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A STUDY ON CLINICO-EPIDEMIOLOGICAL PROFILE AND CORRELATION BETWEEN CRANIAL ULTRASONOGRAPHY FINDINGS AND SEVERITY OF HYPOXIC ISCHAEMIC ENCEPHALOPATHY IN TERM NEONATES WITH PERINATAL ASPHYXIA ADMITTED AT SNCU IN A RURAL MEDICAL COLLEGE AND HOSPITAL IN WEST BENGAL, INDIA

Paediatrics

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ABSTRACT

Introduction: Perinatal asphyxia (PNA) is defined as failure to initiate and sustain breathing after birth. PNA leading to Hypoxic ischemic encephalopathy (HIE) is a dreaded neurological condition of the newborn. **Background:** HIE is one of the important causes of neonatal morbidity and mortality in the first week of life. Neuroimaging plays an essential role in the assessment of brain injury in HIE patients. **Objectives:** 1.To study the clinico-epidemiological profile of term neonates with PNA 2.To study the serial cranial USG findings in asphyxiated term neonates in first week of life. 3. To assess the correlation between concurrent use of serial cranial ultrasonography findings in term neonates with PNA and with regards to the severity of HIE. **Materials And Methods:** This hospital based cross-sectional study was conducted at SNCU of Bankura Smmilani Medical College and Hospital, Bankura. 100 cases of term neonates with HIE admitted at SNCU from 1st December 2021 to 31st January 2022 were taken as study population. All the relevant history was taken based on clinico-epidemiological parameters and detailed clinical- examination was done. Serial cranial USG was perfomed in first week of life. **Result:** In our study among 100 neonates, 62 (62%) cases belonged to HIE-I, 29 (29%) cases with HIE-II, and 9(9%) cases with HIE-III. 42(42%) cases showed normal Cranial USG finding, 24(24%) cases showed cerebral oedema, 14 (14%) cases showed Gr-I IVH, 10(10%) cases showed Gr-II IVH, 6(6%) cases showed Gr-III IVH and 4(4%) cases showed Gr-IV IVH. Among HIE-I neonates, 42(67.7%) cases had normal cranial USG findings and 20(32.2%) cases showed cerebral oedema. In HIE-II neonates, 4(13.7%) cases showed cerebral oedema, 14(48.2%) cases showed Gr-I IVH, 10(34.4%) cases showed Gr-II IVH and 1(3.44%) case showed Gr-III IVH. In neonates with HIE-III, 5 (55.5%) cases showed Gr-III IVH and 4 (44.4%) cases showed Gr-IV IVH. Correlation of cranial USG shows worsening trend with increasing severity of HIE as per Sarnat and Sarnat staging. Chi-square test revealed strong positive correlation. (p= 0.0001, rs=0.9) **Conclusion:** This study concluded that the serial cranial USG findings in PNA neonates when done in first week of life, revealed a strong positive correlation with the severity of HIE. Cranial USG is cost effective, easily available and is ideal for the initial assessment of neonates with HIE.

KEYWORDS

HIE, IVH, PNA, Ultrasonography

INTRODUCTION:

WHO defined birth asphyxia as "failure to initiate & sustain breathing at birth" and based on APGAR [1] score of < 7 at one minute of life. The essential criteria for diagnosing perinatal asphyxia as outlined by ACOG & AAP [2] are: 1) Prolonged metabolic or mixed acidemia (pH <7.0 on cord arterial blood sample) 2) Persistence of an Apgar score of <3 for 5 min or longer [3,4] Clinical neurologic manifestation as seizures, hypotonia, coma or HIE in the immediate neonatal period. 4) Evidence of multiorgan dysfunction in the immediate neonatal period.

Perinatal asphyxia is due to a lack of blood flow or gas exchange to or from the fetus in the period immediately before, during, or after the birth process. Perinatal asphyxia can result in profound systemic and neurologic sequelae due to decreased blood flow and/or oxygen to a fetus or neonate during the peripartum period. Neonatal hypoxic-ischemic encephalopathy refers specifically to the neurologic sequelae of perinatal asphyxia. [5,6]

Neonatal Hypoxic Ischaemic Encephalopathy occurs in one to six per 1000 live full-term births. Of affected newborns, 15–20% of affected newborns die in the postnatal period, and an additional 25% sustain childhood disabilities. [7,8] The presence of an abnormal neurologic examination in the first few days of life is the single most useful indicator that a brain insult has occurred. Neonates with mild encephalopathy do not have an increased risk of motor or cognitive deficits. Neonates with severe encephalopathy have an increased risk of death and an increased risk of cerebral palsy (CP) and mental retardation amongst survivors .[9,10]

PNA can result in systemic effects, including neurologic insult, respiratory distress and pulmonary hypertension, and liver, myocardial, and renal dysfunction. Depending on the severity and timing of the hypoxic insult, a neonate with HIE due to PNA can demonstrate a variety of neurologic findings. Using the Sarnat staging for encephalopathy can be useful. In Sarnat Stage I, the least severe stage, there is generalized sympathetic tone and the neonate may be hyper-alert with prolonged periods of wakefulness, mydriasis and increased deep tendon reflexes. In Sarnat Stage II, the neonate may be lethargic or obtunded, with decreased tone, strong distal flexion, and generalized parasympathetic tone with miosis, bradycardia and increased secretions. Seizures are common in Sarnat Stage II. Sarnat Stage III, the most severe, is characterized by a profoundly decreased level of consciousness, flaccid tone, decreased deep tendon reflexes and very abnormal EEG. Clinical seizures are less common in Sarnat Stage III due to the profound injury in the brain preventing the propagation of clinical seizures.

Neonatal sonography of the brain [11,12 ,13] is now an essential part of newborn care. Current ultrasound technology allows for rapid evaluation of infants in the sick newborn care unit with virtually no risk. The advantage of sonography over computed tomography (CT) or magnetic resonance imaging (MRI) include portability, lower cost, speed, no ionizing radiation, and no sedation. The ultrasound machine is portable, so it can be used at the bedside in the neonatal intensive care unit and obviates transporting the sick infant, can be repeated as often as necessary and has no side effects.

It detects most of the hemorrhagic, ischemic and cystic brain lesions as well as calcifications, cerebral infections and major structural abnormalities in preterm and full-term neonates. The presence of increased echogenicity in the white matter on a day 1 ultrasound examination is also strongly suggestive of an antenatal insult, as this echogenicity takes time to develop. These findings may be important for genetic counselling as well as for medicolegal issues. Sequential

imaging has shown that lesions in the basal ganglia may increase in size during the first week after birth. [14,15]

This current study was undertaken in view of the paucity of such studies in rural medical colleges like ours. Assessment of severity of HIE and its correlation with cranial USG findings would help in proper parent counselling regarding immediate outcome and early institution of stimulation therapy for better management of the neonate.

MATERIALS AND METHODS

Study Design: Descriptive Cross-sectional SNCU based study.

Place: SNCU, Department of Pediatrics, BS Medical College, Bankura, West Bengal, India.

Study Period: 1st December 2021 to 31st January 2022

Sample Size: 100 Cases

Study Population:
100 cases of term neonates with PNA with HIE admitted at SNCU of Bankura Sammilani Medical College and Hospital from 1st December 2021 to 31st January 2022.

METHODS:
After obtaining consent from parents, data was collected on a pre-designed, pre-tested and structured questionnaire. A detailed history of the neonate such as sex, birth weight, and gestational age were noted along with detailed clinical examination was performed. All the clinico-epidemiological parameters along with risk factors of the mother were noted such as age, mode of delivery, color of amniotic fluid, and co-morbid conditions such as Eclampsia, Heart Disease, Diabetes mellitus and Hypothyroidism. The asphyxiated term neonates were graded for HIE according to Sarnat and Sarnat staging. Serial cranial USG was done in first week of life. Scans were performed through anterior fontanelle in both coronal and sagittal planes. USG grading was done according to Papile's grading of IVH.

Papile's grading of IVH:

Grading of IVH	Description
I	No IVH
II	IVH without ventricular dilatation
III	IVH with ventricular dilatation
IV	IVH with parenchymal hemorrhage

*IVH= Intra Ventricular Hemorrhage

The data was analysed by statistical software version SPSS 25. The numerical data are expressed in percentages. P-value less than 0.05 was considered significant.

A) Inclusion Criteria
1. Documented neonate of perinatal asphyxia determined by ACOG & AAP.
2.History of difficult labour with poor or no cry immediately after birth (in cases of babies referred from Out born NICU where APGAR Score is not available)
3. Parents/guardians who have given written consent.

B) Exclusion Criteria
1. No documented history of perinatal asphyxia.
2. Premature neonate.
3. Neonates with congenital malformations.
4. Parents who refused to give written consent.

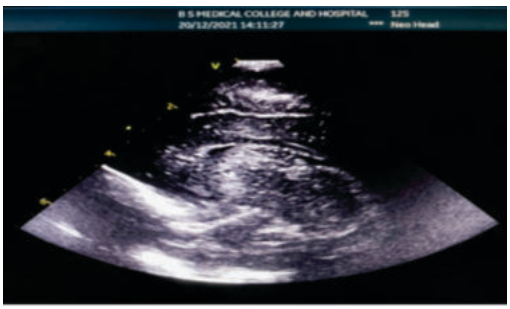

Fig I: Cranial USG - Grade I Germinal Matrix Hemorrhage

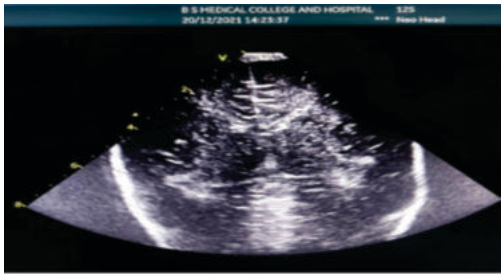

Fig II: Cranial USG - Bilateral lateral ventricles effaced

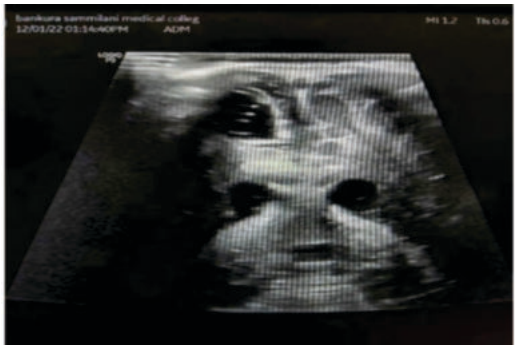

Fig III: Cranial USG - Cystic Encephalomalacia

RESULTS AND ANALYSIS

Table 1: Distribution According To Clinical And Sociode mographic Variables

VARIABLES		NO. OF CASES (n=100)	PERCENTAGE (%)
MATERNAL AGE	18-22	54	54%
	23-27	24	24%
	28-32	12	12%
	33-38	8	8%
	>38	2	2%
PLACE OF DELIVERY	HOSPITAL	91	91%
	HOME	9	9%
MODE OF DELIVERY	VD	65	65%
	LSCS	30	30%
	ASSISTED VAGINAL DELIVERY	5	5%
CHARACTERISTIC OF AMNIOTIC FLUID	CLEAR	58	58%
	MECONIUM STAINED	38	38%
	BLOOD STAINED	-	
	FOUL SMELLING	4	4%
CO-MORBID CONDITION OF MOTHER	ECLAMPSIA	21	21%
	DIABETES MELLITUS	6	6%
	HYPOTHYROIDISM	-	
	HEART DISEASE	-	
SEX OF NEONATE	FEMALE	46	46%
	MALE	54	54%
	AMBIGUITY	-	-
BIRTH WEIGHT	<1500 gm	15	15%
	1501-2500 gm	51	51%
	2501-3000gm	22	22%
	>3001gm	12	12%
GESTATIONAL AGE	37-38 weeks	39	39%
	39-40 weeks	47	60%
	>41 weeks	14	14%

Among 100 neonates, 54(54%) cases had maternal age between 18-22 years, 24(24%) cases had maternal age between 23-27 years, 12(12%) cases had maternal age between 28-32 years, 8 (8%) cases had maternal age between 33-38years and 2(2%) cases had maternal age more than 38 years. As per place of delivery of 91(91%) cases were born at Hospital and 9(9%) were born at Home. According to mode of delivery, 65(65%) cases had VD, 30(30%) cases had LSCS and 5(5%) cases had assisted VD. 58 (58%) cases had clear amniotic fluid, 38 (38%) cases had meconium-stained amniotic fluid, and none had blood-stained and 4(4%) cases had foul smelling amniotic fluid.

According to comorbid condition of the mother, 21(21%) cases had maternal history of Eclampsia, 6(6%) cases had maternal history of Diabetes mellitus and none had maternal history of Hypothyroidism and Heart disease.

Out of 100 neonates, 46(46%) cases were Female and 54(54%) cases were Male. 15(15%) cases had birth weight less than 1500gm, 51(51%) cases had birth weight between 1501-2500gm, 22 (22%) cases had birth weight between 2501-3000gm and 12(12%) cases had birth weight more than 3000gm. 39(39%) cases belonged to 37-38 weeks Gestational week(G.A), 47(47%) cases belonged to 39-40 weeks G.A and 14(14%) cases belonged to more than 41 weeks G.A.

Table 2: Distribution According To Severity Of HIE In Accordance To Sarnat And Sarnat Staging

HIE Grading	No. of cases(n=100)	Percentage
HIE-I	62	62%
HIE-II	29	29%
HIE-III	9	9%

Among 100 neonates, 62 (62%) cases belonged to HIE-I, 29 (29%) cases belonged to HIE-II and 9(9%) cases belonged to HIE-III.

Table 3: Distribution According To Cranial USG Findings

Cranial USG Findings	No. Of Cases(n=100)	Percentage
Normal study	42	42%
Cerebral Edema	24	24%
Grade-I IVH	14	14%
Grade-II IVH	10	10%
Grade-III IVH	6	6%
Grade-IV IVH	4	4%

Among 100 neonates, 42(42%) cases showed normal Cranial USG finding, 24(24%) cases showed cerebral oedema, 14 (14%) cases showed Gr-I IVH, 10(10%) cases showed Gr-II IVH, 6(6%) cases showed Gr-III IVH and 4(4%) cases showed Gr-IV IVH.

Table 4: Correlation Of HIE Grading With Cranial USG Findings

HIE Grading	CRANIAL USG FINDINGS						
	Normal Cranial USG	Cerebral Oedema	Grade-I IVH	Grade-II IVH	Grade-III IVH	Grade-IV IVH	P-Value= 0.0001
HIE-I(62)	42 (67.7%)	20 (32.2%)	-	-	-	-	
HIE-II(29)	-	4 (13.7%)	14 (48.2%)	10 (34.4%)	1 (3.44%)	-	r_s=0.9
HIE-III(9)	-	-	-	-	5 (55.5%)	4 (44.4%)	

Among 62 cases of HIE-I, 42(67.7%) cases had normal cranial USG finding and 20(32.2%) showed cerebral oedema. Among 29 cases of HIE-II, 4(13.7%) cases showed cerebral oedema, 14(48.2%) cases showed Gr-I IVH, 10(34.4%) cases showed Gr-II IVH and 1(3.44%) case showed Gr-III IVH. Among 9 cases of HIE-III, 5 (55.5%) cases showed Gr-III IVH and 4 (44.4%) cases showed Gr-IV IVH. Chi-square test revealed that severity grading of HIE and cranial USG findings are strongly related (r_s= 0.9, p= 0.0001). P value is less than 0.05, hence is considered significant.

DISCUSSION:

In our study, 100 cases of term neonates with PNA with HIE admitted at SNCU of Bankura Sammilani Medical College and Hospital from 1st December 2021 to 31st January 2022 were studied. Majority of mothers were between 18-22 years of age group which accounted for 54(54%). Maternal conditions and the period of pregnancy mainly affect neonatal mortality rates related to perinatal anoxia. The study indicated that young maternal age (20–25 years) and primigravida has been one of the main risk factors of developing birth asphyxia.[16,17]

91(91%) cases were delivered at the hospital and the remaining 9(9%) cases were delivered at home. In our setting, most of the deliveries occurred at hospital but those births which took place at home were found to have a significant risk factor for causing birth asphyxia.[18] Limited resources and uneducated rural settings, where due to the lack of awareness and resources, home births by untrained midwives are customary, led to more PNA cases. [19]

65(65%) cases were born out of VD, 30(30%) cases had LSCS and 5(5%) cases had assisted VD. The study showed the majority of neonates were delivered through VD. Regarding the type of delivery, most births which occurred by VD had a history of PNA. [20, 21] On the other hand, information confronted with the findings of another study showed caesarean delivery under spinal anaesthesia had more prevalence of perinatal asphyxia.[22]

Characteristics of the amniotic fluid showed, that 58(58%) cases had clear amniotic fluid, 38(38%) cases had meconium stained amniotic fluid, none had blood stained and 4(4%) cases had foul smelling amniotic fluid**.** We found meconium stained amniotic fluid as one of the risk factor. [17],[23] According to comorbid conditions of mother, 21(21%) cases had maternal history of Eclampsia, 6(6%) cases had maternal history of Diabetes mellitus and none had maternal history of Hypothyroidism and Heart disease. Hypertension can cause a decrement in blood flow resulting in asphyxia. Pre-eclampsia found to be associated significantly with increased risk of birth asphyxia. [19] A study showed risk factors related to perinatal asphyxia are arterial hypertension, diabetes, use of illicit drugs, alcohol, hypertensive disorders and meconium amniotic fluid etc. [23,24] Among 100 neonates, 46(46%) cases were female and 54(54%) cases were male. Male predominance was found in our study. Male to female ratio is 1.1:1.Similar results were shown by other studies, where there was a higher prevalence of males in the occurrence of perinatal asphyxia (63.3%) . [25] Male to female PNA ratio was 1.6:1. [21]

We found majority of neonates had low birth weight. 15(15%) cases had a birth weight less than 1500gm, 51(51%) cases had birth weight between 1501-2500gm, 22 (22%) cases had birth weight between 2501-3000gm and 12(12%) cases had a birth weight more than 3000gm**.** Another study showed similar results where lower birth weight (<2500gm) was related to perinatal asphyxia**.** [16] Low birth weight was one of the major culprits for causing birth asphyxia. [17]According to Gestational age (G.A), 39(39%) cases belonged to 37-38 weeks, 47(47%) cases belonged to 39-40 weeks and 14(14%) cases belonged to more than 41 weeks**.** Term babies carried a significantly higher association with birth asphyxia, with gestational age 37-<40 weeks. [21]

In our study with 100 neonates, 62 (62%) cases belonged to HIE-I, 29 (29%) cases belonged to HIE-II and 9(9%) cases belonged to HIE-III. Other study showing distribution as-39 neonates were grouped under HIE-I, 49 under HIE-II and 12 under HIE-III. [26]

In Cranial USG, 42(42%) cases showed normal finding, 24(24%) cases showed cerebral oedema, 14 (14%) cases showed Gr-I IVH, 10(10%) cases showed Gr-II IVH, 6(6%) cases showed Gr-III IVH and 4(4%) cases showed Gr-IV IVH. We found 42% cases had no abnormal changes in Cranial USG. As reported from other study, 40% of the participants had no detectable brain changes, which is consistent with HIE findings where a good percentage of the affected brain may not demonstrate structural changes. [27] Similar findings have been reported in many other studies on HIE. [28,29,30]

Out of 62 cases of HIE-I, 42(67.7%) cases had normal cranial USG findings and 20(32.2%) showed cerebral oedema. Among 29 cases of HIE-II, 4(13.7%) cases showed cerebral oedema, 14(48.2%) cases showed Gr-I IVH, 10(34.4%) cases showed Gr-II IVH and 1(3.44%) case showed Gr-III IVH. Among 9 cases of HIE-III, 5 (55.5%) cases showed Gr-III IVH and 4 (44.4%) cases showed Gr-IV IVH. A study from Bangladesh has shown some abnormal findings in 54% cases of perinatal asphyxia, among them most of them (43%) had cerebral edema and 5% had haemorrhage. [31]

In our study correlation between severity grading of HIE and cranial USG findings are strongly related (r_s= 0.9, p= 0.0001).P value is less than 0.05, hence is considered significant.

We observed that severe abnormal cranial USG findings were more likely to be detected in Sarnat Stage III when compared to Sarnat Stages I and II. There was a trend toward severe HIE cranial USG findings with worsening Sarnat scores. [32]

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. [33]

CONCLUSION:

We found in our study that there was a trend toward severe HIE cranial

USG findings with worsening Sarnat scores. We observed significant Cranial USG findings in neonates with even mild to moderate clinical HIE. Chi-square test revealed that severity grading of HIE and cranial USG findings has a strong positive correlation ($r_s = 0.9$, $p = 0.0001$).

This study highlights the convenience and diagnostic efficiency of cranial ultrasound as a screening modality among neonates with PNA to identify those at risk of the adverse short term outcome. Imaging studies are usually done in all neonates with HIE. Ideally, MRI brain is the most sensitive and specific modality for assessment of severity of HIE but MRI is difficult to perform during the acute stage, since it is time consuming and needs deep sedation which is risky in asphyxiated babies. USG is easier to perform without any need for sedation. Serial Cranial USG is very helpful for party counselling regarding the immediate outcome and for frequent follow up visits in rural medical college like ours where patients are lost to follow up.

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Conflict Of Interest: NIL

Author's contribution:

1. Barman M. Conceptualized the study, actually conducted it and drafted the manuscript.
2. Chatterjee S.S. Collected the data, compiled them and performed statistical analysis.
3. Poddar S. and Mandal U. Helped in collection of radiological data, actively helped at every step of the study and contributed some intellectual contents.
4. Pal A .C. Supervised the study, revised the manuscript and finally prepared the manuscript and added many intellectual contents to the same.

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