard deviations below the mean for age and sex. The mean OFC in this study group was 42.4 cm (± 2.2). However this was not classified according to sex. According to data from the National Centre for Health statistics (NCHS), the mean OFC for boys at six months of age is 43.8 cm and for girls is 42.4 cm.[41] In this study a total of 23 infants had microcephaly (14 boys and 9 girls). HIE score was found to be negatively correlated with occipital frontal circumference (OFC) meaning that the higher the HIE score attained the smaller the OFC at six months of age. This is a result of neuronal

damage due to HIE leading to slowed or an arrested brain growth and hence microcephaly. 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 one year of age that had a sensitivity of 65% and specificity of 73%.[42] Similarly, in a study to predict neurological outcome using proton spectroscopy in asphyxiated infants, Roth et al found that the severity of asphyxia was inversely proportional to the velocity of increase in OFC in cm/year.[43] Findings in these studies are similar to the findings in this study in which it was found that the more severe the HIE the smaller the head circumference at six months of age.

In a study by Watemberg et al, microcephally was found to be common among children evaluated for developmental disabilities. The commonest factors related to microcephaly were prematurity, perinatal asphyxia and small for gestational age.[44] The study also showed that in children with cerebral palsy, microcephaly was a risk factor of mental retardation. 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.[42]

9.0 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 six 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 six months of age. It was found that the higher the HIE score, the smaller the OFC.

10.0 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 infant

REFFERENCES:

1. Airede AI, Weerasinge HD. Birth asphyxia: A review. EAMJ 1985; 72:252-257.
2. Low JA. Intrapartum fetal asphyxia: definition, diagnosis and classification. AM J Obstet Gynecol 1997; 176:957-9.
3. Erganderer U, Eriksson M and Zetterstrom R. Severe neonatal Asphyxia. Incidence and predictors of outcome in the Stockholm area. Acta Paediatr Scand, 1983; 72:321-5.
4. Nelson KB, Ellenberg JH. Apgar scores as predictors of chronic Neurological disability. Paediatrics. 1981; 68: 36-44.
5. Fenicel GM. Hypoxic ischaemic encephalopathy in the newborn. Arch. Neurol, 1983; 40: 261-6.
6. Volpe JJ. Neurology of the newborn 3rd Ed. W.B. Saunders, Philadelphia, 1981.
7. Airede AI. Birth asphyxia and Hypoxic-Ischaemic Encephalopathy: incidence and severity. Annals of tropical Paediatrics.1991; 11:331-5
8. Al-Alfy A, Carroll JE, Devarajan LV, Moussa MAA. Term infant asphyxia In Kuwait. Annals of tropical paediatrics. 1990; 10:355-61.
9. Macdonald HM, Mulligan JC, Allen AC, and Taylor PM. Neonatal asphyxia. Relationship of obstetric and neonatal

complication to neonatal mortality in 38,405 consecutive deliveries. J. Paediatr.1980; 96:898-902.

10. Williams THC and Davies DP Medical audit in neonatal Care. Brit. Med. J.1980; 281:1618-20.

11. Kawo NG, Urassa ENJ, Killewo C, and Massawe AW. Asphyxia neonatorum. In Muhimbili Medical Center; Management and associated factors. Tanzania Journal of Paediatrics: 1995; 3 (2) 50-53.

12. Msemo GRL, The short-term outcome of infants with birth Asphyxia in Muhimbili Medical Centre: Dissertation submitted for Partial requirement for the degree of Masters of Medicine 1991.

13. Sykes GS, Molloy PM, Johnson P. Do Apgar score indicate Asphyxia? Lancet: 1983; 1:494-6.

14. Kliegman RM. Fetus and the neonatal infant. Nelson's Textbook of Paediatrics: 15th edition; 1996: 431-442.

5. Casey M, Macintyre DD, Leveno KJ. The continuing value of the Apgar score for the assessment of the newborn infant. NEJM, 2001; 344:467-471.

6. Gilstrop LC, Hauth JC, Jenkins GDV et al. Second stage fetal heart rate abnormalities and type of neonatal acidaemia. Obstet Gynecol 1987; 70:191-5

17. Toh VC. Early predictors of adverse outcome in term infants with post-asphyxial hypoxic ischaemic encephalopathy.Acta paediatr 2000; 89 (3): 343-7.

18. Levene MI, Sands C, Grindulis H and Moore JR. Comparison of two methods of predicting outcome in perinatal asphyxia. The Lancet January 1986; (ii) 67-68.

19. Woods D, Melan A. Hypoxic Ischaemic Encephalopathy. Notes on the newborn infant: 5th edition 1996.

20. Sarnat HB and Sarnat MS. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch. Neurol. 1976; 83: 696-705

21. Raju TNK, Vidyasar D, Papazafiratou C. Cerebral perfusion pressure and abnormal intracranial pressure waveforms: their relation to outcome in severe asphyxia. Crit care Med. 1981; 9:449-53.

22. Coovadia HM, Wittenberg DF. Paediatrics and Child Health: A Manual for health professionals in the third world. 4th Ed 1998: 129-131.

23. Sperling MA. Hypoxia-Ischaemia. Nelson's Textbook of Paediatrics. 15th Edition 1996: 469-471.

24. Aggarwal P, Chaudhari S, Bave S.Clinical predictors of oucome in HIE in term neonates. Annals of Tropical Paediatrics 1998;(18) 117-121.

25. Nelson KB, Ellenberg JH. Neonatal signs as predictors of cerebral palsy. Paediatrics 1979; (164): 225-32.

26. Amiel-Tison C, Cerebral damage in full-term newborn. Aetiological Factors, neonatal status and long term follow up. Biol Neonate 1969; 14: 234-50.

27. Thompson CM, Peterman AS, Liney LL, Hann FM, van der Elst CW and Molteno CD. The value of the Hypoxic Ishaemic Encephalopathy score in predicting neurodevelopmental outcome. Acta paediatrica 1997; 86:757-61.

28. Volpe JJ. Perinatal hypoxic ischaemic brain injury: Symposium on Paediatric Neurology. Paediatric Clinics of North America 1976; 23:383-396.

29. Cheung PY, Robertson CMT. Predicting outcome of term neonates with intrapartum asphyxia. Acta paediatr 2000; 89: 262-71.

30. Leviton A, Nelson KB. Problems with definitions and classification of newborn encephalopathy. Paediatr Neurol 1992; 8: 85-90.

31. Hutchison JH, Cockburn F. Practical Paediatric Problems: Cerebral Palsy. 6th Edition 1991; 567-575.

32. Portman RJ, Carter BS, Gaylord MS, Murphy MG, Thieme RE, Merenstein R.E. Predicting neonatal Morbidity after perinatal

asphyxia: a scoring system. Am J Obstet Gynecol 1990; 192:174-81.

33. Lipper EG, Voorhies TM, Ross G, Vannuci RC, Auld PAM. Early predictors of one Year outcome for infants asphyxiated at birth. Dev Med Child Neurol 1986; 28: 303-9.

34. Boo NY, Chandran V, Zulfiqar MA. Early cranial ultrasound Changes as predictors of outcome during the first year of life in Infants with perinatal asphyxia. J. Paediatr. Child Health 2000; 36(4) 363.

35. Hallioglu O, Topaloglu AK, Zenaroglu A. et al. Denver Developmental screening test II for early identification of infants who develop major neurological deficits as a sequel of HIE. Pediatr. Int. 2001; 43 (4): 400-4

36. Bao YL, Yu RJ, Li ZS. 20 item neonatal behavioral Neurological assessment used in predicting prognosis of Asphyxiated newborns. Clin. Med. J. (Engl) 1993; 106 (3): 211-5.

37. Thornberg E, Thiringer K, Odeback A, Milsom I. Birth asphyxia: incidence, clinical course and outcome in a Swedish population. Acta Paediatr 1995; 84(8) 927-32.

38. Finer NN, Robertson CM, Peters KL, Coward JH. Factors affecting outcome in hypoxic aschaemic encephalopathy in term infants. Am J Dis Child 1983; 137 (1): 21-5

39. Robertson CMI, Finer NN. Term infants with hypoxic ischaemic encephalopathy: outcome at 3.5 years. Dev Med Child Neurol 1985; 274:473-84.

40. Hadders-Algra M, Huisjes HJ, Touwen BC. Perinatal correlates of major and minor neurological dysfunction at school age: A multivariate analysis. Developmental Med and Chlid Neurology 1988; 30: 472-481.

41. Needlman RD. Growth and development. Nelson's textbook of Pediatrics 15th Edition: 1996:38-44.

42. Mercuri E, Ricci D, Cowan FM, Lessing D, Frisone MF, Haataja L et al. Head growth in infants with Hypoxic ischaemic encephalopathy: correlation with neonatal magnetic resonance imaging. Pediatrics 2002; 106:235-43.

43. Roth SC, Edwards AD, Cady EB, Delpy DT, Wyatt JS, Azzopardi D et al. Relation between cerebral oxidative metabolism following birth asphyxia, neurodevelopmental outcome and brain growth at one year. Dev Med Child Neurol 1992; 34 (4): 285-95.

44. Watemberg N, Silver S, Harel S, Lerman-Sagie T. Significance of microcephaly among children with developmental disabilities. Journal of Child Neurology 2000; 17 (2): 117-22.