

EVALUATION OF HYPOXIC ISCHEMIC ENCEPHALOPATHY IN PERINATAL ASPHYXIA BY USING SARNAT AND SARNAT SCORE.

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ABSTRACT

The present study was conducted to evaluate the staging of Hypoxic Ischemic Encephalopathy in Perinatal Asphyxia. Sarnat grading scale has been using for classification for HIE of new born due to insufficient oxygen to the brain which leads to alteration in consciousness, muscle tone, activity, primitive reflexes, heart rate, respiration and pupil, seizures and EEG. Among the 80 babies participated in the study, 21 (26%) had mild clinical features (stage-1), 40 (50%) babies had moderate manifestation (stage-2) and 19 babies (24%) developed severe (stage-3) encephalopathy. Seizures found in 59 (73.75%) babies and 21(26.25%) were non-seizures. Mothers of asphyxiated babies had Obstetric complications and maternal illness like Abnormal presentations and prolonged labour (47.82%), Premature rupture of membranes (28.98%), Pregnancy induced hypertensions (7.29%), Oligohydramnios (4.34%), Abroptio placenta (2.89%) and Cord prolapsed (2.89%). Eleven babies were free from obstetric complications (17.75%). Obstetric complications and maternal illness were significantly correlated with HIE and convulsion (p value< 0.0001).

KEYWORDS: Hypoxic Ischemic Encephalopathy (HIE), Convulsion and Obstetric complications.**INTRODUCTION**

Hypoxic Ischemic Encephalopathy is an abnormal neurobehavioural state in which the main pathogenic mechanism is impaired cerebral blood flow. Asphyxial events occur in 90% of term infants due to antepartum and intrapartum period as a result of impaired gas exchange across the placenta that leads to inadequate provision of oxygen and removal of carbon dioxide and hydrogen ion from the foetus. The remainder of events occur in the postpartum period, secondary due to pulmonary, cardiovascular or neurologic abnormalities. Etiologies of Perinatal hypoxia ischemia are maternal factors such as hypertension, diabetes, cardiac, pulmonary and neurologic diseases, placental infarction, fibrosis, abruption, umbilical cord prolapsed, foetal anaemia, infections, persistent pulmonary hypertension of new born (PPHN).^[1]

The pathophysiology of hypoxic ischemic change is with brief asphyxia showing there is a transient increase, followed by decrease in heart rate, mild elevation in blood pressure, increase in central venous pressure without any disturbance in cardiac output but with diving reflex. In prolonged asphyxia cerebral blood flow becomes dependent on systemic BP in which a low cardiac output leads to hypotension and impaired

cerebral blood flow resulting in anaerobic metabolism and eventual intracellular energy failure due to an increase in the utilization of glucose in the brain and fall in concentration of glycogen, phosphocreatine and ATP. Hypoxia induces vascular dilatation increase glucose availability in which anaerobic metabolism produces lactic acid. Cellular changes occur due to diminished oxidative phosphorylation and ATP production. This energy failure impairs ion pump function, causing accumulation of intracellular Na^+ , Cl^- , H_2O and Ca_2^+ , extracellular K^+ and excitatory amino acid (EAA), neurotransmitters glutamate. Impairment of oxidative phosphorylation can occur during the primary asphyxial episode as well as during a secondary energy failure that usually occurs approximately 6 to 24 hrs after the initial insult. Cell death can be either immediate or delayed and either apoptotic or necrotic. Immediate neuronal death is due to intracellular osmotic overload of Na^+ and Ca_2^+ as seen with excessive EAA acting on ionotropic glutamate receptors. Nevertheless delayed neuronal death occurs secondary to uncontrolled activities of enzymes lipases, proteases and second messenger systems within the cell, perturbation of mitochondrial respiratory electron chain transport and generation of free radicals. EAA also activate AMPA receptor channel leading to oligodendrocyte progenitor cell death.^[2,3]

Reperfusion of ischemic tissue may cause injury as it can promote the formation of excess reactive oxygen species viz. SOD, HO, Hydroxyl, singlet oxygen which can overwhelm the endogenous scavenger mechanism, thereby causing damage to the cellular lipids proteins and nucleic acids as well as to the blood brain barrier.^[4]

Increased intracranial pressure (ICP) or cerebral oedema is the effect of brain damage which peaks at 36 to 72 hours after the insult. Seizures are described in 20% to 50% of infants with HIE and usually starts between 6 to 24 hours after the insults ie. during second energy

failure. They are more often seen in Sarnat stage-II rarely in Sarnat-III and almost never seen in HIE-I. Seizures may be associated with increased cerebral metabolic rate which could lead to further cerebral injury.^[1]

The diagnosis of perinatal HIE requires an abnormal neurologic examination on the first day following birth. The clinical spectrum of HIE is described as stage-1, stage-2 and stage-3 based on Sarnat and Sanat scoring system. Therefore Sarnat and Sarnat grading is used to determine the status of neurological insults of the asphyxiated babies participated in the study.

Fig:1 Staging's of Hypoxic Ischemic Encephalopathy (HIE) (Sarnat et al 1976)^[5]

Signs and Symptoms	HIE STAGES		
	Stage-1 (Mild)	Stage-2 (Moderate)	Stage-3 (Severe)
Level of consciousness	Hyperalert, irritable	Lethargic or obtunded	Stuporous, comatosed
Neuromuscular control	Uninhibited overactive	Diminished spontaneous movement	Diminished or absent spontaneous movement
Muscle tone	Normal	Mild hypotonia	Flaccid
Posture	Mild distal flexion	Strong distal flexion	Intermittent decerebration
Stretch reflexes	Overactive	Overactive/ diminished	Decreased or absent
Segmental myoclonus	Present or absent	Present	Absent
Complex reflexes Suck	Normal	Suppressed	Absent
Moro	Weak	Weak or absent	Absent
Oculovestibular	Strong, low threshold	Weak, Incomplete high threshold	Absent
Tonic neck reflex	Normal	Overactive	Weak or absent
	Slight	Strong	Absent
Autonomic function	Generalized sympathetic	Generalized parasympathetic	Both system depressed
Pupils	Mydriasis	Miosis	Midposition, often unequal;
Respirations	Spontaneous	Spontaneous; occasional apnea	poor light reflex
Heart rate	Tachycardia	Bradycardia	Periodic; apnea
Bronchial and salivary secretions	Sparse	Profuse	Variable
Gastrointestinal motility	Normal or decreased	Increased diarrhoea	Variable
Seizures	None	Common focal or multifocal (6-24 hrs)	Uncommon (excluding decerebration)
Electroencephalic findings	Normal (awake)	Early: generalized low-voltage, slowing (continuous delta and theta) Later-periodic pattern(awake); seizure focal or multifocal; 1.0 to 1.5 Hz spike and wave	Early; periodic pattern with isopotential phases Later; totally isopotential
Duration of symptom	<24 hours	2-14 days	Hours to weeks
Outcome	About 100% normal	80% normal; abnormal if symptoms more than 5 days	About 50% die; remainder with severe sequelae

MATERIALS AND METHODS

The study was conducted for the doctoral research at department of Anatomy in collaboration with department of Paediatrics and department of Biochemistry JIPMER, Pondicherry during 2008 to 2011. The design of the study was cleared by Institutional ethics committee and Research council. Inclusion criteria for selection of the asphyxiated babies and controls were term appropriate with gestational age babies and weight. Preterm and post term, large gestational age (LGA) and small gestational age (SGA) and babies with congenital malformations were excluded. Neonatal asphyxia can be diagnosed by the presence of the following criteria Apgar score <3 at 5

mins, changes in fetal heart rate <60 beats/min, meconium stained liquor, clinical evidence of Hypoxic ischemic encephalopathy (HIE). HIE was evaluated by using Sarnat and Sarnat score.

Protocol for Grading the Stages of HIE^[5]

Staging of Hypoxic ischemic Encephalopathy by Sarnat & Sarnat Score

HIE- Stage-I

- The symptoms of HIE stage-1 are maximal during the first 24hours after birth and then progressively diminish. Consciousness is not impaired except for a brief interval of lethargy immediately after birth.

- The characteristic features are jitteriness- a hyperalert state in which there are prolonged periods of wakefulness, irritability and excessive responsiveness to stimulation. The typical response to stimulation is a low frequency, high amplitude shaking of limbs and jaw.
- Muscle tone is normal when newborn is at rest or suspended vertically or horizontally.
- The anterior fontanelle is soft, cranial nerve function is normal and convulsion do not occur.
- EEG is usually normal.
- Duration of the insult is the first 24 hours.
- Outcome will be 100% normal
- Hypotonia is severe. The newborn lies motionless with legs extended and fully abducted and arms remain in any position they fall.
- There is no grasp reflex, no flexion movement of the head and resistance of limbs.
- Pupillary and doll's eye reflexes are normal, but oculomotor palsies may be present.
- Sucking and swallowing reflexes are depressed or absent.
- Convulsions increase with frequency and severity of encephalopathy.
- EEG markedly suppressed.
- Duration- Hours to weeks
- Outcome - 50% die; remainder develops severe sequelae

HIE- Stage-II

- Children with moderate HIE are lethargic or obtund for at least during the first 12 hours after birth.
- Hypotonia is present at rest and spontaneous movement of the limb is decreased.
- Proximal weakness in which the muscle about the shoulder are weaker than the muscle around the pelvis.
- The period between 48 and 72 hours after birth is a critical interval during which the encephalopathy either worsens or improves.
- Lack of improvement leading to convulsion and cerebral oedema.
- EEG always abnormal
- Duration of the insult 2-14 days
- Outcome ,80% normal; abnormal if symptoms last for more than 5 days

HIE- Stage-III

- Newborns are stuporous and comatosed immediately after birth.
- Respirations are irregular or periodic
- Apnea and convulsion begin during the first 24 hours after birth and progress to tonic and multifocal before the end of 1st day.

STATISTICAL ANALYSIS

The association between groups were analysed by Carl Pearson Correlation coefficient by using Graph pad (InStat, San Diego, USA).

RESULTS

The asphyxiated babies recruited in this study were affected neurological insult and they were classified into three stages viz. Stage-I, Stage-II and stage-III based Sarnat and Sarnat scoring system. Therefore all babies with asphyxia had HIE. Among the 80 cases 21(26.25%), 40(50%) and 19(23.75%) were grouped in HIE-I, HIE-II and HIE-III respectively. There were 50 (62.5%) males and 30(37.5%) female children had HIE in which 10 (12.5%) males and 11(13.75%) females in HIE-I, 28 (35%) males and 12 (15%) females in HIE-II and 12 (15%) males and 7(8.75%) females in HIE-III. 59(80%) (Table 1). HIE babies had convulsion in which 40(50%) and 19(30%) were males and female babies respectively (Table 2). Obstetric complications and maternal illness significantly correlated with severity of stages of Hypoxic ischemic Encephalopathy (p value< 0.0001). Convulsion was positively associated with Obstetric complications and maternal illness (p value<0.05) (Fig.1).

Table 1: Showing distribution of cases with gender according to HIE staging.

Gender	HIE-I		HIE-II		HIE-III		Total (%)
	n	%	n	%	n	%	
Male	10	12.5	28	35	12	15	50 (62.5%)
Female	11	13.75	12	15	7	8.75	30(37.5%)
Total	21	26.25	40	50	19	23.75	80(100%)

Table 2: Exhibiting Distribution of Convulsion based on HIE staging's.

HIE staging	Number of cases		Cases with Convulsion	
	Male	Female	Male	Female
HIE-I	10(12.5)	11(13.75%)	0(%)	0(%)
HIE-II	28(35%)	12(15%)	28(35%)	12(15%)
HIE-III	12(15%)	07(8.7%)	12(15%)	7(15%)
Total	50(62.5%)	30(37.4%)	40(50%)	19(30%)
	80(100%)		59(80%)	

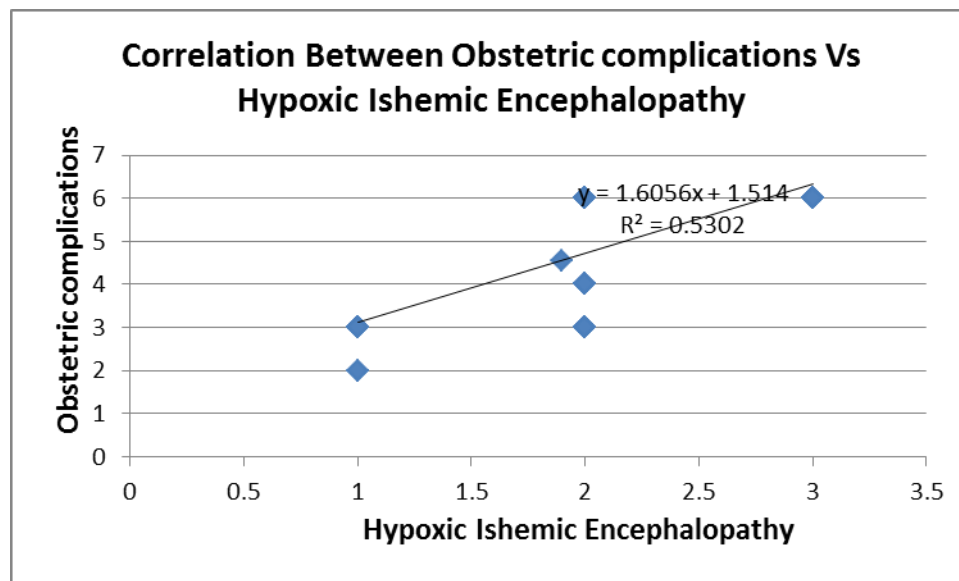


Figure:2 Depicting Correlation coefficient (Pearson) between Hypoxic Ischemic Encephalopathy and Obstetric complications. This correlation line $y=1.605x+1.514$ was drawn from the data obtained from Perinatal asphyxia cases (n=69) which showed R2 value of 0.530 (r value 0.7532 and p value < 0.0001).

DISCUSSION

This study was designed to understand the Protocol of Sarnat and Sarnat score for grading the stages of hypoxic ischemic encephalopathy. Sarnat and Sarnat et al explored the three staging of Hypoxic Ischemic Encephalopathy by the following signs and symptoms viz. Level of consciousness, Neuromuscular control, Muscle tone, Posture, Stretch reflexes, Segmental myoclonus, Complex reflexes Suck, Moro, Oculovestibular, Tonic neck reflex, Autonomic function, Pupils, Respirations, Heart rate, Bronchial and salivary secretions, Gastrointestinal motility, Seizures, Electroencephalic investigations.

Cowan et al reported that the brain images showed acute insult in the immediate period leads to neonatal brain injury in which the MRI or post mortem examinations in 351 full term infants with neonatal encephalopathy, early seizure acquired antenatally and early post partum period.^[6] Our study agrees the previous report in which Hypoxic Ischemic Encephalopathy with seizures were due to disturbance in the oxygenation to the brain of the babies during antenatal and post natal period causes alteration in gene expression and protein synthesis which attributes DNA damage.^[4] Yoon BH et al documented that antenatal exposure to intra amniotic inflammation and evidence of a systemic fetal inflammatory response (funisitis) are strong and independent risk factors for the subsequent development of cerebral palsy.^[7] In our study antepartum insults like intramniotic inflammation causes HIE which was significantly correlated with micronucleus score. Low JA et al suggested that periodic monitoring of heart rate, fetal blood gas and acid base balance can be useful fetal assessment paradigm for intrapartum asphyxia in which intervention and delivery may have prevented the progression of mild asphyxia and modified the degree of

moderate or severe asphyxia in some cases^[8] Though obstetric complications of the cases of current study leads to foetal distress which later hampering the blood circulation to vital organs of the baby results significant DNA damage. Another study of Low JA et al states that risk factors included severe intrapartum fetal hypoxia, moderate and severe newborn respiratory complications in which 26% of mild and moderate contributed encephalopathy and 66% of cases were severe encephalopathy.^[9] Our study agrees with the previous reports that 26.25%, 50% and 23.75% had HIE-1, HIE-2 and HIE-3 respectively.^[9] Low JA et al reported that Intrapartum asphyxia with a severe metabolic acidosis accounts for complications in all newborn systems.^[10] Our study agrees with previous reports as correlation of multiorgan dysfunction in perinatal asphyxia with DNA damage.^[16] Blair et al reported that all spastic cerebral palsy was intrapartum asphyxia in the possible cause of the brain damage.^[11] The current study agrees Apnea, Hypotonic and convulsion were significantly manifested in HIE-2 and 3 stages. Hull J et al reported that the fall in incidence of hypoxic ischemic encephalopathy has occurred during a period of falling perinatal mortality rate. It was instructive to find that infants born vaginally and without obstetric intervention formed of larger fraction of the severely affected infants in later period.^[12] Our study agrees the previous reports as obstetric complications in perinatal asphyxia shows significant DNA damage^[15] (Fig.1). Ashwal.S et al recommended, observations of coma, brain stem reflexes with abnormalities of EEG, CBF within 24-48 hours is suggestive of brain death in newborn.^[13] In the current study we found that the manifestations of HIE such as absence of grasp, pupillary and flexion, suckling and swallowing reflexes, comatosed, EEG markedly reduced and 35% of the babies were expired.^[14]

CONCLUSION

Sarnat and Sarnat Score is a unique Diagnostic Tool for Evaluation of staging Hypoxic Ischemic Encephalopathy in Perinatal Asphyxia.

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