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Original Research Paper

A Study On Clinico- Neuro- radiological Correlation and Immediate Outcome of Perinatal Asphyxia in Neonates Admitted in Tertiary Care Hospital, Tirupati

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ABSTRACT

Background: Perinatal Asphyxia (PA) is the most common cause of neonatal mortality. Hypoxic-ischemic encephalopathy is the foremost concern in an asphyxiated neonate. Neuroimaging with cranial ultrasound, computed tomography (CT), and Magnetic resonance imaging (MRI) are valuable tools in the work-up of patients with birth asphyxia. This study was conducted to study the clinico-neuroradiological correlation in birth asphyxia and its immediate outcome. **Materials and methods:** This prospective, observational study was conducted among 110 new borns with birth asphyxia over a period of one year to study clinico-neuro radiological manifestations admitted to the Department of Pediatrics, Sri Venkateswara Medical College, Tirupati. Neonates with major congenital malformations and meningitis were excluded from the study and after taking informed consent. All the admitted asphyxiated babies after clinically staging as Hypoxic Ischemic Encephalopathy I ,II,III as proposed by Sarnat and Sarnat staging were subjected to neuroimaging investigations Neurosonogram, CT brain, and MRI brain. At the time of discharge, the outcome has been assessed by Seizure control, Feeding pattern, and clinical neurological evaluation. **Results :** In our study majority of babies were male new borns (61.8%) , and more than half of the cases (51.8%) were reported as HIE stage-II. Neurosonogram identified 38 cases (34.5%) as abnormal. Among these 40.6% of the cases showed focal echogenic lesions. MRI identified 48 cases (43.6%) as abnormal, among which 47.9% of the cases (n=23) showed T2 hyperintensities. Clinical outcome at discharge showed feeding abnormalities in 12 cases , 6 had paladi feeding, 3 had swallowing difficulty, and one had Ryle's tube feeding. Abnormalities in tone were observed in 16 cases, in which all are hypertonia. Fifty-eight cases required AEDs for seizures.Out of 110 cases, all the cases (100%) got discharged. 78.2% of cases had a good outcome, and 21.8% of cases had a poor outcome. **Conclusions:** Radiological investigations such as Neurosonogram and MRI are good predictors of a poor outcome in perinatal asphyxia cases. Prompt treatment by the Paediatrician immediately after the birth will be helpful in preventing untoward events in these cases.

Key words – Perinatal Asphyxia, Outcome, Neurosonogram, Magnetic Resonance Imaging (MRI)

INTRODUCTION:

Perinatal Asphyxia (PA) is one of the most common causes of neonatal and under-5 mortality. The estimated incidence of perinatal asphyxia is 1 to 6 per 1000 live births, represents the 3rd most common cause of neonatal death (23%)[1,2]after preterm birth (28%), and severe infections (26%). Perinatal asphyxia is an important cause of stillbirths of the total 2.7 million stillbirths that occur globally, around 1.2 million occur during the intrapartum period, largely due to asphyxia.[3]The National Neonatal Perinatal Database (NNPD) reported perinatal asphyxia to be the commonest cause of stillbirths, accounting for 45.1% of all such cases.[4]Almost all (98.2%) asphyxia related deaths occur during the 1st week of life, with 73% occurring within 24 hrs of birth.[5] Hypoxic-ischemic encephalopathy is the foremost concern in an asphyxiated neonate because, contrary to other system derangements, this has the potential to cause serious long-term neuromotor sequelae among survivors in the form of cerebral palsy, seizures, intellectual disability, and learning disabilities.[6-9] Neuroimaging with cranial ultrasound, computed tomography (CT), Magnetic resonance imaging (MRI) are valuable tools in the work-up of patients with birth asphyxia.Currently, MRI is considered as gold standard in the diagnosis of perinatal asphyxia. If decisions are delayed, there is a possibility that the infant will survive with very severe long term disabilities, as the end of life decisions are relying more and more on the results of imaging performed in the first days of life.[10]

AIMS

To study the clinico-neuroradiological manifestations in birth asphyxia and its immediate outcome .

MATERIALS AND METHODS

A prospective, observational study was conducted among all new borns with birth asphyxia over a period of year from March 2019 to February 2020to study cliniconeuro radiological manifestations admitted to the Department of Pediatrics, Sri Venkateswara Ramnarain Ruia Government General Hospital tertiary care teaching hospital attached to Sri Venkateswara Medical College, Tirupati. A total of 198 newborns presenting with an APGAR score of < 7 at 5 min of age and Failure to initiate and sustain breathing at birth are enrolled in the study excluding the neonates with major congenital malformations and meningitis are excluded from the study and after taking informed consent. Among 198 new borns, 75 died and 13 left against medical advice during the study so 110 new borns were included in the study. Clinical examination of all the admitted asphyxiated babies was done. The evaluation was done, including the general examination such as anthropometry, signs and stages of hypoxic-ischemic encephalopathy (HIE) as proposed by Sarnat and Sarnat were assessed. Data collected from all subjects was entered in predesigned proforma.

Routine investigations include blood sugar, serum electrolytes, renal parameters, were done. Neuroimaging investigations like Neurosonogram by ESOATE, and MRI brain by Philips INGENIA 1.5 Tesla are advised depending on the clinical presentation and correlated accordingly through Sarnat-Sarnat staging. Early outcomes were recorded in the form of clinical improvement, presence of HIE 1/2/3 and death. At the time of discharge, the outcome has been assessed by Seizure control ,Feeding pattern and clinical neurological evaluation Those babies with no feeding difficulties and taking breastfeeds, having seizures controlled well or a baby being on single AED at the time of discharge and neurologically normal clinical assessment are said to be having good outcome. Those babies with feeding difficulties like a baby on spoon/ tube feeds, having refractory seizures or seizures controlled with two or more AED's at the time of discharge, and abnormal neurological clinical assessment categorized as poor outcome.

Data analysis:

Data was entered into MS-EXCEL and statistical analysis was carried out after validating the data. Microsoft Word and Excel, along with SPSS 22, manufactured by International Business Management USA, was used to generate graphs and tables. Results were expressed as frequencies and percentages a p-value of 0.05 was considered statistically significant.

RESULTS

In the present study, majority i.e., 61.8% of the subjects were male new borns and 38.2% of the subjects were female new borns.(Table 1) Among all newborns,86.4% were full term and 13.6% were preterm deliveries.(Table 1), 71.8% of the mothers had NVD and 28.2% had LSCS. Majority (70.9%) were out born. 75.5% of the mothers were primigravida.(Table 1).In the present study 70.9% of the cases were admitted on Day 0 and 22.7% on Day 1(Table1)

Among study subjects 61.8% cases had APGAR of >5 at 5 minutes, 20.9% had APGAR 3 - 5 at 5 min and 17.3% had <3 APGAR at 5 minutes and majority of the cases i.e., 51.8% of the cases had stage 2 HIE, 40% had stage 1 and 8.2% had stage 3 HIE. (Table 1) In the present study, 34.5% of the cases had Abnormal NSG findings (Table 2). The most common abnormality detected in Neurosonogram is focal echogenic lesions found in 40.6%, others being Periventricular Leukomalacia in 27%, Increased echogenicity in 18.4% and multiple cysts, B/L symmetric echogenicity and Intraventricular hemorrhage were 5.4% each. (Table 2) In the present study, among stage 2 HIE , 50.9% of cases had abnormal NSG and 100% of cases with stage 3 HIE had abnormal NSG and the difference was found to be statistically significant(table 3) None of the stage 1 HIE had any neurosonogram abnornmality .(Table 3)

In the present study, 43.6% of the cases had Abnormal MRI findings (Table 2) and the most common abnormality being T2 hyperintensities in 47.9%. 25% cases had Periventricular Leukomalacia, 16.7% had restricted diffusion and 10.4% had haemorrhage In the present study, 68.4% of cases with HIE stage 2 had abnormal MRI and 100% of cases with stage 3 HIE had abnormal MRI and the difference was found to be statistically significant.(table 3) None of the stage 1 HIE had any abnormality in MRI. In the present study most common pattern of abnormality observed was deep Grey matter abnormality accounting for 13.6% of cases with abnormal MRI followed by Cortical Injury(10.9%) , Periventricular leukomalacia (10.9%) and mixed pattern in 8.1% of cases . In the present study, 74.7% babies born to primi mothers and 88.9% of the babies born to Multipara mothers respectively had good outcome.(Table 4) In the present study 26.3%, 65.2% and 97% of cases with APGAR <3, 3-5 and >5 at 5 minutes respectively had good outcome and 73.6%, 34.7% and 2.9% of cases with APGAR <3, 3-5 and >5 at 5 minutes respectively had poor outcome and the difference was found to be statistically significant. (Table 4) In the present study, 100% of cases with HIE stage 1, 73.7% of cases with HIE stage 2 had good outcome, and 100% of the cases with HIE stage 3 had poor outcome, and the difference was found to be statistically significant.(Table 4) In the present study, majority i.e., 78.2% of cases had Good outcome and 21.8% of cases had Poor outcomes of HIE.(Table 4) In the present study, 10.9% had feeding problems. Among the cases with feeding problems, 50% had problem with Paladai, 25% had swallowing difficulty, 16.7% had sucking difficulty and 8.3% had problem with Ryle's tube feeding. Abnormalities in tone were observed in 16 cases in which all had hypertonia , neurobehavioural abnormalities include excessive cry , non-cuddlable seen in 4.5% cases and non -consolable in 5.4% cases ,irritability in 3.6% cases and 58(52.7%) cases required AED for seizures.(Table 5) Occurrence of clinical abnormalities were more in stage -3 and stage -2 cases when

compared with stage -1 cases as shown in table 6 and the association was statistically significant . In stage -2 cases seizures required antiepileptic drugs was the most frequent abnormality followed by neurobehavioural, tone and feeding abnormalities as shown in Table 5.

DISCUSSION

In our present study , among 110 new borns , most cases were males (61.8%) females were (38.2%). The males to females ratio were 1.6:1.which was correlating to the study conducted by Futrakul S et al [11] which showed 61.5% were male and 38.5% were female. Data from the 1991 to 2000 California state wide hospital discharge database showed a birth asphyxia incidence of 4.9 per 1000 live births among males compared with 4.2 per 1000 live births among females. Male gender, after adjusting for ethnicity, socioeconomic status, and birth weight, was associated with an increased risk of birth asphyxia.[12] The median gestational age of the neonates was 37 – 42 weeks in this study. Out of them, 78 were referred and admitted on the same day of birth. In the present study, primigravida mothers were 75.5%, and multigravida was 24.5% which indicates that primigravida as one of the main risk factor of developing perinatal asphyxia, which was also reported in previous studies.[12,13] 86.4% of the cases were Full term, and 13.6% were Preterm deliveries. In contrary, Preterm delivery emerged as one of the significant risk factor of birth asphyxia as reported in past studies.[14] In the present study, neonates born with an APGAR score of <3 at 5 minutes 17.3%, 3-5 were 20.9%,>5 were 61.8% . In neonates with APGAR <3 at 5 min 73.6% had a poor outcome, neonates with APGAR >5 97% had a good outcome, and neonates with 3-5 APGAR 65.2% had a good outcome, and 34.7% had a poor outcome. Better outcome was reported in high APGAR score neonates in comparison to low APGAR score. This was evident as a strong correlation between poor outcome and low APGAR score at 5 min with p value 0.000, statistically significant.(table 4) Markedly lower rate of survival in APGAR (0-3) neonates beyond five minutes were reported by the studies conducted by Moster D et al. [15]Casey BM et al. [16]Vahabi S et al.[17] and Li F et al. [18], Futrakul et al [10]and Ellis et al[19]. It was found that new borns with APGAR scores of 0 to 3 had a 386-fold increased risk for neonatal death[15].

In the present study, majority of the neonates were HIE stage-2 (51.8%), followed by HIE stage-1 (40%) and HIE stage-3 (8.2%). Neuroimaging studies are the best way to know the extent of asphyxial injuries and to differentiate asphyxial injury from developmental or acquired abnormalities. Ultrasonography, although easily performed, is of limited value in the evaluation of the asphyxiated infant. MRI is the preferred imaging tool for delineating the nature & extent of asphyxial damage in the clinically stable neonate. In the present study, 65.4% of neonates had normal neurosonogram findings, and 34.5% had abnormal findings. In that all the HIE stage 1 cases were normal, and all the HIE stage 3 cases were abnormal majority of the HIE stage-2 cases were identified as abnormal (50.9%), and the difference was found to be statistically significant. Daneman et al[21]. proved that cranial ultrasound remains an extremely useful modality for evaluating the full term neonatal brain. Badrawy et al[22]. showed in their study that 37% of preterm had abnormal cranial ultrasound findings. MRI is the best imaging modality for the early assessment of brain injury in asphyxiated neonates. MRI can visualize cerebral hypoxic-ischemic lesions with higher resolution, sensitivity, and specificity than neurosonogram and CT. It is able to detect 75-100% of cerebral lesions resulting from asphyxia, particularly those affecting white-matter, basal ganglia, and thalamus. MRI has the advantage of noninvasive and not exposing the new born to ionizing radiation. T2 weighted MRI imaging is better for detecting ischemic lesions and imaging differentiating

between white and grey matter. Diffusion-weighted imaging is best for the detection of ischemic lesions within the white matter. With the use of MRI in newborns with HIE, it is possible to predict the pattern of the later neurodevelopmental deficit. In the present study, 56.3% of neonates had a normal MRI, and 43.6% had abnormal findings. Among MRI reported all the HIE stage 1 cases as normal and all the HIE stage 3 cases as abnormal. HIE stage 2 cases that were abnormal not identified by neurosonogram were identified by MRI (68.4%), which indicates that the MRI is identifying the severity of the cases appropriately, and the difference was found to be statistically significant.

MRI was performed in asphyxiated neonates within the first ten days of life. In a parietal or parieto-occipital distribution, focal parenchymal hemorrhages were common in the series by Keeney and colleagues.[23] A study found a strong correlation between early and late sequential MRI in HIE neonates treated with therapeutic hypothermia.[24] In particular, the localization, extension and severity of hypoxic-ischemic brain injury in the two scans have been shown to be strongly correlated. This study results suggest that MRI in the first days of life may be a useful prognostic tool for clinicians and help in medical issues such as the end of life decisions. In the present study, majority i.e., 78.2% of cases had a good outcome, and 21.8% of cases had poor outcome.100% of cases with HIE stage 1, 73.7% of cases with HIE stage 2 had a good outcome, and 100% of the cases with HIE stage 3 had a poor outcome in the form of severe neurological disability, and the difference was found to be statistically significant. A study performed by Robertson CM et al. [20]showed that the surviving neonates with stage 3 HIE, as well as those with stage 2 and those neonates with feeding and swallowing difficulties, should be referred to a developmental therapist. Neonates with continuing seizures or difficult to treat neonatal seizures should have post-discharge medical supervision by a physician with knowledge of epilepsy. At the time of discharge, 52.7% cases required antiepileptic drugs for seizures at the time of discharge which was consistent with study conducted by Mullingan et al [25] 10.9% had feeding problems. Among which , 50% had a paladi feeding , 25% had swallowing difficulty, 16.7% had sucking difficulty, and 8.3% had a Ryles tube feeding. Abnormalities in tone were observed in 14.5% cases of which had hypertonia; neurobehavioural abnormalities include excessive cry and non-cuddlable seen in 4.5% cases and non-consolable in 5.4% cases, irritability in 3.6% cases. Occurrence of clinical abnormalities was more in stage-3 and stage-2 cases when compared with stage-1 cases. In stage-2 cases, seizures that required antiepileptic drugs was the most frequent abnormality, followed by neurobehavioural, tone, and feeding abnormalities. The presence of seizures increases a new borns risk of cerebral palsy 50 to 70 fold. Snyder ey et al. [26] observed poor feeding in 64%, abnormal muscle tone in 70%, seizure in 30%, and loss of neonatal reflexes in 64% of cases. A recent literature review has reported the rate of individual long-term neurodevelopmental outcomes after HIE: 45% of sequelae were represented by cognition and developmental delay or learning difficulties, 29% by cerebral palsy, 26% by blindness or vision defects, 17% by gross motor and coordination problems, 12% by epilepsy, 9% by hearing loss or deafness, and 1% by behavioral problems.[27] A recent review of the literature by Ellenberg et al.[28] has revealed that cerebral palsy rate ranges from less than 3% to more than 50% in different studies. The study by Graham et al.[29] has shown that HIE results in cerebral palsy in at least 14% of cases. Furthermore, van Handel et al.[30] investigated the behaviour at school age in children who had been affected by neonatal encephalopathy, demonstrating that they had a problematic behaviour,

with social and attention problems. Neonates with severe encephalopathy (stage 3) are generally believed to have a uniformly dire prognosis[31]. MRI has emerged as potentially one of the most useful tools for prognostication in HIE. Significant injury to the cortex or subcortical nuclei is associated with both intellectual and motor disability, but the severity varies depending on the regions involved and severity of injury to this region. Discrete lesions in the subcortical nuclei or less severe parasagittal injuries are associated with a normal cognitive outcome and only mild motor impairments.

CONCLUSION

Radiological investigations such as Neurosonogram and MRI are good predictors of poor outcome in perinatal asphyxia cases. Prompt treatment by the Paediatrician immediately after the birth will be helpful in preventing untoward events in these cases.

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Table 1. Distribution of study subjects based on various variables

Variables	Number of subjects n=100	Percentage
Male	68	61.8%
Female	42	38.2%
NVD	79	71.8%
LSCS	31	28.2%
Type of Admission		
Inborn	32	29.1%
Out born	78	70.9%
Gravida		
Primi	83	75.5%
Multi	27	24.5%
Maturity		
Full-term	95	86.4%
Preterm	15	13.6%
Age at admission		
0 Day	78	70.9
1 Day	25	22.7
2 Days	2	1.8
3 Days	2	1.8
4 Days	3	2.7
Total	110	100
APGAR at 5 minutes		
<3	19	17.3
3-5	23	20.9
>5	68	61.8
Stage of HIE		
Stage 1	44	40
Stage 2	57	51.8
Stage 3	9	8.2

Table 2 – Distribution of various radiological findings in study subjects

NSG finding	HIE staging		
	Stage-I (n=44)	Stage-II (n=57)	Stage-III (n=09)
Normal study	44 (100%)	29 (49.1%)	00
Focal echogenic lesions	00	12 (19.2%)	03 (33.3%)
Increased echogenicity	00	06 (10.5%)	01(11.1%)
Multiple cysts	00	01 (1.7%)	01(11.1%)
Bilateral symmetric echogenicity	00	01(3.5%)	01(11.1%)
Periventricular leukomalacia	00	08(14%)	02(22.2%)
Intraventricular hemorrhage	00	01 (1.7%)	01(11.1%)
MRI finding	HIE staging		
	Stage-I (n=44)	Stage-II (n=57)	Stage-III (n=09)
Normal study	44 (100%)	18 (31.5%)	00
T2 hyperintensities	00	19 (33.3%)	04(44.4%)
Restricted diffusion	00	06 (10.5%)	02(22.2%)
Hemorrhage	00	04 (7%)	01 (11.1%)
Periventricular leukomalacia	00	10 (17.5%)	02(22.2%)

Table 3 – Correlation between neuroimaging findings with HIE Staging in study subjects

HIE Staging	NSG	
	Normal	Abnormal
Stage 1	44 (100%)	0
Stage 2	28 (49.1%)	29 (50.9%)
Stage 3	0	9 (100%)
Total	72 (65.4%)	38 (34.5%)
Yates' Chi-square = 37.615, df= 2, p-value = 0.000, S		

HIE Staging	MRI	
	Normal	Abnormal
Stage 1	44 (100%)	0
Stage 2	18 (31.6%)	39 (68.4%)
Stage 3	0	9 (100%)

Total	62 (56.4%)	48 (43.6%)
Yates' Chi-square = 55.006, df= 2, p-value = 0.000, S		

Table 4 - Correlation of outcome of study subjects with variables

Gravida	Outcome		Total
	Good	Poor	
Primi	62 (74.7%)	21 (25.3%)	83 (100%)
Multi	24 (88.9%)	3 (11.1%)	27 (100%)
Total	86 (78.2%)	24 (21.8%)	110 (100%)
Yates' Chi-square = 1.645, df= 1, p-value = 0.199			
APGAR at 5 minutes	Outcome		
	Good	Poor	
<3	5 (26.3%)	14 (73.6%)	
3-5	15 (65.2%)	8 (34.7%)	
>5	66 (97%)	2 (2.9%)	
Total	86 (78.2%)	24 (21.8%)	
Chi-square = 41.69, df= 2, p-value = 0.000, S			
HIE staging	Outcome		
	Good	Poor	
Stage 1	44 (100%)	0	
Stage 2	42 (73.7%)	15 (26.3%)	
Stage 3	0	9 (100%)	
Total	86 (78.2%)	24 (21.8%)	
Yates' Chi-square = 39.301, df= 2, p-value = 0.000, S			

Table 5 –Distribution of cases by outcome of HIE

Clinical Outcome		No. of Cases (%)
Feeding Problems:	Normal	98(89.1%)
	Swallowing difficulty	3 (25%)
	Sucking difficulty	2 (16.7%)
	Ryle's tube feeding	1 (8.3%)
	Paladi (Gokurnam)	6 (50%)
Tone abnormalities:	Normal	94 (85.4%)
	Hypertonia	16 (14.5%)
Neuro behavioral abnormalities:	Normal	90 (81.8%)
	Excessive Cry	05 (4.5%)

	Non-Consolable	06 (5.4%)
	Non-Cuddlable	05 (4.5%)
	Irritability	04 (3.6%)
Seizures required AEDs on discharge:	Yes	58 (52.7%)
	No	52 (47.2%)

Table 6 - Distribution of cases by outcome in relation with HIE staging

Clinical abnormality	HIE staging			
	Stage-I (n=44)	Stage-II (n=57)	Stage-III (n=09)	P value
Feeding Abnormalities	00	03	09	0.000, S
Tone Abnormalities	00	07	09	0.000,S
Neuro behavioral abnormalities	00	11	09	0.000,S
Seizures required AEDs on discharge	00	49	09	0.000,S