A DISSERTATION ON

NEURO DEVELOPMENTAL OUTCOME OF NEW BORNS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY

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CERTIFICATE

This is to certify that this dissertation entitled "NEURO DEVELOPMENTAL OUTCOME OF NEW BORNS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY" submitted by DR.K. SATHISHKUMAR to the faculty of Pediatrics, The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the requirement of the award of M.D. Degree Branch VII (Pediatric Medicine) is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I, Dr. K. SATHISHKUMAR solemnly declare that the dissertation titled "NEURO DEVELOPMENTAL OUTCOME OF NEWBORNS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY" has been prepared by me.

This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the requirement for the award of M.D., degree Examination (Pediatric Medicine) to be held in FEBRUARY 2006.

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CONTENTS

INTRODUCTION

Perinatal (Birth) Asphyxia describes a lack of oxygen, blood flow and gas exchange to fetus / new born. Hypoxic Ischemic encephalopathy is an important consequence of perinatal hypoxia.

Birth asphyxia and Hypoxic ischemic encephalopathy(HIE) are associated with increased risk of mortality & morbidity. Mortality in a full term asphyxiated newborn is about 10-20%.

Early neonatal deaths are an important cause of the high infant mortality. Apart from Low Birth Weight & Neonatal infections asphyxia contributes a significant proportion of the mortality in early neonatal period.

HIE is associated with long term neurodevelopmental sequelae. Overall more severe the encephalopathy greater is the risk of sequelae. They may be major neurological sequelae like cerebral palsy, mental retardation, epilepsy, visual and auditory impairment or mild motor deficits in later life or subtle neurological abnormalities. Even in the absence of obvious neurological deficits in newborn period there may be long term functional impairments.

Regular follow up of these babies helps in early identification of the developmental delay. Early identification and appropriate intervention may reduce the severity of later disability.

BIRTH ASPHYXIA & HIE

Asphyxia refers to a combination of hypoxia, hypercarbia and metabolic acidosis.

Definition :

American Academy of Pediatrics defines Perinatal Asphyxia as an insult to fetus or newborn due to a lack of oxygen (hypoxia) and or a lack of perfusion (ischemia) to various organs of sufficient magnitude & duration to produce more than fleeting functional and / or biochemical changes.

Substantial & prolonged intrauterine Asphyxia is said to be present if

a) Documented Apgar score of 0-3 at 5 min

b) Cord Umbilical artery pH of < 7.0 and a base deficit of > 12

National Neonatology forum of India :

NNF suggested that birth asphyxia should be diagnosed when

1. Baby has gasping and inadequate breathing or no breathing at 1 min.

It is a simple & useful definition which can be used in community & corresponds to 1 min Apgar score of 3 or less.

APGAR SCORE

Sign	0	1	2
Heart rate	Absent	Slow< 100 bpm	> 100 bpm
Respiration	Absent	Slow, irregular	Good, crying
Muscle tone	Limp	Some flexion	Active motion
Reflex irritability (catheter in nares, tactile stimulation)	No response	Grimace	Cough, sneeze, cry
Color	Blue or pale	Pink body, blue extremities	Completely pink

Low Apgar scores may be present in non asphyxiated infants also. Despite limitations, Apgar scoring is conventionally used to assess condition of newborn at 1 min after birth.

Incidence of perinatal asphyxia :

The incidence of perinatal asphyxia is about 1 to 1.5% of live births and is inversely related to gestational age and birth weight.

Pathophysiology :

In term neonates 90% of asphyxial insults occur antepartum or intrapartum due to placental insufficiency.

During normal labour, uterine contractions, cord compression, increased O2 consumption by mother & fetus, maternal dehydration & alkalosis cause most babies to be born with little O2 reserve.

In addition to the above normal factors any process that

1. impairs maternal oxygenation
2. decreases blood flow from mother to fetus
3. impairs gas exchange across placenta / in the fetus and
4. increase fetal O2 requirement will increase risk of perinatal asphyxia

In the presence of hypoxic ischemic challenge to fetus compensatory reflexes are initiated causing shunting of blood to brain, heart and adrenals (diving reflex)

Target organs of perinatal asphyxia are brain, heart, lungs, kidney, liver, bowel and bone marrow.

HYPOXIC ISCHEMIC ENCEPHALOPATHY

HIE is the most important consequence of perinatal asphyxia. Neonatal encephalopathy is defined as a state of altered level of consciouness without etiological implications.

Hypoxic Ischemic Encephalopathy describes encephalopathy as defined above with objective evidence of hypoxia / ischemia (asphyxia)

It should be emphasised that HIE is first one out of a number of etiologies in the differential diagnosis of neurological depression in neonate.

Asphyxia may be suspected and HIE reasonably included in differential diagnosis of neonatal depression / neurologic dysfunction if the following have been documented.

1. 5 to 10 min Apgar score < 3
2. Neonatal seizures within first 24 – 48 hrs
3. Need for positive pressure resuscitation for more than 1 min or more than 5 min until first cry
4. Burst suppression patterns on EEG
5. Prolonged fetal acidosis

Pathophysiology:

Brain hypoxia & ischemia from systemic hypoxemia and reduced cerebral blood flow are primary triggers of HIE. Initially compensatory increase in Cerebral Blood Flow occurs.

With prolonged asphyxia Cerebral Blood Flow becomes pressure passive. As BP falls , brain hypoxia occurs leading to decrease in glycogen & ATP. There is a concomitant increase in lactate & fall in PH.

Following initial phase of energy failure metabolism may recover only to deteriorate in second phase (delayed injury)

Reperfusion injury is a second determinant of extent of brain damage. By 6-24 hrs after initial injury, a new phase characterized by apoptosis occurs. This phase may continue for days to week.

Biochemical changes :

Both hypoxia & ischemia increase the release of excitotoxic aminoacids like glutamate. ExcitotoxicAminoacids through action at inotropic glutamate receptors (NMDA) open ion channels allowing Ca2+ and Na+ to enter cell inducing immediate neuronal death from osmolar load.

Further these excitotoxins by direct activation of NMDA channel provoke excessive Ca2+ influx. This in turn leads to a delayed neuronal death by

1. Activation of undesirable second messenger system. (lipases and proteases)
2. Pertubation of mitochondrial respiratory electron chain transport
3. Generation of free radicals & leukotrienes
4. Generation of Nitric oxide

Reperfusion of previously ischemic tissue promotes formation of excess oxygen free radicals. (eg. Superoxide ion, hydrogen peroxide, hydroxyl radical) which may damage cellular lipids, proteins & nucleic acids. Reperfusion also brings with it neutrophils which along with activated microglia release injurious cytokines (IL – 1 β & TNF -α)

Pathological Lesions :

- ***Parasagittal cerebral necrosis*** : This lesion is bilateral, usually symmetrical, and occurs in the cerebral cortex and subcortical white matter, especially in the parietooccipital region. These regions represent the border zones of perfusion from major cerebral arteries.

- ***Status marmoratus :*** In this lesion, the basal ganglia, especially the caudate nucleus, putamen, and thalamus, demonstrate neuronal loss, gliosis, and hypermyelination, leading to a marble white discoloration of these regions. This is the least common type of neuropathology, and its full evolution may take months to years.

- ***Focal and multifocal ischemic brain necrosis*** : These lesions are relatively large, localized areas of necrosis of cerebral parenchyma, cortex, and subcortical white matter. The most frequently affected region is the zone perfused by the middle cerebral artery.

- ***Periventricular leukomalacia*** : This lesion is characterized by necrosis of white matter, seen grossly as white spots adjacent to the external angle of the lateral ventricles. These sites are the border zones between penetrating branches of major cerebral arteries. These lesions are more common in preterm than in term infants.

Clinical Manifestations of HIE :

The spectrum of HIE ranges from mild to severe. The initial phase lasts for about 12 hrs after the insult & consists of signs of cerebral dysfunction. Clinical manifestations and course vary depending on HIE severity.

* Mild HIE
    - Muscle tone may be increased slightly and deep tendon reflexes may be brisk during the first 24 hrs.
    - Transient behavioural abnormalities, such as poor feeding, irritability or excessive crying or sleepiness, may be observed.
    - By 1-2 days of life, the CNS examination findings become normal

* Moderately severe HIE
    - The infant is lethargic, with significant hypotonia and diminished deep tendon reflexes.
    - The grasping, Moro, and sucking reflexes may be sluggish or absent.
    - The infant may experience occasional periods of apnea
    - Seizures may occur within first 24 hours of life

- Full recovery within 1-2 weeks is possible and is associated with a better long term outcome.
- An initial period of well-being may be followed by sudden deterioration, suggesting reperfusion injury; during this period, seizure intensity might increase.

* Severe HIE

- Stupor or coma is typical. The infant may not respond to any physical stimulus.
- Breathing may be irregular, and the infant often requires ventilatory support.
- Generalised hypotonia and depressed deep tendon reflexes are common.
- Neonatal reflexes (eg. Sucking, swallowing, grasping, Moro) are absent.
- Disturbances of ocular motion, such as skew deviation of the eyes, nystagmus, bobbing, and loss of "doll's eye" (ie, conjugate) movements may be revealed by cranial nerve examination.
- Pupils may be dilated, fixed, or poorly reactive to light
- Seizures occur early and often and may be initially resistant to conventional treatments. The seizures are usually generalized, and their frequency may increase during the 2-3 days after onset,

correlating with the phase of reperfusion injury. As the injury progresses, seizures subside and the EEG becomes isoelectric or shows a burst suppression pattern. At that time, wakefulness may deteriorate further, and the fontanelle may bulge, suggesting increasing cerebral edema.

- Irregularities of heart rate and BP are common during the period of reperfusion injury, as is death from cardio respiratory failure.

* Infants who survive severe HIE
  - The level of alterness improves by days 4-5 of life
  - Hypotonia and feeding difficulties persist, requiring tube feeding for weeks to months.

*** Involvement of multiple organs besides the brain is a hall mark of HIE**

- Severely depressed respiratory and cardiac functions and signs of brainstem compression suggest a life- threatening rupture of the vein of Galen (ie. Great cerebral vein) with a hematoma in the posterior cranial fossa.
- Reduced myocardial contractility, severe hypotension, passive cardiac dilatation, and tricuspid regurgitation are noted frequently in severe HIE
- Patients may have severe pulmonary hypertension requiring assisted ventilation. Renal failure presents as oliguria and during recovery, as

high output tubular failure, leading to significant water and electrolyte imbalances.

- Intestinal injuries may not be apparent in the first few days of life. Poor peristalsis and delayed gastric emptying are common; necrotizing enterocolitis occurs rarely.

Sarnat & sarnat clinical stages is used to estimate the severity of asphyxial insult to infants more than 36 wks gestational age on an individual basis at the bed side.

Sarnat and Sarnat's Clinical stages of Hypoxic Ischemic Encephalopathy

	Stage 1	**Stage 2**	**Stage 3**
Level of consciousness	Hyperalert	Lethargic or obtunded	Stuporous
Neuromuscular control			
Muscle tone	Normal	Mild hypotonia	Flaccid
Posture	Mild distal flexion	Strong distal flexion	Intermittent decerebration
Stretch reflexes	Overactive	Overactive	Decreased or absent
Segmental myoclonus	Present	Present	Absent
Complex Reflexes			
Suck	Weak	Weak or absent	Absent
Moro	Strong; low threshold	Weak; incomplete; high threshold	Absent
Oculovestibular	Normal	Overactive	Weak or absent
Tonic neck	Slight	Strong	Absent
Autonomic Function	Generalised sympathetic	Generalised parasympathetic	Both systems depressed
Pupils	Mydriasis	Miosis	Variable; often unequal; poor light reflex
Heart Rate	Tachycardia	Bradycardia	Variable
Bronchial and Salivary secretions	Sparse	Profuse	Variable
Gastrointestinal Motility	Normal or decreased	Increased ; diarrhea	Variable

Seizures	None	Common ; focal or multifocal	Uncommon (excluding decerebration)
Electroencephalogram Findings	Normal (awake)	**Early :** low – voltage continuous delta and theta **Later :** periodic pattern (awake) **Seizures :** focal spike and wave.	Early : periodic pattern with Isopotential phases Later : Totally isopotential
Duration	< 24 hrs	2-14 days	Hours to weeks

LAB TESTS

1. Serum creatine kinase brain fraction CKBB at 4 and 10 hours of life > 15 IU was found to be associated with mortality or neurological sequelae.
2. CKBB together with protein S – 100 (> 8.5 µg/l) & decreased cord blood PH is found to have high specificity & sensitivity in predicting moderate to severe encephalopathy

EEG :

EEG with clinical signs may help in evaluating & classifying the severity of damage (eg. Seizure foci) EEG should be obtained early in moderate to severe cases. Background EEG activity is better indicator of prognosis than ictal patterns.

1. Generalised depression of background rythm & voltage are early findings.
2. Burst suppression pattern is particularly ominous.

Cranial Ultrasound :

It provides quick assessment of brain lesions. It reveals hemorrhages & periventricular changes and less well the extent of edema.

CT Scan :

It is more useful in assessing the degree of edema when performed early (2-4 days). CT may not be useful in predicting sequelae in premature infants because of excess water & lower myelin content.

It is useful in demonstrating focal ischemic lesion.

MRI :

MRI particularly with diffusion weighted images is the diagnostic modality of choice & is also prognostically useful

Prognosis of perinatal asphyxia :

Birth Asphyxia severe enough to damage the fetal brain irreversibly usually kills before / soon after birth (one fourth of cases). The remainder however even those with seizures will be overwhelmingly normal.

Outcome :

1. Overall full term asphyxiated infants have a mortality of 10 to 20% . The incidence of neurologic sequelae in survivors is 20 to 45 %. Approximately 40% of these are mild and 60% are severe

2. Analyzed according to Sarnat's stages of severity virtually 100% of newborns with stage 1 have normal neurologic outcome 80% of those with stage 2 are normal neurologically & virtually all children with stage 3 either die (one half) or develop major neurologic sequelae (Cerebral palsy, epilepsy, mental retardation)

3. The risk of CP in asphyxiated newborns is elevated 5-10% versus 2 per 1000 in general population. Data from national collaborative perinatal project [4] (U.S.) suggests that perinatal factors of labour and delivery contribute little to mental retardation &seizure.

Indicators of Poor Outcome :

Unfavourable signs :

1. Severe prolonged asphyxia
2. Sarnat stage 3 encephalopathy
3. Seizures of early onset (< 12 hrs) and that which are difficult to control.
4. Elevated Intracranial pressure
5. Persistence of abnormal neurologic signs at discharge (> 1-2 wks)
6. MRI showing abnormal signal intensities
7. Elevated CKBB level
8. Persistant oliguria for first 36 hrs of life
9. Interictal background abnormalities in EEG (Burst suppression, isoelectric potential)
10. Intraventricular hemorrhage grade II or more in Ultrasound cranium
11. Ischemia & infarction over parasagittal area

Neurologic Sequelae :

The precise neurologic sequelae following asphyxia will reflect location, identity & extent of neuronal damage. Cerebral palsy of various types, Epilepsy, Auditory & visual impairment are major sequelae. Minor motor difficulties, ADHD, language & learning difficulties also occur.

During follow up detailed neurological & developmental examination should be conducted to identify early clinical markers of developmental delay.

DEVELOPMENTAL ASSESSMENT:

The importance of early diagnosis and treatment of children with developmental de-lay has emerged in recent years as a matter of growing concern . Early identification of children with delayed development has important implications for their treatment and in preventing risks of future disabilities and secondary problems related to family dysfunction, peer difficulties, and school failure.

Developmental screening is a brief testing procedure designed to identify children who should be subjected for intensive diagnostic assessment. Screening refers to the detection of unsuspected deviations from normal development that would not otherwise be identified in routine pediatric practice. The goal of screening is to identify, as early as possible, developmental disabilities in children at high risk so that a treatment or remediation can be initiated at an early age when it is most effective.

The three approaches to screening include informal, routine and focussed developmental screening.

I. **Informal screening** is based on observing the child during a routine pediatric check up and asking parents about their concerns about child's development. Upper limits of normalcy have been used as cut off points to help identify delay.

Such an approach is not a very sensitive way of screening as it is only useful for not missing major delays.

Guidelines for Screening :

1. Screening instruments should be
    a. Reliable and valid
    b. Culturally relevant
    c. Used only for their specified purpose
2. Multiple sources of information should be used.
3. Developmental screening should be done only by trained personnel.
4. Screening should be on a recurrent and periodic basis.
5. Family members should be part of the screening process.

II. **Routine formal screening** entails systematic developmental screening of all children with the help of standardized screening instruments. However, such an approach is highly time consuming. In our country, as well as in other developing countries, with enormous populations, routine formal screening is neither feasible nor cost effective.

III. **Focussed screening** involves developmetal screening of the following groups of children.

a) Children whose parents express developmental concerns or in whom teachers and physicians suspect problems.

b) Newborns with condition that have known to have high risk for developmental delay. ex. Hypoxic ischemic encephalopathy.

Developmental Screening Tests :

Several developmental screening tests are available for use in infants and children. There are several well accepted criteria by which various tests are judged to be appropriate for use in screening programs. It is recommended that screening test should be simple, brief, convenient to use, cover all areas of development, have adequate construct validity be applicable to a wide age range, and have referral criteria that are both specific and sensitive.

By far the most commonly used screening test is the Denver Development Screening Test (DDST). The DDST is used to screen children from two weeks through 6 years of age in four developmental domains; gross motor, fine motor adaptive, personal social and language skills.

Trivandrum Developmental Screening Chart (TDSC)

Commonly used revised DDST has 125 items and takes about 20-30 min to perform by a trained individual.

TDSC is a modification of Baroda scale & it contains about 17 items. These items include testing the gross motor, fine motor, social & adaptive and language skills of the child. Tests for vision & hearing are also included in it. They include tests to assess whether child holds head steady, rolls from back to stomach, raises self to sitting position, stands up by furniture, walk with help, walks alone, walk backwards, walk upstairs with help, social smile, pat a cake, throws ball, points to parts of doll (3 parts), transfer objects hand to hand, fine prehension pellet, says two words, eyes follow pen / pencil, turns head to sound of bell/ rattle etc appropriate to the age.

Following elicitation of history from the mother assessment is done using TDSC. A line is a drawn over the corresponding vertical age line in the chart appropriate to the child's age. The left hand side of each horizontal dark line represents age at which 3% of children passed the items & right end represents 97%.

All the milestones to the left of the age line are tested. Testing standards for few motor skills have been provided by Child Development Centre(CDC). A normal child would have achieved all the milestones to the left of the age line.

A child who has not achieved one or more skills completely to the left of the age line is suspected to have developmental delay. Repeat testing may have to be done a few days later.

TDSC can be used for children from 0-24 months. It contains only 17 items & is not time consuming (5-7 mins) and can be used in busy office practices. It can be used by paraprofessionals also as it is simple to perform. It is only a screening test. Any delay has to be confirmed by proper & complete neurodevelopmental assessement.

CDC Grading of Motor Milestones

Head Holding : Completed 4 months

Grade0 - No head holding at all

I - Head erect & steady momentarily

II - Dorsal suspension – lifts head along with body

III - prone position - elevates on arms, lifting chest

IV - Holds head steady while mother moves around

V - Head balanced at all times

Sitting : Completed 8 months

Grade0 - Not sitting

I - Sits momentarily

II - Sits for > 30 seconds leaning forward

III - Sits with back straight

IV - while sitting can turn around & manipulate a toy

V - self rises to sit

Standing : Completed 12 months

0 - Not able to stand

I - holding furniture momentarily

II - takes few steps with both hands held

III - stands without support, stands alone with legs apart

IV - stands himself up

V - Stands without support to take a few steps.

Assessment :

0, I, II - Abnormal for that age

III, IV, V - Normal

LITERATURE REVIEW

1. Figueras – Aloy J et al, the study conducted to find out the incidence of neurodevelopmental delay showed about 11.2 % of babies with hypoxic ischemic encephalopathy were found to have neurological impairment.

2. Birth Asphyxia – Incidence, clinical course and outcome in a Swedish population. Acta. Pediatrics, 1995,
   Neurological abnormality of 10% was observed among the 65 babies who had HIE.

3. Robertson et al in 1993. The outcome in mild and severe form of HIE is predictable but in moderate form, it is uncertain. However the babies had variable degree of deficit.

4. Freeman J.M.et al., 25% of the babies with HIE were found to be neurologically abnormal on follow up.

5. Neonatology division children's hospital of Pittsburg. Out of the 65 babies with asphyxia who were followed up for 4.8 years 35.4% of babies had neurological impairment.

6. Ellis M. et al., Outcome at 1 year of neonatal encephalopathy in Kathmandu, Nepal. By 1 year ofage,45 (44%) of the infants with Neonatal encephalopathy had died, 18 (18%) had severe impairments and two(2%) had minor impairments. Of the 18 children with major impairment, 14(78%) had spastic tetraplegic cerebral palsy and eight (44%) had multiple impairments.

7. Glenny Dixon et al, Early developmental outcomes after newborn encephalopathy. Overall 39% of patients had a poor outcome as defined by death, cerebral palsy, or a significant degree of developmental delay. 62% of those with severe encephalopathy had a poor outcome compared with 25% of those with moderate encephalopathy. Patients with a history of seizures were 3 times more likely to develop cerebral palsy than patients without. Overall, 28 (10.1%) of patients had cerebral palsy.

8. Funayama CA et al, Hypoxic – ischemic encephalopathy in new born infants. Acute period and outcome.

   The HIE I group had no motor sequelae. In HIE II group 34.5% showed cerebral palsy and 17.7% neuromotor retardation. Epilepsy occurred in 17.5% of cases with HIE grade II, only among those with neuromotor sequelae.

9. Asakura H. et al, Perinatal risk factors related to neurologic outcomes of term new borns with asphyxia at birth : a prospective study. Of the 152 newborns in 1 year prospective follow up. The incidence of a poor neurologic outcome was 13.8% among the subject. The risk of a poor outcome was increased by 13 fold in neonates with adverse neurological signs and 31 fold in those with hypoxic ischemic encephalopathy.

10. Pierrat V. et al, Prevalence, causes and outcome at 2 years of age of newborn encephalopathy : Population based study. 90 neonates with moderate or severe newborn encephalopathy were followed up for 2 years. 14 infants had a poor outcome.

11. Zhou.XJ., et al., Follow up study of mental development in high risk children. There was significant correlation between developmental assessment at 6 and 12 months and mental development at 7years. The evaluation of development at 12 months is of predictive value for long term outcome.

12. Zupan et al., Neurological prognosis of term infants with perinatal asphyxia. Mild encephalopathies have constantly a good prognosis.

Moderate and severe encephalopathies are associated with poor outcome (death or severe handicap) in 25% to 100% of cases.

13. Oswyn G, et al Perinatal asphyxia at Port Moresby General Hospital : a study of incidence, risk factors and outcome. All 34 of the babies with grade 3 hypoxic ischemic encephalopathy (HIE) either died (30) or had serious neurological impairment.

14. Sorenson LC et al, Neonatal asphyxia – prognosis based on clinical findings during delivery and the first day of life. Neither complications of pregnancy, gestational age, the sex of the infant, passage of meconium before delivery, abnormal fetal heart rate nor birth weight seemed to have any interrelationship with outcome. The best predictor of outcome after intrapartum asphyxia was the severity of postasphyxial encephalopathy. The Apgar score was more depressed among the infants with poor outcome.

15. Mercuri E., et al, Head growth in infants with hypoxic – ischemic encephalopathy : correlation with neonatal magnetic resonance imaging. At 12 months, microcephaly was present in 48% of the infants with HIE, compared with 3% of the controls. Suboptimal head growth was documented in 53% of the infants with HIE,

compared with 3%of the controls. Suboptimal head growth predicted abnormal neurodevelopmental outcome with a sensitivity of 79% and a specificity of 78%.

16. Leuthner SR et al : Low Apgar score & definition of birth Asphyxia. Non reassuring fetal heart rate pattern, prolonged labour, meconium stained fluid , low 1 min apgar score & mild to moderate acidemia have no predictive value for long term neurological injury without encephalopathy or seizures.

17. Karin B et al, Apgar scores as predictor of chronic Neurologic disability. Low apgar scores were risk for cerebral palsy. But 55% of children with cerebral palsy had 1 min score of 7-10 & 73% with CP had 5 min score of 7-10. About 12% of 99 babies with Apgar score of 0-3 at > 10 min had CP. 11% of them had mental retardation & about 50% of them had seizures. 8 of these had other significant disabilities.

18. Meharban Singh : Care of the Newborn 6th edition. HIE is a better predictor of subsequent handicap than poor Apgar scores. EEG abnormalities , intraventricular hemorrhage > grade II on

Neurosonogram & CT Brain abnormalities are associated with adverse outcome.

19. John.P.Cloherty : Manual of Neonatal Care : 5th edition Neurologic sequelae in survivors of HIE is 20 to 45%. Incidence is greater with severe encephalopathy. Perinatal factors of labour & delivery contribute little to the incidence of mental retardation, seizures & cerebral palsy. Sarnat stage 3 encephalopathy, early onset seizures (<12 hrs), abnormal extended apgar score are some indications of poor outcome.

AIMS & OBJECTIVES

Aims of the study are

1. To study the incidence and types of neurologic sequelae at one year of age in babies admitted with neonatal hypoxic ischemic encephalopathy in the newborn ward in Institute of child health & research centre, Government Rajaji Hospital, Madurai.
2. To study the correlation of severity of Hypoxic ischemic encephalopathy to neurodevelopmental outcome.

3. To study the perinatal factors affecting neurodevelopmental outcome

METHODOLOGY

Study Design :

It is a prospective Analytical cohort study

Study Population:

The babies born between april 2004 and july 2004 & admitted with Hypoxic ischemic encephalopathy in newborn ward in Institute of child health and research centre madurai were included in the study.

Study Duration :

The babies were followed up for upto 1 year of age (from April 2004 to July 2005.)

Sampling :

Simple Random Sampling

Sample Size :

For an alpha error of 0.05 and power of 0.8 taking into account mortality & drop rate a total of 100 babies were included in the study.

Inclusion criteria :

1. Term Newborn babies weighing > 2 kg admitted in Newborn ward ICH & RC Madurai
2. H/o birth asphyxia defined by
   a. Apgar score of < 7 at 5 min and /or
   b. Need for positive pressure ventilation > 1min after birth
3. Presence of features of hypoxic ischemic encephalopathy :
   a.Altered consciousness
   b. Abnormal tone & reflexes
   c. Seizures
4. Thick meconium stained babies with HIE

Exclusion Criteria :

1. Babies with HIE who died during hospital stay
2. Depression from maternal anesthesia / analgesia
3. Babies weighing < 2 kg
4. Premature babies
5. Babies with cyanotic congenital heart disease
6. Babies with CNS malformation / other severe congenital malformation
7. Babies with sepsis / meningitis

Methodology :

After admission in the newborn ward the babies to be studied were registered. Detailed antenatal and birth history was taken & anthro pometry was done. By clinical neurological examination babies were grouped by Sarnat & Sarnat staging of HIE. Clinical course during hospitalization was studied. All the above details were recorded in a standard proforma (Annexure 2)

Babies who died during hospital stay due to complications of HIE were excluded from the study. Necessary investigation like EEG, USG cranium and CT scan was done.

After discharge the babies who survived the hospitalization were followed up at well baby clinic in ICH & RC upto the age of one year. The follow up was done every 3 months at 3,6,9 and 12 months of age.

At each follow up visit mothers were given a questionnaire regarding babies milestones. ***Neuro developmental assessment of babies was done using Trivandrum developmental screening chart. (Annexure1).*** Babies were assessed for achieved milestones at each follow up. Babies who did not achieve milestones completely to left of age line on TDSC were considered to have developmental delay. A repeat testing was done 2 weeks later.

Clinical Neurological Examination :

Complete neurological examination of babies was done. Special emphasis was given on

1. Presence of cranial nerve palsies
2. Strabismus
3. Examination for hypertonia / hypotonia by scarf sign, adductor angle and passive movements of limbs.
4. Examination for weakness of muscle groups
5. Deep Tendon Reflexes were elicited for presence of hyperreflexia

Measurement of Head circumference was done at each follow up.

Clinical visual and auditory evaluation was done at every visit. Babies with abnormalities were subjected to thorough ophthalmic examination and otoacoustic emission testing.

Neonatal reflexes :

Special emphasis was given to elicitation of

1) Moro reflex
2) Grasp reflex
3) Asymmetric tonic neck reflex

Children were observed for the persistence or asymmetry of these reflexes.

Necessary investigation & appropriate treatment was also given to these babies during follow up period.

OBSERVATION & ANALYSIS

A total number of 100 babies were enrolled for the study & were followed up for 1 year.

Hospital admission data for 4 months April to July 2004.

TABLE - 1

Total no. of live births	6000
Total no. of admission in newborn ward	560
Total no. of cases of birth asphyxia	132

Out of 132 babies admitted with birth asphyxia excluding babies with prematurity, Birth weight < 2 kg etc, 100 babies were registered & followed up in the well baby clinic up to the age of one year & the neurodevelopmental status was evaluated periodically at the interval of three months.

Statistical Analysis :

Computer analysis of data utilizing the software – Epidemiological Information Package – 2002 (Epi Info 2002) – developed by the Centers for Disease Control and Prevention, Atlanta for World Health Organization.

Mean, Standard deviation and 'p' values were calculated using this package. Chi square test was used to calculate 'p' value.

ANALYSIS OF OUTCOME MEASURES

Neuro developmental outcome :

100 babies were followed up at the well baby clinic upto the age of 1 year and their neurodevelopmental status was evaluated periodically at intervals of 3 months using.

1. Clinical Neurological examination including testing of vision & hearing
2. Developmental Screening using Trivandrum Developmental Screening Chart (Annexure 1)

Developmental delay in the study was defined by failure to achieve milestones appropriate for the age based on TDSC.

Basic statistics

TABLE - 2

HIE	I	II	III	Total
Enrolled	39	48	13	100
Completed follow up	28	42	11	81
Drop out	11	6	2	19
Drop out %	28	12.5	15.5	19

Neurodevelopmental Status :

At 3 months of Age

TABLE - 3

Neurodevelopmental status	No.	%
Normal	55	55
Abnormal	32	32
Drop out	13	13

During the first evaluation at 3 months of age, 55% of babies were normal & 32% were abnormal. 13 babies did not come for follow up. Dropout rate was 13%.

At 6 months :

TABLE - 4

Neurodevelopmental status	No.	%
Normal	64	64
Abnormal	21	21
Drop out	15	15

9 babies who showed developmental delay at 3 months were found to be normal during next follow up visit. 2 more babies in addition to earlier 13 babies did not come for follow up.

At 9 months :

TABLE - 5

Neurodevelopmental status	No.	%
Normal	63	63
Abnormal	19	19
Drop out	18	18

2 babies who were abnormal at 6 months were found to be normal at 9 months. 3 more babies did not come for followup. All the babies who were normal at 6 months continued to be normal.

At 12 months :

TABLE - 6

Neurodevelopmental status	No.	%
Normal	62	62
Abnormal	19	19
Drop out	19	19

At 1 yr of age, 62 babies were normal (62%), 19 babies were abnormal and a total of 19 babies had not come for follow up.

Developmental Delay - Breakup Age wise

TABLE - 7

Months	I	II	III	Total
3	4	16	12	32
6	1	9	11	21
9	0	8	11	19
12	0	8	11	19

Babies who were found to be abnormal at 9 months persisted to have developmental delay at 1 year. Babies who were normal at 3 to 6 months, remained normal thereafter.

Incidence of developmental delay - at 1 year of age.

TABLE - 8

Babies enrolled	Completed Follow up	Developmental delay	%
100	81	19	23.4

Out of the 100 babies enrolled for the study about 19% dropped out by the end of 1 year. 81 out of the 100 babies came for regular follow up for the

study period of one year. By the end of 1 year 19 babies out of the 81 were observed to have developmental delay based on Trivandrum Developmental Screening chart. That is about 23.4 % of children with Hypoxic ischemic encephalopathy were found to be abnormal at 1 year of age.

Incidence of developmental delay in relation to HIE stages

TABLE - 9

	Follow up	Developmental delay	%
I	28	0	0
II	42	8	19
III	11	11	100

Out of the 28 babies with HIE stage 1 who completed follow up none had any developmental delay. That is Developmental delay in HIE stage 1 was zero percentage.

Out of the 42 babies HIE stage II , 8 babies were found to be abnormal at 1 year of age. That is 19% of the babies with HIE stage II had developmental delay.

And all of the 11 babies with HIE stage III (100%) had developmental delay.

Other Disabilities :

Motor Disabilities at 1 year of age

TABLE - 10

	I	II	III	Total
Spastic quadriparesis	0	2	3	5
Generalised Hypotonia	0	0	1	1
		Total		6

Motor disabilities were found in 6 out of 81 babies, ie. About 7.5%. Spasticity was the most common abnormality detected (83%) and it was found only in HIE stage III and Stage II.

Visual Disabilities at 1 yr of age

TABLE - 11

HIE Stage	I	II	III	Total
Convergent squint	0	5	3	8
Squint with Amblyopia	0	1	0	1
Cortical blindness	0	1	1	2
		Total		11

About 13.5% of children with HIE were found to have visual disability and most common was convergent squint. The disabilities were more common in HIE Stage II and Stage III. Cortical blindness was found in 2 out of 11 children (18%).

Hearing Defects

Babies who where found to have hearing defects by clinical examination otoacoustic emission testing was done. Out of the 5 babies who were found to have hearing defects by clinical examination 2 were found to have deafness by otoacoustic emission testing.

HIE Stage II - 1

HIE Stage III - 1

Seizures Disorder

TABLE - 12

HIE Stages	I	II	III	Total
Generalised tonic clonic	0	2	0	2
Myoclonic	0	1	0	1
Total				3

About 3 children out of 81 persisted to have recurrent convulsions.(3.7%) Convulsions in all 3 cases needed atleast 2 anticonvulsants for effective control.

Microcephaly

Correlation of Head circumference at 1 year of age with HIE Staging

TABLE - 13

Head Circumference in cm	HIE Stage		
	I	II	III
Mean	43.75	41.15	38.7
Standard Deviation (S.D)	0.68	1.72	0.75

Mean Head circumference of babies with HIE stage III was significantly lower compared to that of HIE stage II & stage I. HIE stage I babies had a mean head circumference in the normal range

Correlation of Head circumference with HIE stages

TABLE - 14

HIE Stage	Actual difference of Mean	S.E.(d) Standard Error of difference between means
HIE I & II	2.6	0.28
HIE I & III	5.05	0.26
HIE II & III	2.45	0.34

Comparing the head circumference of babies with HIE I , HIE II, & HIE –III the actual difference of mean was more than twice the standard error of difference between Means (S.E.(d))

PERINATAL RISK FACTORS & OUTCOME

To study impact of the perinatal risk factors on neurodevelopmental outcome.

MATERNAL FACTORS :

1. Antenatal Immunisation & Antenatal check up :

82 of 100 mothers (82%) had two doses of tetanus toxoid & atleast two antenatal checks. 18 out of 100 mothers did not have even one antenatal check up and they were un immunized.

2. Parity :

TABLE - 15

Total no. of Pregnancies	Numbers	%
One	62	62
Two	26	26
Three	8	8
Four	2	2
> Four	2	2

Out of the 100 babies, born with birth asphyxia about 62 out of 100 mothers were primi (62%). & only 10 were above second gravida.

Correlation of Parity with developmental delay

TABLE - 16

Parity	Developmental Delay		Relative risk	P value
	Yes	No		
Primi	12	38	0.82	> 0.05
≥ Two	7	24		

3. Maternal Illness :

TABLE - 17

Maternal Illness	Numbers	%
APH	3	3
PIH	22	22
Cardiovascular disease	2	2
Diabetes mellitus	1	1
Antenatal infections	4	4
Total	32	32

Out of 100 mothers 32 of them (32%) had some form illness complicating pregnancy. In this study preg`nancy induced hypertension (PIH) was the most frequent maternal illness associated with birth asphyxia.

Correlation of Maternal Illness with developmental delay.

TABLE - 18

Maternal Illness	Developmental Delay		Relative Risk	P value
	Yes	No		
Present	9	16	2.11	>0.05
Absent	10	46		

4. Mode of delivery :

TABLE - 19

Mode of delivery	Numbers	%
Labour natural	79	79
Forceps	9	9
LSCS	12	12
Vacuum	0	0

79 out of 100 mothers (79%) delivered Vaginally, 9 deliveries required forceps application (9%) & 12 babies were delivered by Caesarean section (12%). Vacuum application is not practiced in our institution.

Correlation of Mode of delivery with developmental delay

TABLE - 20

Mode of Delivery	Developmental Delay		Relative Risk	P value
	Yes	No		
Labour Natural	15	46	1.22	>0.05
Others	4	16		

5. Meconium stained liquor :

Meconium stained liquor was documented in 22 out of 100 mothers (22%)

Correlation of Meconium stained liquor with developmental delay

TABLE - 21

Meconium stained Liquor	Developmental Delay		Relative Risk	P value
	Yes	No		
Present	3	11	0.89	> 0.05
Absent	16	51		

6. Mode of Presentation :

Majority of the deliveries were by vertex presentation 89%. Breech presentation was observed in only 11% of the babies.

Correlation of Mode of presentation with developmental delay

TABLE - 22

Mode of presentation	Developmental Delay		Relative Risk	P value
	Yes	No		
Vertex	16	58	0.50	> 0.05
Breech	3	4		

NEONATAL FACTORS :

1. Sex

TABLE -23

Sex	No.	%
Male	62	62%
Female	38	38%

62 out of the 100 babies with birth asphyxia were males – 62% and 38% were females. Male to Female ratio is 1.6 : 1

Correlation of Sex with developmental delay

TABLE - 24

Sex	Developmental Delay		Relative Risk	P value
	Yes	No		
Male	12	40	0.95	>0.05
Female	7	22		

2.Birth Weight :

TABLE - 25

Birth Weight (wt in gms)	Numbers	%
2000 – 2500	37	37
2500 – 3000	49	49
> 3000	14	14

Those babies having birth weight below 2000 gms were excluded form the study. 37% of babies were between 2 – 2.5 kgs, 49% between 2.5 & 3.0 kg & 14% above 3.0 kg

Correlation of Birth weight with developmental delay

TABLE - 26

BirthWeight	Developmental Delay		Relative Risk	P value
	Yes	No		
≤ 2.5 kg	7	25	0.89	>0.05
> 2.5 kg	12	37		

3. Time of first cry :

TABLE - 27

Time of First cry	Numbers	%
< 5 min	27	27
5 – 10 min	25	25
10 – 20 min	21	21
20 min – 1 hr	19	19
> 1 hr	8	8

About 27 % of babies cried within 5min, 25% of babies between 5-10 min, 22% of babies cried between 10-20 min. and 20% of babies cried between 20 min. to 1 hr. About 8 % of babies cried after 1 hr or later. Thus about 27 % of babies had only mild degree of asphyxia.

Correlation of Time of first cry with developmental delay

TABLE - 28

Time of first cry	Developmental Delay		Relative Risk	P value
	Yes	No		
> 20 min	10	14	4.52	<0.001
≤ 20 min	9	48		

4. Apgar Score at 5min of birth

TABLE - 29

Apgar Score	No.	%
0 – 3	38	38
4 – 7	62	62

38 out of the 100 babies were found to have an apgar score of less than or equal to 3 consistent with significant asphyxia

Correlation of Apgar Score at 5 min with developmental delay

TABLE - 30

Apgar score at 5 min	Developmental Delay		Relative Risk	P value
	Yes	No		
0 – 3	9	26	1.18	>0.05
4 – 7	10	36		

5. Apgar Score at 20 min.

TABLE - 31

Apgar Score	No.	%
0 – 3	22	22
4 – 7	78	78

Out of the 38 babies who had apgar score of less than or equal to 3 about 16 babies had a better apgar score of more than 3 at 20 min. only 22% of the babies had apgar score of less than 4 at 20 min.

Correlation of Apgar score at 20 min with developmental delay

TABLE - 32

Apgar score at 20 min	Developmental Delay		Relative Risk	P value
	Yes	No		
0 – 3	11	18	2.46	< 0.001
4 – 7	8	44		

6. Resuscitation at 1 min of birth :

TABLE - 33

Resuscitation at 1 min	No.	%
Routine	38	38
PPV at 1 min	62	62

62 out of 100 babies required positive pressure ventilation either by bag mask or endotracheal tube (62%)at 1 min after birth.

PPV at 1 min TABLE - 34

Resuscitation	No.	%
Bag mask ventilation	58	93.5
Endo tracheal intubation and ventilation	4	6.5

About 38% of babies required only routine resuscitation & had mild asphyxia.62% of the babies required positive pressure ventilation at 1 min after birth. 93.5% of these babies required bag and mask ventilation and about 6.5 % of these babies required intubation & ventilation.

Correlation of Resuscitation at 1 min with developmental delay

TABLE - 35

Resuscitation at 1 min	Developmental Delay		Relative Risk	P value
	Yes	No		
PPV	14	37	1.21	> 0.05
Routine	5	25		

7. Sarnat & Sarnat Staging :

Babies who developed hypoxic ischemic encephalopathy as evidenced by altered consciousness, abnormality of tone and presence of convulsions were classified into 3 groups based on Sarnat and Sarnat clinical staging.

39 babies out of 100 developed hypoxic ischemic encephalopathy - Sarnat & Sarnat Stage I. 48% of babies developed HIE Stage II & 13% of babies developed HIE stage III

Breakup of cases according to HIE stages

TABLE - 36

HIE Stage	No.	%
I	39	39
II	48	48
III	13	13

Babies with severe encephalopathy – HIE stage III were found to be less in number compare to HIE stage I and HIE stage II

Correlation of Sarnat & Sarnat Staging with developmental delay

HIE stage I with HIE Stage II

TABLE - 37

Sarnat Stage	Developmental Delay		Relative Risk	P value
	Yes	No		
I	0	28	α (Infinite)	<0.01
II	8	34		

HIE stage I with HIE Stage III

TABLE - 38

Sarnat Stage	Developmental Delay		Relative Risk	P value
	Yes	No		
I	0	28	α (Infinite)	<0.001
III	11	0		

HIE stage II with HIE Stage III

TABLE - 39

Sarnat Stage	Developmental Delay		Relative Risk	P value
	Yes	No		
II	8	34	5.25	<0.001
III	11	0		

8. Duration of hospital Stay:

TABLE - 40

Duration of hospital Stay	No.	%
≤ 10 days	71	71
> 10 days	29	29

Duration of hospital stay of babies was arbitrarily classified into less than or equal to 10 days and more than 10 days. About 71% of babies were discharged within 10 days and 29% of the babies after 10 days.

Correlation of duration of hospital stay with developmental delay

TABLE - 41

Duration of Hospital Stay	Developmental Delay		Relative Risk	P value
	Yes	No		
> 10 days	12	13	3.84	< 0.001
≤10 days	7	49		

9. Convulsions :

TABLE - 42

Convulsions	No.	%
Present	51	51
Absent	49	49

About 51% of babies had atleast 1 episode of convulsions. 48 out of 51 babies with convulsions belonged to HIE Stage II and 3 babies belonged to HIE Stage III.out of the 51 babies only 43 completed follow up

Correlation of Convulsions with developmental delay

TABLE - 43

Convulsions	Developmental Delay		Relative Risk	P value
	Yes	No		
Present	15	28	3.31	>0.05
Absent	4	34		

10. Time of onset of convulsions.

N = 51

TABLE - 44

Time of onset	No.	%
< 12	22	22
12 – 24	18	18
> 24	11	11

22 out of the 51 babies developed convulsions within 12 hrs of birth (43%) and remaining 29 babies had developed convulsions after 12 hrs (57%).

Correlation of Time of onset of convulsion with developmental delay

TABLE - 45

Time of onset of convulsion	Developmental Delay		Relative Risk	P value
	Yes	No		
≤ 12 hrs	10	8	2.77	< 0.05
> 12 hrs	5	20		

INVESTIGATIONS :

11. Ultra sound cranium

TABLE - 46

USG cranium – Result	No.	%
Normal	92	92
Abnormal	8	8

USG cranium was taken in most babies in the first week. Few babies whose general condition was poor neurosonogram was done before discharge. About 92% of the babies with HIE had normal Neurosonogram findings. About 8% had abnormalities.

Out of 8 babies with abnormal neurogram 6 had cerebral edema, 1 had intraventricular hemorrhage & 1 had altered periventricular echogenicity.

Correlation of Ultra sound Cranium with developmental delay

TABLE - 47

Ultra sound Cranium	Developmental Delay		Relative Risk	P value
	Yes	No		
Abnormal	6	2	4.21	< 0.001
Normal	13	60		

12. Electroencephalogram :

TABLE - 48

EEG	No.	%
Normal Study	23	38.5
Abnormal record	37	61.5

EEG could be done only for 60 of the 100 babies. These included all babies in HIE stage II & 12 babies in HIE stage III

Out of the 60 babies 23 had a normal EEG (38.5%) &37 babies had abnormal EEG record (61.5%)

Types of abnormalities in EEG :

1. Poorly formed (low voltage) background waves in delta range. No abnormal discharge. Diffuse cerebral dysfunction.
2. Diffuse slowing with back ground beta to delta waves. Sharp wave discharges +

Correlation of Electroencephalogram with developmental delay

TABLE - 49

EEG	Developmental Delay		Relative Risk	P value
	Yes	No		
Abnormal	11	25	1.40	>0.05
Normal	5	18		

DISCUSSION

Birth Asphyxia and the consequent hypoxic ischemic encephalopathy are the common clinical problems encountered in the newborn ward. 23.5 % of the admission in the new born ward of Institute of Child Health and Research Centre, Madurai are birth asphyxiated babies.

Out of 100 babies followed up neurodevelopmental evaluation was completed in 81 babies (81%) upto one year of age. 19 babies did not complete the follow up.

Incidence of neurologic sequelae:

19 out of 81 babies i.e 23.4% were neurodevelopmentally abnormal at one year of age. In a similar study conducted by Asakura . H et al [33] showed 13.8 % children with HIE had poor neurologic outcome.

The incidence of neurologic sequelae was found to be 14% in babies with HIE (Robertson C Finer) [10]. Similar results were obtained in a study by Thornberg E et al (Acta Pediatrica 1995) [15]

The higher incidence of neurological impairment observed in present study may be due to high incidence of birth asphyxia in our community and

also due to apparently normal babies (HIE stage I) not completing follow up. Also since Govt. Rajaji Hospital, Madurai is a tertiary care centre more number of complicated (Obstetric) cases are referred. The present study correlates with the observation that about 25-30% of babies are found to have permanent sequelae following HIE (Nelson et al) [30]

Severity :

No baby with HIE Stage I had developmental delay and all babies with HIE Stage III had developmental delay. The incidence of sequelae in moderate HIE was found to be about 19% which is slightly lower than that resulted in the study of Robertson C Finer et al (24%).[10]

Types of delay :

Motor disabilities occurred in about 7.5% of all children with HIE. That is 31.5% of children with developmental delay (by TDSC) had motor disabilities. The risk was highest in HIE III (36%). Spastic quadriparesis was the most common abnormality found (83%).

Visual disabilities :

Visual disabilities occurred in about 11 children (13.5% of asphyxiated children). Strabismus was most common (72.0%) but was without visual

impairment in most children. Cortical blindness with visual loss was present in 2 out of 11 patients. (18%)

Hearing deficits :

Hearing deficits occurred in minority of asphyxiated children (2.5%). Early detection by otoacoustic emission testing helped in early referral for intervention.

Seizure disorder :

Seizure disorder with recurrent convulsions in infancy was noted in 3 children. All were from HIE stage II encephalopathy (3.7%).

Microcephaly :

Mean Head circumference was comparatively lower in children with HIE II & III compared to HIE I. Children with significantly less optimal head growth had development delay. Head circumference was normal in all children with normal neurological status. Similar results were obtained in study relating HIE to head growth (Pediatrics 2000)[24]

RISK FACTORS :

The factors significantly associated with neurodevelopmental deficit were HIE stage II, HIE stage III, delayed onset of first cry for more than 20 minutes, Low apgar score at 20 min. presence of convulsions, early onset of convulsions (< 12hrs), duration of hospital stay for more than 10 days and abnormal Ultra sound cranium.

These findings correlate well with other studies.

Sarnat & Sarnat HIE staging :

HIE stages showed marked correlation with neurodevelopmental deficit. None of the babies who had HIE stage I during neonatal period developed neurodevelopmental deficit. But HIE stage II and stage III were significantly associated with neurodevelopmental deficit. 8 of the 48 babies who were in Sarnat and Sarnat stage II and all the 11 babies with Sarnat and Sarnat stage III had neurodevelopmental deficit at one year.

In one study conducted in Swedish population [15] the observation made was similar, that is the neurodevelopmental outcome correlated well with the severity of HIE.

Robertson et al in 1993[21] in his study concluded that the outcome in mild and severe form of HIE is predictable but in moderate form, it is uncertain. However the babies had variable degree of deficit.

Delayed onset of First Cry :

The incidence of neurologic of sequelae was greater with delayed first cry >20 min ($p < 0.001$)

Apgar Score :

The incidence of developmental delay correlated well with Apgar score at 20 min. ($p < 0.001$) in this study. This correlates well with study by Nelson et al [32] that incidence of cerebral palsy increased with presence of low Apgar scores (1% at 5 min to 57% at 20 min)

Convulsions :

In our study, presence of convulsions and early onset of convulsions < 12 hrs was associated with increased risk of developmental delay($p<0.001$).

This correlates with study done by Thornberg et al [8] which showed seizures increased risk of sequelae by 2-5 fold. 67% had died or developed sequelae. Early onset of seizures increases risk of adverse outcome (75% with seizures at < 4 hrs had developmental delay.)

Duration of Hospital stay :

Hospital stay (persistent neurological abnormality) of more than 10days was associated with greater risk of neurologic sequelae in our study

The study by Scott H et al 1976 showed that 74% of asphyxiated infants who were normal neurologically by 2 weeks had no abnormal neurologic sequelae

EEG :

30.5% with abnormal record developed neurologic sequelae. but this was not statistically significant ($p>0.05$)

Children with Normal / maturally delayed interictal EEG patterns have 86% normal development. Mild depression or normal background was associated with normal outcome (Volpe) [8].

Only markedly abnormal record predicted subsequent morbidity or mortality(Clancy R et al). [8]

USG cranium :

6 out of 8 children with abnormal findings on ultra sound cranium had developmental delay (75%).($p < 0.001$) .

8 out of 9 infants with normal scan had normal outcome (Siegel MJ. HIE in terms infants).

The result correlates well with other studies. (Neur Croat 1992) [19]

Other Perinatal factors :

Other factors like maternal, illness, meconium stained liquor, mode of presentation, birth weight, mode of delivery, sex, apgar score at 5 min, parity and resuscitation at one minute were not significantly associated with neurodevelopmental deficit.

This is similar to this results obtained in studies relating to prognostic implication of perinatal factors. (J.Obstet 2000) [25]

Developmental Screening :

In this study, an attempt was made to find out the earliest time of assessment which can predict neurodevelopmental abnormality. Although neurodevelopmental assessment at the age of 3 months was able to detect neurodevelopmental delay significant proportion of them became normal as child grew older.

It was also observed that none of babies found to be abnormal at the age of 9 months became normal at the of 1 year. But those babies found to be normal in the assessment at 6 months persisted as normal till end.

Hence it is inferred from this study that assessment at the age of 6 months confirms normal neurodevelopmental status and assessment at the age of 9 months predicts abnormal neurodevelopmental outcome. However, these high risk babies must be followed up for longer period of time to detect subtle abnormalities which may appear later as the child grows older. It is essential that any deviation from normal neurodevelopmental should be detected early so that early interventional measures can be initiated as early as possible.

CONCLUSION

1. In this study out of 81 babies who completed follow up, 23.4% showed neurodevelopmental deficits.
2. The types of neurological sequelae found in HIE apart from delayed milestones were spastic cerebral palsy, hearing loss, visual impairment, epilepsy, and microcephaly.
3. The risk factors for neurodevelopmental deficit observed in this study are sarnat and sarnat HIE stage III , sarnat and sarnat HIE stage II , presence of convulsions, early onset convulsions of < 12 hrs, delayed first cry for more than 20 minutes duration of hospital stay > 10 days and abnormal USG cranium.
4. It is inferred from this study that the earliest age to detect definite neurodevelopmental abnormality is 9 months and the earliest age for predicting normal neurodevelopment is 6 months.
5. Approximately ¼ of the survivors developed neurodevelopmental deficit at one year. This emphasizes the need for early detection and intervention for reducing the severity of the disability.

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PROFORMA (ANNEXURE)

NEURO DEVELOPMENTAL OUTCOME IN CHILDREN WITH BIRTH ASPHYXIA

NAME : I.P. NO. :

AGE : ADDRESS :

SEX :

ANTENATAL H/O

1. HYPEREMESIS - Y/N
2. DRUG INTAKE - Y/N -IFA OTHERS
3. EXANTHEMATOUS ILLNESS - Y/N
4. ANTEPARTUM HEMORRHAGE - Y/N
5. DIABETES MELLITUS - Y/N
6. HYPERTENSION - Y/N
7. PREECLAMPSIA - Y/N

NATAL H/o :

1. PLACE OF DELIVERY :
2. MODE OF DELIVERY : NORMAL

   I) ASSISSTED
   II) CAESAREAN
3. MATERNAL SEDTION : Y/N
4. MECONIUM STAINED LIQUOR : Y/N
5. CRIED AFTER : MIN

RESUSCITATION:

i) SUCTION & O2
ii) BAG & MASK VENTILATION
iii) BAG & TUBE VENTILATION
iv) MECHANICAL VENTILATION

APGAR SCORE :

1 MIN
5 MIN
20 MIN

BIRTH WEIGHT :

SIBLING H/o

ON ADMISSION IN NEWBORN UNIT :

1.	General Condition	:	
2.	Cry	:	
3.	Activity	:	
4.	Colour	:	
5.	HR	:	
6.	RR	:	
7.	CVS	:	
8.	RS	:	
9.	P/A	:	
10.	CNS	:	TONE NEONATAL REFLEXES ANTERIOR FONTANELLE SPINE & CRANIUM

SARNAT STAGING :

1. CONSCIOUSNESS
2. MUSCLE TONE
3. TENDON REFLEXES
4. MYOCLONUS
5. SUCKING
6. MORO RESPONSE
7. GRAPING
8. OCULOCEPHALIC REFLEX

9. PUPILS
10. RESPIRATION
11. HEART RATE
12. CONVULSION

INVESTIGATIONS :

ULTRA SOUND CRANIUM

ELECTRO ENCEPHALOGRAM

TRIVANDRUM DEVELOPMENTAL SCREENING CHART – BASED FOLLOW UP

H/O

MILESTONES :

CONVULSIONS :

OTHERS :

EXAMINATION :

HEAD CIRCUMFERENCE :

TONE :

POWER :

DTR :

PLANTAR :

NEONATAL REFLEXES :

VISION :

HEARING :

TRIVANDRUM DEVELOPMENTAL SCREENING CHART BASED DEVELOPMENTAL ASSESSMENT

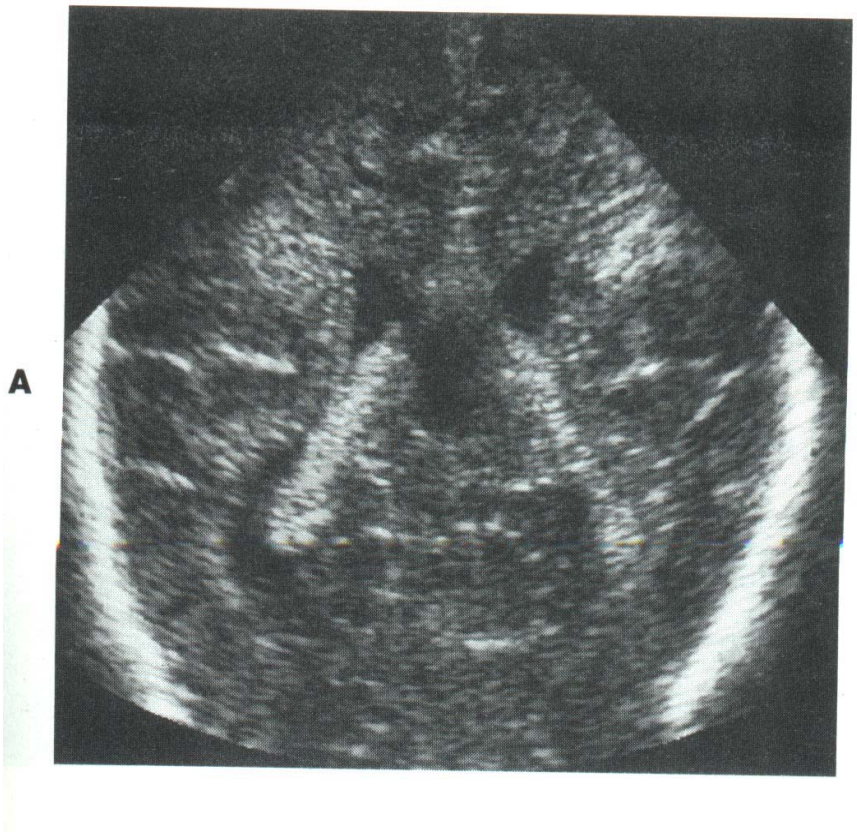
RESULTS :

CONCLUSION :

ABBREVIATIONS

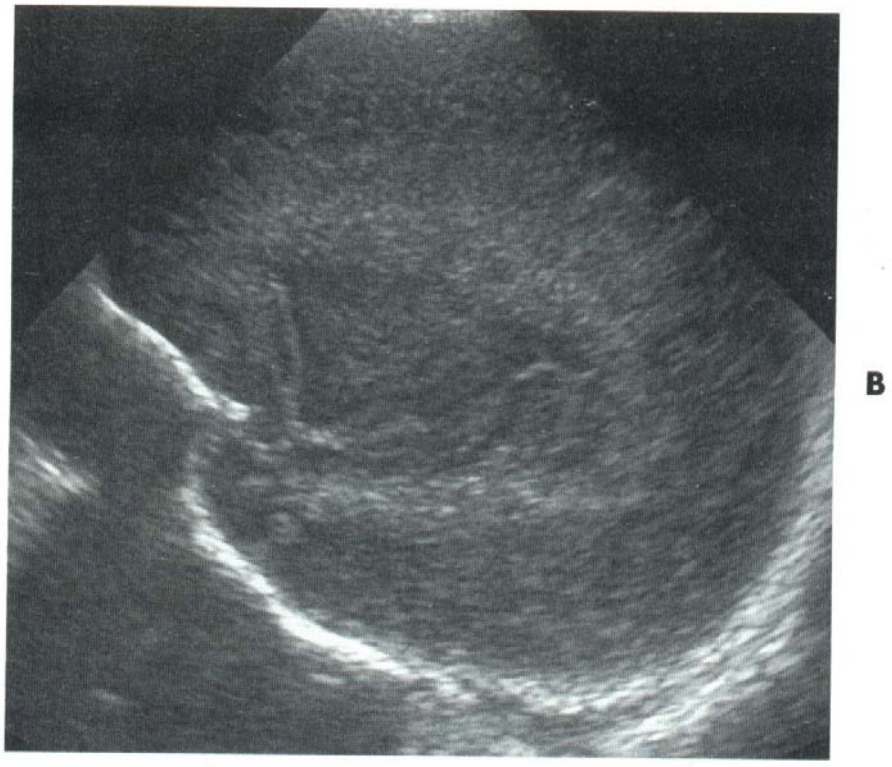
ADHD	-	ATTENTION DEFICIT HYPERACTIVITY DISORDER
APH	-	ANTEPARTUM HEMORRHAGE
ATP	-	ADENOSINE TRIPHOSPHATE
CDC	-	CHILD DEVELOPMENT CENTRE
CKBB	-	CREATINE KINASE BRAIN FRACTION
CNS	-	CENTRAL NERVOUS SYSTEM
CP	-	CEREBRAL PALSY
CT	-	COMPUTED TOMOGRAPHY
DDST	-	DENVER DEVELOPMENT SCREENING TEST
EEG	-	ELECTRO ENCEPHALOGRAM
HIE	-	HYPOXIC ISCHEMIC ENCEPHALOPATHY
ICH & RC	-	INSTITUTE OF CHILD HEALTH RESEARCH CENTRE
LN	-	LABOUR NATURAL
MRI	-	MAGNETIC RESONANCE IMAGING
NMDA	-	N- METHYL, D – ASPARTATE
PIH	-	PREGNANCY INDUCED HYPERTENSION
PPV	-	POSITIVE PRESSURE VENTILATION
USG	-	ULTRASOUND

PERIVENTRICULAR LEUKOMALACIA



Coronal sonogram : Bilateral increased echogenecity just lateral and superior to lateral ventricles

CEREBRAL EDEMA



Sagittal Sonogram : Diffuse cerebral edema with silhouetting of the sulci

MASTER CHART

S . No.	Mother's Name	Sex	Maternal illness present / Absent	Mode of Delivery	Meconium stained liquor	Birth weight	Time of First cry in mins	Apgar < 3 score at 20 min Y/N	Resuscitation at 1 min routine / PPV	Sarnat Staging	Time of onset of convulsions <12hrs Y/N	Duration of hospital stay	USG cranium	EEG
1.	Revathy	M	P	Forceps	P	2.25	5	N	R	I	-	3	N	-
2.	Reta Mary	M	P	LSCS	A	2.45	10	N	R	I	-	3	N	-
3.	Karthiga	F	A	L. N	P	2.7	5	N	PPV	I	-	4	N	-
4.	Saraswathi	M	P	Forceps	A	2.2	10	N	R	I	-	3	N	-
5	Kauupathal	M	A	L. N	P	2.3	5	N	PPV	II	N	11	N	A
6	Sakrtabanu	M	P	L. N	P	2.6	20	Y	PPV	III	N	13	N	A
7	Dhanalakshmi	F	A	Forceps	A	2.2	20	N	R	II	N	6	N	N
8	Mardayee	M	A	L. N	A	3.4	5	N	PPV	II	N	8	N	A
9	Muthumari	F	P	L. N	A	2.4	5	N	R	I		3	N	
10	Devi shree	F	A	L. N	A	2.75	20	N	R	II	N	12	N	N
11	Venkateswari	F	P	LSCS	A	2.25	20	Y	PPV	II	Y	11	N	A
12	Sevanammal	M	A	L. N	A	2.8	5	N	R	II	N	8	N	A
13	Aruna	M	P	L. N	P	2.8	10	N	PPV	II	N	7	N	N

14	Eswari	M	P	L. N	A	2.1	10	N	R	I		3	N	-
15	Selvi	F	A	LSCS	A	2.55	20	y	PPV	II	Y	11	N	A
16	Durgeswari	M	A	L. N	A	2.4	20	N	R	II	Y	7	N	A
17	Valarmathi	M	A	L. N	A	2.75	1hr	Y	PPV	III	-	14	N	A
18	Muthuselvi	M	A	L. N	P	2.25	5	N	PPV	I	-	4	N	-
19	Sri Devi	M	P	L. N	P	3.3	20	N	PPV	II	N	7	N	N
20	Jeyarani	M	A	L. N	A	2.35	5	N	R	I	-	4	N	-
21	Amirthavalli	F	P	Forceps	A	2.8	10	Y	PPV	III	Y	11	N	A
22	Kuruvathal	F	A	L. N	A	3.4	10	N	PPV	II	N	6	N	N
23	Nallamani	M	P	L. N	A	2.9	1hr	N	R	II	N	7	N	A
24	Thulasi	F	P	LSCS	A	2.45	5	N	R	I	-	3	N	-
25	Papathi	M	A	L. N	P	2.5	>1hr	Y	PPV	II	Y	10	A	A
26	Mala	M	A	L. N	A	2.3	10	N	PPV	II	N	6	N	A
27	Sumathi	F	A	L. N	A	2.5	1hr	N	R	II	Y	7	N	A
28	Shanthi	M	P	L. N	A	2.25	10	N	PPV	II	N	12	N	N
29	Rakku	M	A	L. N	A	3.6	5	N	PPV	I	-	3	N	-
30	Natchiammal	F	P	LSCS	A	2.1	20	N	R	I	-	3	N	-
31	Pavalakodi	M	A	L. N	A	2.7	20	N	R	II	N	11	N	A
32	Tamilselvi	M	A	L. N	A	2.8	10	N	PPV	II	N	7	N	A

33	Selva meena	F	P	L. N	P	3.2	10	N	PPV	II	N	7	N	N
34	Veerajothi	M	A	L. N	A	2.75	1hr	Y	PPV	III	Y	12	N	A
35	Arokyaselvi	F	A	L. N	A	2.6	20	N	PPV	II	N	7	N	N
36	Noorjahan	M	P	L. N	P	2.1	5	N	R	I	-	4	N	-
37	Pappa	F	A	LSCS	P	3.8	10	N	R	I	-	4	N	-
38	Chellammal	M	A	L. N	P	2.4	10	N	PPV	II	N	11	N	N
39	Jeyalakshmi	F	P	L. N	A	2.5	1hr	Y	PPV	III	-	12	N	A
40	Deepalakshmi	F	A	L. N	A	3.5	20	N	PPV	II	N	7	N	N
41	Veerammal	M	A	Forceps	A	2.3	1hr	N	PPV	II	Y	11	A	A
42	Vijayalakshmi	M	A	L. N	A	2.7	5	N	R	I	-	5	N	-
43	Saradha	M	P	L. N	P	3.9	20	N	R	I	-	5	N	-
44	Thangam	F	A	L. N	A	2.1	1hr	N	R	II	Y	12	N	N
45	Kanimozhi	M	A	L. N	A	2.8	5	N	PPV	II	N	7	N	N
46	Katheeja	F	A	L. N	P	2.5	1hr	N	PPV	II	Y	12	N	N
47	Aarthi	F	A	LSCS	A	2.2	>1hr	Y	PPV	III	-	11	A	A
48	Durgeswari	M	P	L. N	A	2.9	5	N	R	II	N	8	N	N
49	Jeyarani	M	A	L. N	A	2.35	20	N	R	I	-	3	N	-
50	Muthuselvi	F	A	Forceps	P	3.2	1hr	Y	PPV	II	Y	7	A	A
51	Vasanthi	M	A	L. N	A	2.4	5	N	PPV	II	N	6	N	N

52	Chellammal	M	P	L. N	A	2.6	10	N	PPV	II	N	7	N	N
53	Sundari	F	A	L. N	A	2.25	10	N	R	I	-	3	N	-
54	Sikkandar Beevi	M	A	L. N	A	2.7	>1hr	Y	PPV	II	Y	11	N	A
55	Vairamani	F	P	L. N	A	2.1	>1hr	y	PPV	II	Y	7	N	A
56	Lakshmi	M	A	L. N	A	2.8	5	N	PPV	I	-	3	N	-
57	Muthumari	M	P	LSCS	p	2.4	5	N	R	I	-	4	N	-
58	Jyothi	F	A	L. N	A	2.9	10	N	R	I	-	4	N	-
59	Maruthu pandi	M	A	L. N	A	2.3	10	N	PPV	I	-	5	N	-
60	Chitra	M	P	L. N	A	3.5	5	N	R	I	-	5	N	-
61	Periyanatchi	F	P	L. N	A	2.2	10	N	R	I	-	5	N	-
62	Raja lakshmi	M	A	Forceps	A	2.5	5	N	R	I	-	5	N	-
63	Vanilla	M	A	L. N	A	2.2	5	N	R	II	-	4	N	-
64	Pandi	F	A	L. N	A	2.6	1hr	N	R	II	Y	7	N	A
65	Thangam	F	P	LSCS	A	3.45	20	N	PPV	II	Y	12	N	A
66	Irulayee	M	A	L. N	A	2.5	20	N	PPV	II	N	6	N	N
67	Devi	M	A	L. N	P	2.4	1hr	Y	PPV	II	-	14	N	A
68	Amutha	M	A	L. N	A	2.8	10	N	PPV	III	N	7	N	N
69	Latha	F	A	L. N	A	2.5	5	N	R	I	-	3	N	-
70	Sangeetha	F	P	LSCS	A	2.2	>1hr	Y	PPV	I	Y	11	N	A

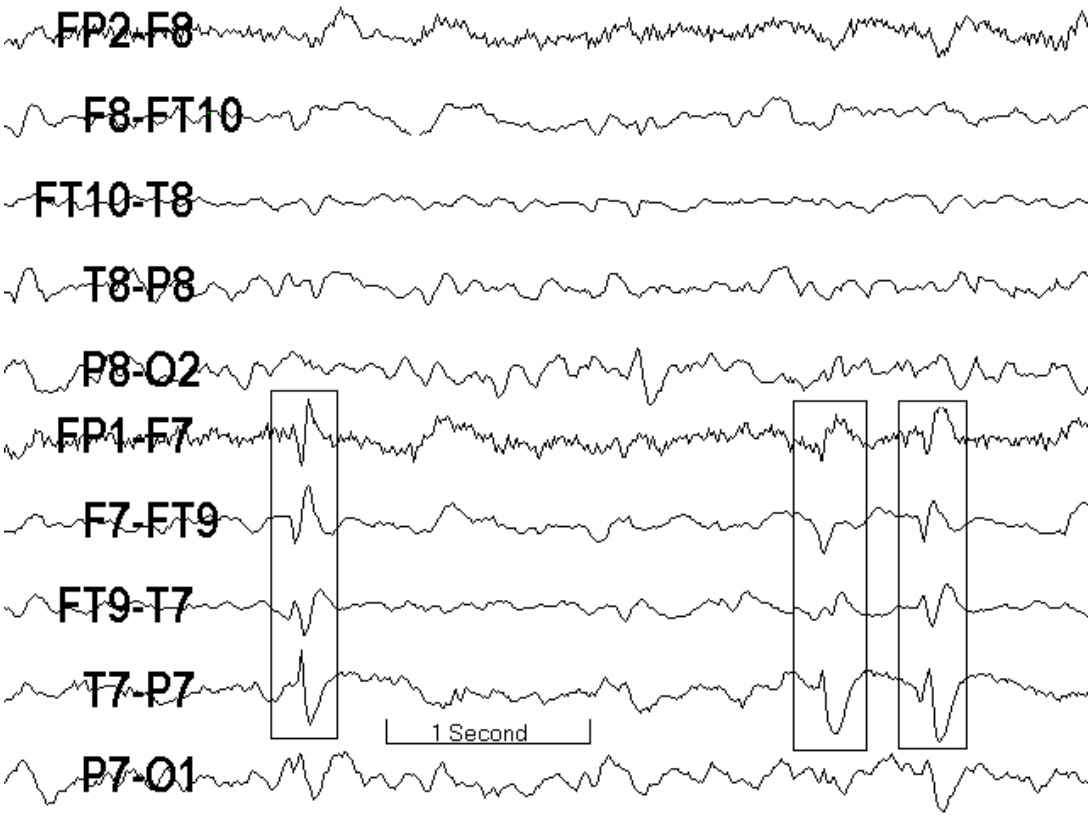
71	Manimegalai	M	A	L. N	A	2.6	5	N	PPV	I	-	3	N	-
72	Pandimeena	M	P	L. N	A	2.7	5	N	R	I	-	5	N	-
73	Akila	M	A	L. N	A	2.9	>1hr	N	R	II	Y	9	N	A
74	Ponnazhaghu	M	A	L. N	A	2.5	10	N	R	I	-	4	N	-
75	Gandhimathi	M	A	L. N	A	2.5	1hr	N	PPV	III	-	12	N	A
76	Muneeswari	F	A	L. N	A	2.6	1hr	Y	PPV	III	-	11	N	A
77	Selvi	M	A	L. N	P	2.3	10	N	PPV	I	-	4	N	-
78	Annalakshmi	M	A	L. N	P	2.7	20	N	R	I	-	4	N	A
79	Panchavarnam	M	A	L. N	A	3.1	5	N	PPV	II	N	10	N	-
80	Meena	F	A	Forceps	A	2.4	5	N	PPV	I	-	3	N	-
81	Vasuki	M	P	L. N	A	2.8	10	N	R	I	-	5	N	-
82	Priya	F	A	L. N	A	2.9	10	N	PPV	I	-	4	N	A
83	Lakshmi	M	A	L. N	A	2.3	1hr	Y	PPV	III	-	11	N	A
84	Divya	F	P	L. N	A	2.5	20	N	PPV	II	N	8	N	N
85	Vanitha	F	A	L. N	P	2.9	1hr	N	R	II	N	8	N	A
86	Mahalakshmi	M	A	LSCS	P	3.75	1hr	Y	PPV	I	Y	12	A	A
87	Rani	M	A	L. N	A	2.7	20	Y	PPV	I	N	11	N	A
88	Jeyasudha	M	P	L. N	A	2.2	5	N	PPV	II	-	3	N	-
89	Mareeswari	F	A	L. N	A	2.8	5	N	PPV	II	-	4	N	-

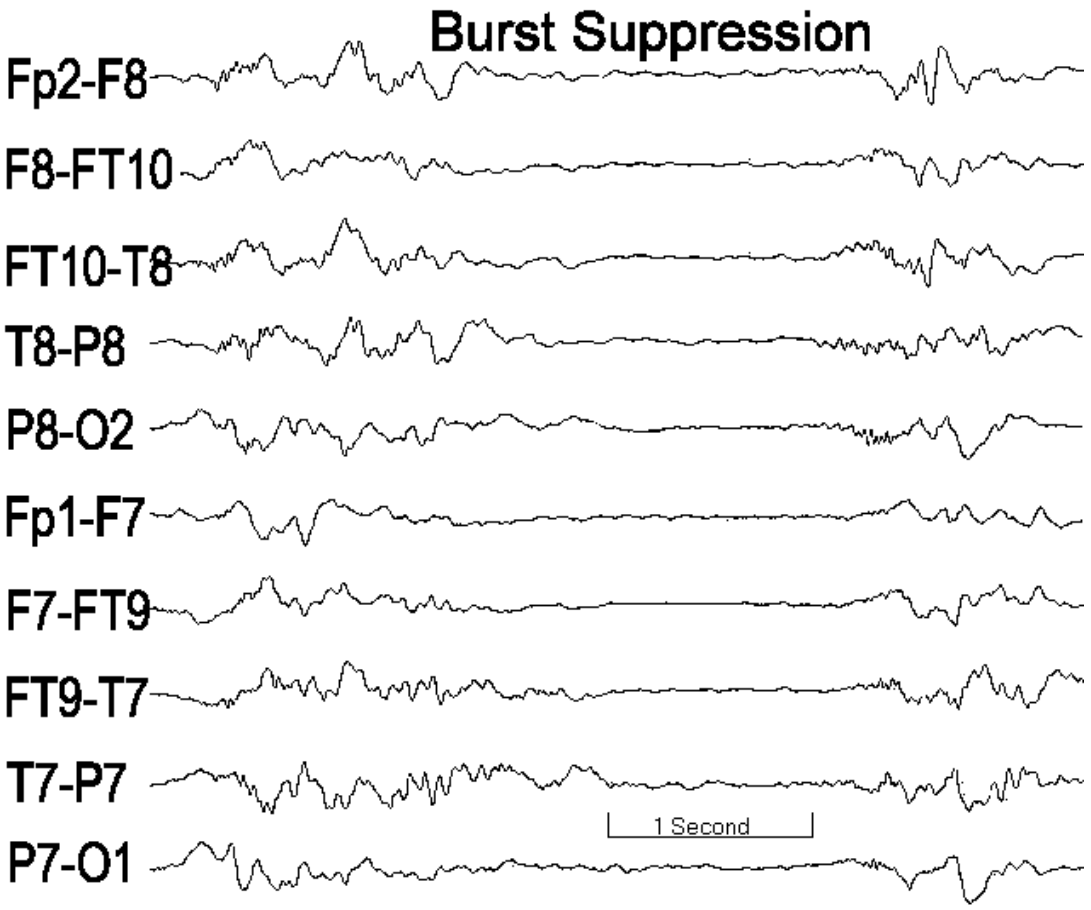
90	Fathima	M	A	L. N	A	2.7	>1hr	Y	PPV	II	Y	7	N	A
91	Kavitha	F	P	Forceps	A	2.6	20	Y	PPV	III	-	13	N	N
92	Thiraviyam	M	A	L. N	A	2.1	1hr	N	PPV	II	Y	9	A	A
93	Kamatchi	F	A	L. N	A	2.5	>1hr	N	PPV	II	Y	11	N	N
94	Vasantha	M	A	L. N	A	2.6	1hr	N	R	II	N	8	N	N
95	Raghavi	M	A	L. N	A	2.8	20	N	PPV	II	Y	14	N	N
96	Vimala	M	A	L. N	P	2.2	1hr	Y	PPV	III	-	9	A	N
97	Muneeswari	M	A	L. N	A	2.9	10	N	PPV	I	-	3	N	-
98	Jeyasheela	F	P	LSCS	A	3.2	10	N	PPV	I	-	3	N	-
99	Anuratha	M	A	L. N	A	2.3	20	Y	PPV	III	-	12	A	N
100	Mageswari	F	A	L. N	A	2.6	10	N	PPV	I	-	4	N	-

Y - YES P - PRESENT

N - NO A - ABSENT

FOCAL EPILEPTIFORM DISCHARGES




Burst Suppression
Fp2-F8
F8-FT10
FT10-T8
T8-P8
P8-O2
Fp1-F7
F7-FT9
FT9-T7
T7-P7
1 Second
P7-O1

OTOACOUSTIC EMISSION TEST

OtoRead

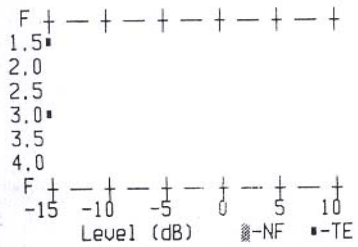
OTOACOUSTIC EMISSIONS TEST

Right

TE 64 sec avg U7.62

NAME: R. Hari Haran 9 month

F	P	TE	NF	SN
1.5	83	-15	-16	1
2.0		-19	-17	-2
2.5		-26	-26	0
3.0		-15	-21	6 P
3.5		-20	-22	2
4.0		-20	-23	3



Right : Refer

R Aravind

ARAVIND KUMAR. R.
AUDIOLOGIST

OtoRead

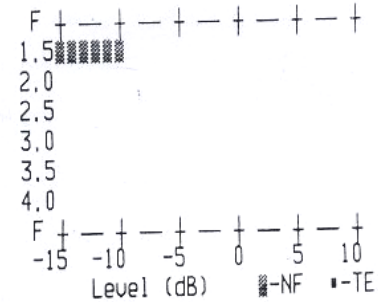
OTOACOUSTIC EMISSIONS TEST

Left

TE 64 sec avg U7.62

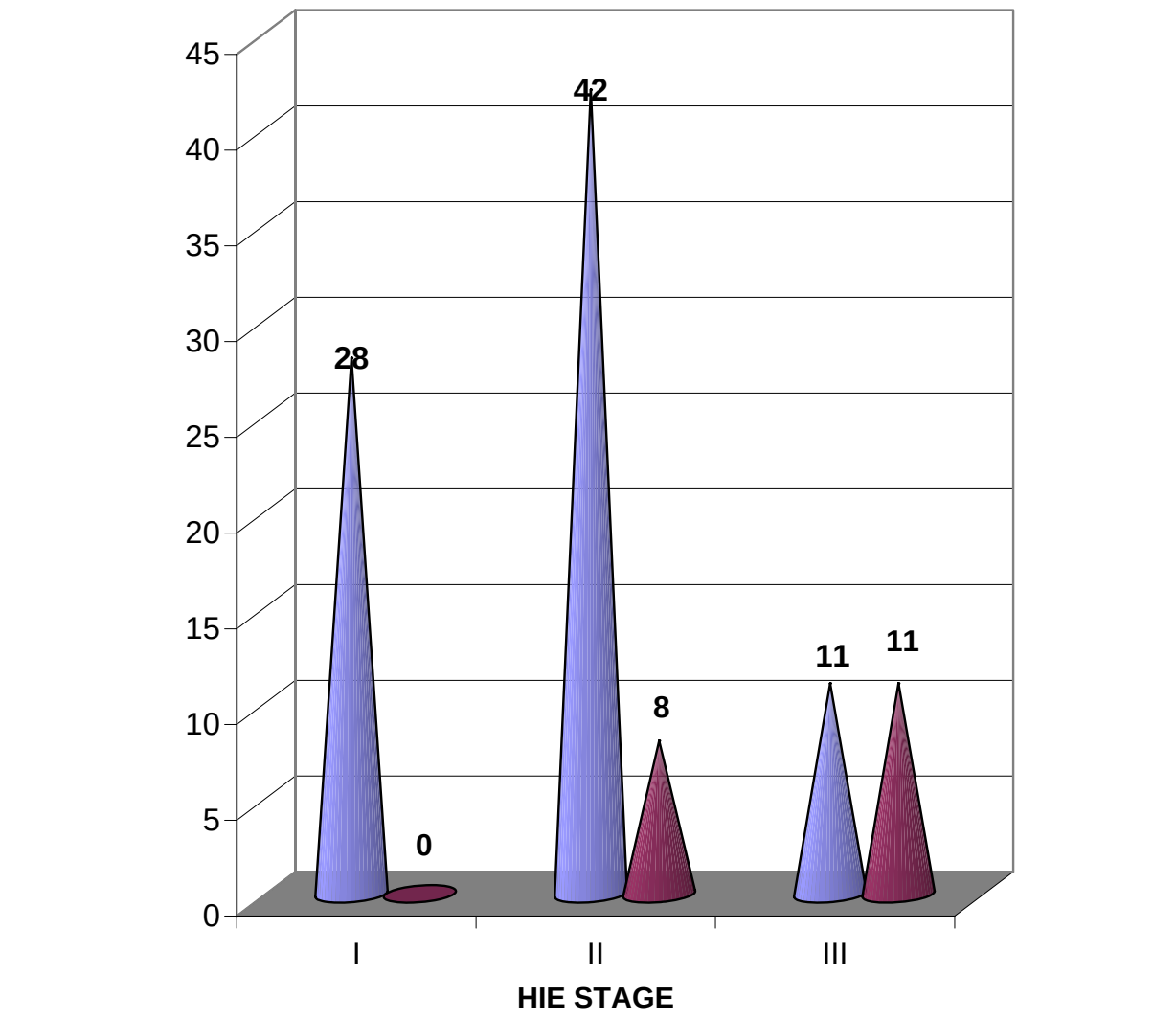
NAME: R. Hari Haran 9 month

F	P	TE	NF	SN
1.5	83	-13	-10	-3
2.0		-16	-17	1
2.5		-26	-21	-5
3.0		-24	-25	1
3.5		-22	-22	0
4.0		-22	-24	1



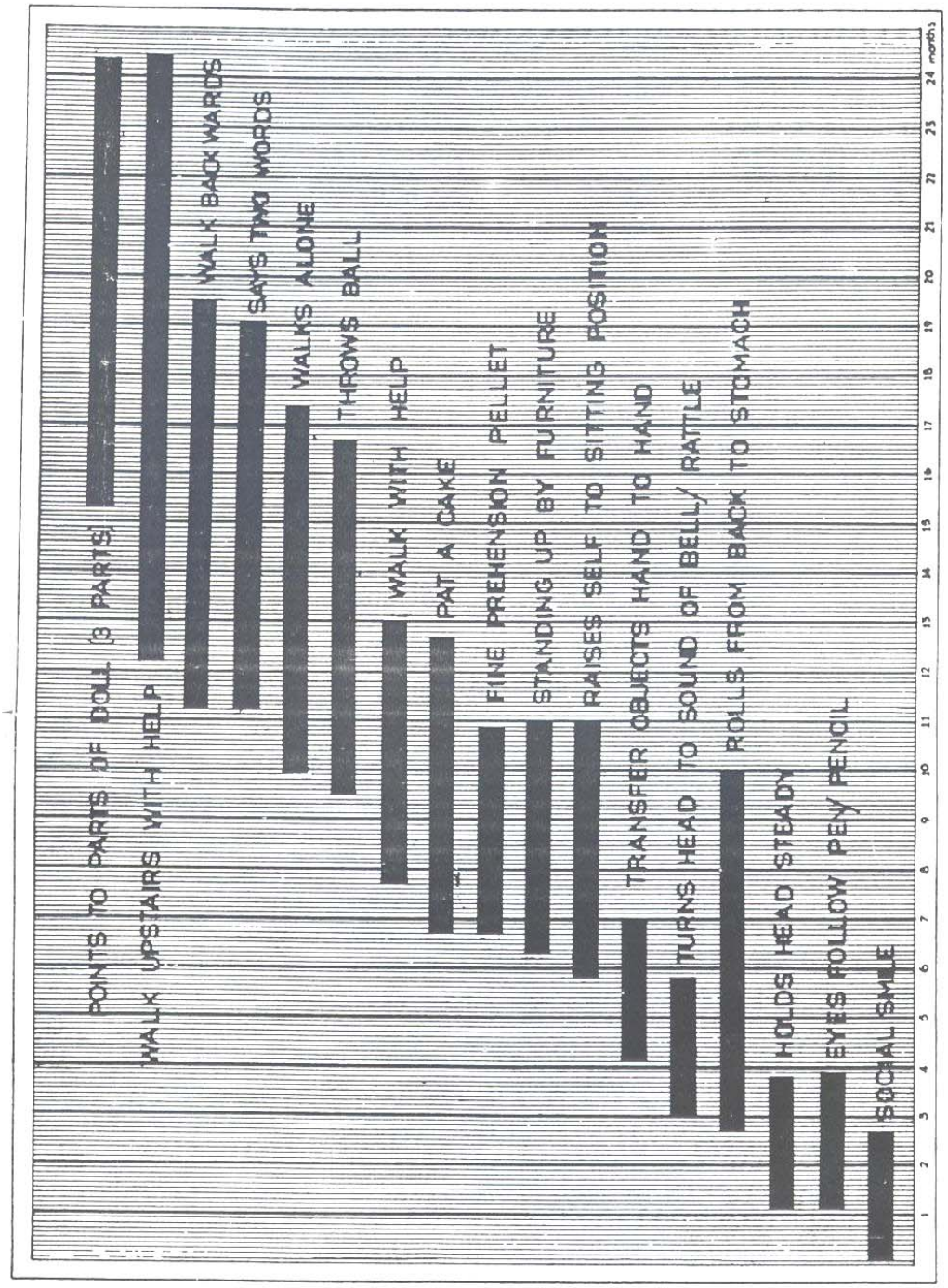
Left : Refer

DEVELOPMENTAL DELAY - AT 1 YEAR OF AGE



Trivandrum Developmental Screening Chart

ANNEXURE-I



Based on Baroda norms.

M.K.C. Nair, Babu George, Elsie Philip. Indian Pediatr 1991; 28: 869-72.

CHILD DEVELOPMENT CENTER PROJECT, S.A.T. HOSPITAL, TRIVANDRUM