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International Journal of Current Research
Vol. 9, Issue, 12, pp.63363-63366, December, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

ROLE OF CRANIAL USG IN TERM NEONATES WITH HYPOXIC ISCHAEMIC ENCEPHALOPATHY AND ITS CO-RELATON WITH NEURODEVELOPMENTAL OUTCOME

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ARTICLE INFO

Article History:
Received 07th September, 2017
Received in revised form
23rd October, 2017
Accepted 09th November, 2017
Published online 31st December, 2017

Key words:

Perinatal Asphyxia,
Hypoxia,
Encephalopathy.

ABSTRACT

Background: Perinatal asphyxia leading to hypoxic-ischemic encephalopathy (HIE) is still leading cause of infant and under-five mortality and significant morbidity in developing countries. Cranial USG is a sensitive, cheap and non invasive tool for early diagnosis of HIE and persistence of these lesion on serial USG can be correlated with subsequent neuro-developmental outcome.

Method: This prospective observational study was conducted in SNCU and NICU of a tertiary care hospital of India on term neonates with perinatal asphyxia.

Results: 72% babies on day 3, 60% of babies on day 7 and 44% babies on 6 weeks of life had some changes in USG Brain**.** Most of the babies with definite USG changes had stage 3 (Sarnat & Sarnat) stage of HIE. Among 72% , having early abnormal USG findings, 64% were found to have abnormal neurological findings in Amiel-Tison scale and 56% in TDSC developmental scale on follow up at 6 weeks.

Conclusion: Cranial Ultrasonography specially in early stage have role in detecting lesions and correlating with subsequent neurodevelopmental outcome which will help in early diagnosis and early intervention in neurologically cripple child.

Citation: Dr. Biswajit Das, Dr. Debasree Guha and Dr. Paramita Mukhopadhyay, 2017. "Role of cranial usg in term neonates with hypoxic ischaemic encephalopathy and its co-relaton with neurodevelopmental outcome", *International Journal of Current Research*, 9, (12), 63363-63366.

INTRODUCTION

Despite major advances in monitoring technology and knowledge of fetal and neonatal pathologies, perinatal asphyxia or, more appropriately, hypoxic-ischemic encephalopathy (HIE), remains a serious condition that causes significant mortality and long-term morbidity. The incidence of hypoxic-ischemic encephalopathy is reportedly high in countries with limited resources; however, precise figures are not available. Birth asphyxia is the cause of 23% of all neonatal deaths worldwide (Bulletin of WHO*,* 2009). It is the fifth largest causes of death of children younger than 5 years (8.5%) (Joy E Lawn *et al*., 2007). More than a million children who survive birth asphyxia develop problems such as cerebral palsy, mental retardation, learning difficulties, and other disabilities (Bryce *et al*., 2005). Cranial ultrasonography (CUS) of the brain is the diagnostic modality of choice in the screening of infants who are at risk of brain injuries. The reason for the increasing acceptance of ultrasonography includes its convenience (portability), safety, non invasiveness, wide spread availability and excellent resolution.CUS of neonatal brain is sensitive for the detection of edema, hemorrhage, periventricular leukomalacia and hydrocephalus. Resistive index of the middle cerebral arteries, if correlated with gestational age, can add more information (Christine P. Chao *et al*., 2006). An attraction of ultrasonography of the neonatal brain is the potential of securing information early on about the short term prognosis and risk of later neurodevelopmental handicap in survivors of HIE. However, these lesions observed on ultrasound may not have a simple and straight relationship to neurodevelopmental outcome as shown by a number of published literatures on follow up data. It is true that when there are positive scan findings, the risk of neurodevelopmental sequelae in a population of infants with similar scan findings might be known, but whether the individual baby will or will not develop those sequelae cannot yet be judged with certainty from the scan findings (Jacquie Waller *et al.,* 2006). The objective of this study was *to* determine the role of cranial ultrasonography in identifying the different lesions of Hypoxic ischemic encephalopathy in term neonates and it's correlation with neurodevelopmental outcome.

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MATERIALS AND METHODS

This prospective observational study was conducted in Sick Newborn Care Unit (SNCU) and NICU of Department of Pediatric Medicine and Department of Radiology of R. G.Kar Medical College and Hospital, a tertiary care hospital in

eastern India. Period of the study was 1 year from April 2015-March 2016. 50 babies born in our institution with history of perinatal asphyxia were included in this study. Those babies were assessed clinically for grading of HIE (Sarnat & Sarnat staging) after birth & USG brain at 3 days, 7 days, 6 weeks and 6 months along with Neurodevelopmental assessment with the help of Amiel-Tison (ATN) methods & Trivandrum Developmental Screening Chart (TDSC). Proper informed consent was taken from the parents of the babies and permission was taken from the Institutional Ethics Committee prior to the study. Babies included were full term (37 completed gestational week) and birth weight ≥ 2500 gm, singleton pregnancy, with either a/b/c

a) Apgar score <6 at 5 minutes of birth
b) Delay in establishing spontaneous respiration more than 5 minutes
c) Required positive pressure ventilation at birth to establish spontaneous respiration or Evidence of encephalopathy e/f
e) Seizure alone
f) Any two of the following criteria lasting > 24 hours.
   - Difficulty in maintaining respiration (central cause)
   - Difficulty in feeding (Central Cause)
   - Abnormal muscle tone and reflexes (Hypo or hypertonia)

Babies with Septicemia (sepsis screen positive), congenital anomaly, severe birth trauma, suspected intrauterine infection/ inborn error of metabolism, Meconium aspiration syndrome were excluded from study. All term babies with history of perinatal asphyxia as per inclusion criteria were assessed clinically by using Sarnat & Sarnat staging and USG scan was performed with the electronic ultrasonography machines equipped with 3.5, 5 & 7.0-MHz transducers at 3 days, 7 days and 6 weeks after birth.

Clinical Findings of three stages of HIE include (Summarization of Sarnat & Sarnat Staging)-

Stage I (first 12 to 24 hours): hyper alertness, hyper excitability, seizures, apnea, jitteriness, weakness;
Stage II (24 to 72 hours); coma, respiratory arrest, apnea, abnormal oculomotor reflexes, impaired pupillary response.
Stage III (>72 hours); persistent stupor, abnormal suck, swallow and gag, weakness and severe hypotonia.

All the data will be collected and compiled during the period of study. At the end of the study data will be subjected to a suitable complete statistical analysis to document any significant difference between different cohorts.

Data Analysis

Distribution of study population on stages of encephalopathy showed that most of the babies, 54% have features of Stage 2 encephalopathy and only 12% babies have clinical features of severe hypoxemic brain damage, in form of Stage 3 encephalopathy.

Cranial ultrasound findings

Day 3 findings

A completely normal scan was found in 14 of the 50 infants. The remaining 36 had some changes. Diffuse white matter increased echogenicity (DWMIE) were present in 35, Effacement of the convolutional markings (ECM) in 36 babies, Obliteration of the surrounding fluid spaces (OSFS) in 26, Ventriculomegaly in 8, coarsening of the brain echotexture (CBE) in 12, intraventricular haemorrhage in six, Intra-parenchymal hemorrhage (IPH) in 2 and cerebral atrophy (CA) in none of the babies were found.

Table 1. Findings of definite changes in USG Brain in different stages of HIE

	Stage 1	Stage 2	Stage 3
	Definite changes	Definite changes	Definite changes
DAY3	7	22	6
DAY7	2	12	6
6 WEEKS	0	7	5
Chi-Square test	P=0.1479		
Contingency coefficient	0.33		
DF	4		

Day 7 findings

A completely normal scan was found in 20 of the 50 infants. The remaining 30 had some changes. Diffuse white matter increased echogenicity (DWMIE) were present in20 of the50, Effacement of the convolutional markings (ECM) in 22 babies, Obliteration of the surrounding fluid spaces (OSFS) in 20, Ventriculomegaly in 10, coarsening of the brain echotexture (CBE) in 24, intraventricular haemorrhage in 4, Intra-parenchymal hemorrhage (IPH) in 4 and cerebral atrophy (CA) in none of the babies were found.

6 weeks findings

A completely normal scan was found in 28 of the 50 infants. The remaining 22 had some changes. Diffuse white matter increased echogenicity (DWMIE) were present in12 of the50, Effacement of the convolutional markings (ECM) in 8 babies. Obliteration of the surrounding fluid spaces (OSFS) in 8, Ventriculomegaly in 12, coarsening of the brain echotexture (CBE) in 8, intraventricular haemorrhage in 3, Intra-parenchymal hemorrhage (IPH) in 6 and cerebral atrophy (CA) in 6 of the babies were found.

Usg brain & atna

Neurological examination was normal in 14 and abnormal in 36 infants out of 50 infant studied. Of the 14 infants who had a normal cranial ultrasound scan, 10 had a normal and 4 and abnormal neurological examination (ATNA). Of the 36 infants with abnormal ultrasound findings, 4 had a normal and 32 abnormal neurological examination (ATNA).

Developmental Scales (TDSC)

Of the 50 infants examined, 20 babies were normal and 30 were abnormal TDSC score. Ten of the 50 infants assessed had normal scores on all the subscales (both ATNA & TDSC). The other 18 had mild delay on at least one subscale. Six had moderate and another six had severe delay on TDSC study. 12 of the 50 infants with normal ultrasound scans had a normal score on TDSC and 2 had at least one abnormal score. 8 of the 36 infants with abnormal ultrasound scans had normal and 28 had abnormal scores on TDSC.

Table 2. Findings of USG Brain abnormalities

Age	Diffuse white matter increased echogenicity (DWMIE)	Effacement of the convolutional markings (ECM)	Obliteration of the surrounding fluid spaces (OSFS)	Ventricul omegaly	coarsening of the brain echotexture (CBE)	Inter ventricular hemorrhage (IVH)	Intra-parenchymal hemorrhage (IPH)	cerebral atrophy (CA)
D3	35 (70%)	36 (72%)	26 (52%)	8 (16%)	12 (24%)	6 (12%)	2 (4%)	0 (0%)
D7	20 (40%)	22 (44%)	20 (40%)	10 (20%)	24 (48%)	4 (8%)	4 (8%)	0 (0%)
6 weeks	12 (24%)	8 (16%)	8 (16%)	12 (24%)	8 (16%)	3 (6%)	6 (12%)	6 (12%)
Mean	22.33 (44.46%)	22 (44%)	18 (36%)	10 (20%)	24.67 (25.12%)	4.33 (8.66%)	4 (8%)	2 (4%)

Table 3. USG Brain & Neurodevelopmental Outcome Correlation with Risk Factors

ATNA	TDSC	RISK FACTORS						
		Low apgar score	Resuscitation				Usg brain findings	Diagnosis Sarnat staging
			MOIST O2	PPV	PPV & CC	INTUBATION	D3, D7, 6WEEKS	
OPTIMAL 14	OPTIMAL 20	4-6	N-12	N-2	N-0	N-0	WNL-10 DWMIE -2 ECM-2	1
MILD 20	MILD 18	4-6	N-8	N-8	N-2	N-2	WNL-4 DWMIE -12 ECM-10 IVH-2 OSFS-14	2
MODERATE 10	MODERATE 6	0-3	N-0	N-2	N-5	N-3	WNL-2 DWMIE -8 ECM-6 IVH-4 OSFS-8 IPH-2 CA-2	2
SEVERE 6	SEVERE 6	0-3	N-0	N-1	N-2	N-3	DWMIE -6 ECM-6 IVH-4 OSFS-5 IPH-2 CA-5	3
TOTAL N-50	N-50		20	13	9	8		

Table 4. USG Brain & Neurodevelopmental Outcome results

Usg brain	ATNA		TDSC	
	Optimal	Abnormal	Optimal	Abnormal
Uneventful n-14	N-10	N-4	N-12	N-2
Eventful N-36	N-4	N-32	N-8	N-28

DISCUSSION

Estimates of the incidence of perinatal asphyxia vary depending on the definitions used. In resource rich countries, the incidence of severe perinatal asphyxia (causing death or severe neurological impairment) is about 1/1000 live births (Levene *et al*., 1985; Thornberg *et al*., 1995). In resource-poor countries, perinatal asphyxia is probably much more common. The 1996 guidelines from the AAP and ACOG for hypoxic-ischemic encephalopathy (HIE) indicate that all of the following must be present for the designation of perinatal asphyxia severe enough to result in acute neurological injury.

- Profound metabolic or mixed acidemia (pH <7) in an umbilical artery blood sample, if obtained
- Persistence of an Apgar score of 0-3 for longer than 5 minutes
- Neonatal neurologic squelae (e.g., seizures, coma, hypotonia)
- Multiple organ involvement (e.g., kidney, lungs, liver, heart, intestines)

Worldwide, perinatal asphyxia is a major cause of death and of acquired brain damage in newborn infants. The prognosis depends on the severity of the asphyxia. Only a minority of infants with severe encephalopathy after perinatal asphyxia survive without disability. However, there are limited population-based data on long-term outcomes after perinatal asphyxia, such as cerebral palsy, developmental delay, visual and hearing impairment, and learning and behavioral problems. The clinical signs and symptoms depend on the severity, timing and duration of the insult. The infant's gestational age needs to be taken into consideration in the evaluation. Symptoms usually evolve over a period of 72 hours (1976 Sarnat and Sarnat). CUS is helpful to exclude structural abnormalities and to detect calcifications and cysts, atrophy or cerebral hemorrhage. Sequential cranial ultrasound examinations following a recent hypoxic-ischemic insult are helpful for assessing the evolution of injury, and particularly for defining the pattern of lesions and the timing of their onset (Roberto Antonucci *et al*., 2014). A observational study Cally J. Tann *et al* from a resource limited country; Uganda had showed in 21% of cases with HIE having major abnormalities in early CUS (<36 hours) (Cally J. Tann *et al*.,

2016) Another study from Bangladesh by TaranaYasmin *et al* have shown some abnormal findings in 54% cases of perinatal asphyxia, among them most of them (43%) had cerebral edema and 5% had haemorrhage (TaranaYasmin *et al*., 2016). Study by Nagraj *et al* from India showed 24.6% neonates who had abnormal Apgar scores, 52.9% with mild asphyxia, 50% with moderate asphyxia, and 80% with severe asphyxia had abnormal findings on cranial ultrasound of which evidence of intracranial bleed and periventricular echogenicity were most common. Correlation between cranial ultrasound findings of neonates with perinatal asphyxia was statistically significant (P = 0.003) (NiranjanNagaraj *et al*., 2016). We performed cranial ultrasound and neurological assessments in a cohort of 50 infants regarded as normal at birth. Thirty six of the 50 infants (72%) showed some ultrasound changes. As in previous studies, we observed a significant incidence of haemorrhages (9%) and asymmetrical ventricles (16%). We also observed that an additional 44.67% showed diffuse increased white matter echogenicity. Some 36% of theinfants had an Obliteration of the surrounding fluid spaces (OSFS). In our study correlation between findings of USG brain and neurodevelopment showed Out of 50 babies studied USG brain was uneventful in 14 babies (28%) and eventful in 36 babies (72%). Among those 50 babies (ATNA) Amiel-Tiscon Neurological Assessment was optimal in 14 babies (28%) mild changes noted in 20 babies (40%), moderate in 10 babies (20%) and severe changes noted in 6 babies (12%).TDSC scoring shows that 20 babies (40%) are optimal, mild changes noted in 18 babies (36%), moderate in 6 babies (12%) and severe changes noted in 6 babies (12%). An article by Mary A Rutherford *et al* about 2 decades ago had shown Regular ultrasound scanning identified 40 term infants with perinatal asphyxia in their study with a poor outcome. A normal ultrasound or isolated findings of intraventricular haemorrhage, subarachnoid haemorrhage or transient flares were associated with a normal outcome in 13 of 14 infants (Mary A Rutherford *et al*., 1994). Another study from the southern part of India have revealed The incidence of abnormal neurological outcome was 14%, abnormal tone-14%, developmental delay-12%, seizures-12% and microcephaly 12 at 6 months of age. There is significant association (p=0.11) between HIE stages and abnormal neuroimaging. Babies with HIE stage I had normal neuroimaging findings (Sirajuddin Nazeer *et al*., 2017) Another study conducted by KhaledAbdulqawi *et al* where cranial ultrasound found to have a positive predictive value of 78% and negative predictive value of 58.3% respectively (Abdulqawi *et al*., 2011).

Conclusion

Our study has revealed that despite of having some limitations, early and as well as follow up cranial USG have a role in identifying significant lesions in Hypoxic ischemic encephalopathy specially in resource limited countries or regions and these changes also correlates with subsequent neuro-developmental outcome as suggested by abnormal neurological findings in Amil Tison And TDSC scale in babies with history of perinatal asphyxia and positive USG findings of HIE after birth.

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