

Cranial Ultrasound in Detection of Neurological Lesions in Preterm Neonates in a Tertiary Care Hospital - A Prospective Observational Study

Nandkishor Gupta^{1*}, Badri kumar Gupta², Prem Yadav³ and Sadan Mukhi³

¹Department of Anatomy, Uttar Pradesh University of Medical Sciences, Uttar Pradesh, India

²Department of Pediatric, Universal College of Medical Sciences, Rupandehi, Nepal

³Department of Radiology, Universal College of Medical Sciences, Rupandehi, Nepal

Correspondence should be addressed to Nandkishor Gupta, Nkgupta_mahe@yahoo.co.in

Received: September 16, 2020; Accepted: September 28, 2020; Published: October 05, 2020

ABSTRACT

BACKGROUND

Incomplete formation and maturation of the central nervous system makes it extremely vulnerable to injury, in the case of premature neonates. This can result in a broad range of neurodevelopmental abnormalities. Cranial ultrasound is a sensitive tool for the early detection of these. Preterm neonates, defined as childbirth occurring at less than 37 completed weeks of gestation, is a major determinant of neonatal mortality and morbidity because of their greater risk for intraventricular hemorrhage (IVH) and hypoxic ischemic encephalopathy (HIE). The morbidity associated with preterm birth often extends to later life, resulting in enormous physical, psychological and economic costs. Currently, many imaging modalities are available like cranial ultrasonography, computed tomography and magnetic resonance imaging to detect the intracranial abnormalities in these neonates. However advantages of cranial ultrasonography are easy availability, not expensive, easy to perform, quick, can be done at bedside, repeatable and radiation free. The aims of the study were to identify the severity of brain injuries by grading the neurosonographic findings and to correlate the clinical presentations with the neurosonographic findings.

MATERIAL AND METHODS

This study is done in department of pediatrics in neonatal intensive care unit in Universal College of Medical Sciences, a tertiary care hospital, Bhairahawa. This cross-sectional study comprise of 60 preterm neonates, referred to department of radio-diagnosis for cranial ultrasonogram. Ultrasound examination of the neonatal brain done through anterior fontanelle in coronal and sagittal planes within 1st week using healthcare logiq p6 pro ultrasound machine.

RESULTS

In this cross-sectional study of 60 neonates, 46 were male and 14 were female. Among 60 babies, 30 (50%) showed normal study and remaining 30 (50%) showed abnormal scan. Among the cases which were abnormal on scan most common finding was GMH (33.3%) and next commonest was periventricular leucomalacia (PVL- 16.7%) noted in 10 babies.

Citation: Nandkishor Gupta, Cranial Ultrasound in Detection of Neurological Lesions in Preterm Neonates in a Tertiary Care Hospital - A Prospective Observational Study. J Clin Cases Rep 4(S5): 26-32.

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CONCLUSION

Cranial ultrasonography is the best point of care neuroimaging method available for high-risk neonates. It is critical as an investigatory modality in NICU and effectively documents morphology of cerebral damage.

KEYWORDS

Cranial ultrasonography; Hypoxic ischemic encephalopathy; Germinal matrix hemorrhage; Periventricular leukomalacia; Preterm neonates

INTRODUCTION

Neonatal sonography of the brain is now an essential part of newborn care, particularly in high risk and unstable premature infants. Cranial ultrasound is the most available and easily repeatable imaging technique for the neonatal brain showing brain development and the most frequently occurring forms of cerebral injury in the preterm and terms. Preterm neonates defined as childbirth occurring at less than 37 completed weeks of gestation. There are three sub-categories of preterm birth based on gestational age: extremely preterm (<28 weeks), very preterm (28 to <32 weeks) and moderate to late preterm (32 to <37 weeks) [1]. Preterm neonates have a higher mortality and morbidity because of their greater risk for intraventricular hemorrhage (IVH) and hypoxic ischemic encephalopathy (HIE) also known as periventricular leukomalacia (PVL), which can lead to poor neurodevelopmental outcomes [2]. Hypoxic-ischemic encephalopathy (HIE) is most common clinically encountered problem in neonatal ICU and is significantly associated with neurological demise and cerebral palsy in neonates. Even in developed countries, neonates having moderate to severe hypoxic-ischemic encephalopathy death or moderate to severe disability occurs in 53% - 61% of infants. In hypoxic-ischemic encephalopathy, neonates brain shows high levels of cerebral blood flow measured at 12 hours - 24 hours of life have been associated with more severe brain injury [3]. Intraventricular hemorrhage occurs in 40% of preterm neonates who weigh less than 1500 g, 90% of hemorrhages occur within first 3 postnatal days and the remainder by 10 days. However, Intraventricular

hemorrhage is usually clinically occult and detection requires a screening USG [4]. Germinal matrix hemorrhage (GMH) is the most common cerebral insult that affects the premature infant. GMH occurs in the germinal matrix which is densely vascular and present at the caudothalamic groove until 35 weeks - 36 weeks gestation. Therefore the risk of hemorrhage is markedly reduced in infant older than 36 weeks. Infants at greatest risk for GMH are less than 32 weeks gestation, and the risk increases with extent of prematurity [5]. The grading system for GMH on NSG is given by Papile et al., 1978 to assess prognosis. Grade I: Subependymal hemorrhage, Grade II: Intraventricular hemorrhage (IVH) without ventricular dilatation, Grade III: IVH with ventricular dilatation and Grade IV: IVH with intraparenchymal hemorrhage [6]. Periventricular leukomalacia is the second most frequent lesion of the infant brain, following haemorrhage into the germinal matrix or ventricle. PVL is now considered the principal form of brain injury among preterm infants. PVL is the major reason for developing a variety of neurological sequelae including motor dysfunction, delayed cognitive development, visual impairment and epilepsy seen in 3% to 10% of premature neonates. Early identification may facilitate future preventive strategies. In the recent years, the incidence of all grades of hemorrhage has decreased because of increased antenatal steroid use and improved neonatal care. As cost containment has become a more pressing issue, the need for and frequency of screening USG has been raised [4]. The advantages of sonography over CT and MRI include easy to operate, non invasiveness, accuracy, portability, lower cost, rapid diagnosis, wide availability, repeatability, lack of

ionizing radiation, no need for sedation, bed side availability for unstable infants and suitable for screening [7].

MATERIAL AND METHODS

This hospital based prospective observational cross-sectional study was conducted in Neonatal Intensive Care Unit department of pediatrics in Universal College of Medical Sciences, a tertiary care hospital over a period of 1 year, from May 2019 to May 2020. Other neonates were excluded from study according to exclusion criteria. A total Sixty high-risk neonates admitted to NICU were selected as per the inclusion criteria on nonrandomized purposive sampling basis and were subjected to neurosonography on the selected days. If CUS revealed various findings, repeat neurosonogram were done to follow-up sequel if any. Informed consent was obtained from the parents/guardian regarding the inclusion of the neonate in the study. Assessment of factors placing the neonate in a high-risk category was done taking detailed maternal history reviewing antenatal records. All perinatal details were recorded, and detailed clinical examination was done including anthropometric measurements. Vital parameters were recorded within 24 hours - 48 hours of admission, and complete neurological examination was done during baby's stay in NICU. Gestational age was assessed as LMP of mother as well as per modified Ballard's scoring method for all preterm neonates. Evaluation with baseline routine investigations (septic and metabolic workup) and lumbar puncture in case of neonatal convulsions and neonatal sepsis, chest X-ray in all respiratory distress cases was done. Cranial ultrasound of the high-risk neonate fulfilling the inclusion criteria was performed. Follow-up cranial ultrasound was done in case of findings revealed and for preterm neonates. Morphology of cranial ultrasound findings was studied and recorded, and clinical correlation with various findings on cranial ultrasound was done. Neonates were followed until recovery and discharge from NICU.

Inclusion Criteria

Neonatal convulsions, birth asphyxia and hypoxic ischemic encephalopathy (HIE), respiratory distress, neonatal sepsis, preterm neonates, neonates born out of traumatic/instrumental labor, metabolic disturbances with convulsions, congenital malformation of central nervous system, and neural tube defects.

Exclusion Criteria

Transient tachypnea of newborn, babies with only hyperbilirubinemia, babies >28 days.

Ethical Clearance

The approval of Institutional Review Committee of Universal College of Medical Sciences, Bhairahawa, Nepal was taken before the initiation of experiment. Registration No. UCMS/IRC/222/18. All the protocols and experiments were conducted in compliance with the ethical principles and guidelines.

Sample Size

The sample size was calculated using the following formula:

$$\begin{aligned}n &= z^2pq/d^2 \\ &= (1.96)^2 \times 4 \times 96/52 \\ &= 59\end{aligned}$$

Where n = required sample size

- P = prevalence of disease (estimated to be approximately 4%)
- q = 100-p
- z = 1.96 (taken at 95% confidence interval)
- d = allowable error (taken as 5%)
- Sample size calculated by above formula is approximately 59.
- The sample size included in the study was 60.

Statistic Analysis

The data obtained by questionnaire as per the case proforma were analyzed with the help of SPSS version 22 (Statistical Package for the Social Science) program. Frequency of the qualitative variables was presented in the percentage. Value of continuous variables was

presented as mean ± SD. Data were analyzed using Chi square test for qualitative variables and analysis of variance (ANNOVA) was used for comparison of mean of continuous variables. Statistical significance was set at P value <0.05.

RESULTS

During the study period, a total 60 newborn with clinically suspected HIE were evaluated. There were 46(76.7%)male and 14(23.8%) female neonate with male to female ratio of 3.2:1. However 44(73.3%) were delivered by normal vaginal delivery, 14(23.3%) were delivered by caesarian section and breech presentation were 2(3.4%). 14(23.3%) were between 28 to 32 weeks gestational age and 46(76.7%) were between 33 weeks to 36 weeks gestational age. 5(8.3%) neonates were born very low birth weight, 25(41.7%) were born low birth weight and 30(50%) were weight more than 2 kg. 33(55%) were primi mother and 27(45%) were multi. Antenatal steroids 45(75%) mother had received and 15(25%) mother had not received (Table 1).

S.No.	CATEGORY	Distribution	Frequency	Percentage
1	Sex	Male	46	76.7
		Female	14	23.3
2	Mode of Delivery	Vaginal	44	73.3
		LSCS	14	23.3
		Breech	2	3.4
3	Gestational Age (weeks)	28-32	14	23.3
		33-36	46	76.7
4	Birth weight (kg)	<1.5	5	8.3
		1.5-2	25	41.7
		>2	30	50
5	Gravida	Primi	33	55
		Multi	27	45
6	Antenatal Steroid Administration	Received	45	75
		Not received	15	25

Table 1: Demographic data of preterm babies (n = 60).

Out of total cases 50 babies were found to have stage 2 HIE comprising of total of 83.3% whereas stage 3 and stage 1 HIE were 10% and 6.7% respectively (Table 2).

HIE Stages	No of Cases	%
Stage 1	4	6.7
Stage 2	50	83.3
Stage 3	6	10
Total	60	100

Table 2: Distribution of various stages of HIE.

Out of total cases studied 40 were presented with seizures as major clinical presentation comprising of 66.7% followed by hypotonia and delayed cry which were both at 35% of total. Other significant clinical findings included absent suckling, poor suckling and apnoea at 28.3%, 23.3% and 26.7% respectively (Table 3).

Clinical Presentations	No of Babies	%
Seizures	40	66.7
Lethargy	5	8.3
Absent Suckling	17	28.3
Poor Suckling	14	23.3
Flaccidity	2	3.3
Irritable/Excessive Cry	2	3.3
Weak Cry	4	6.6
Delayed Cry	21	35
Absent Cry	4	6.6
Sudden Onset Pallor	2	3.3
Hypotonia	21	35
Hypertonia	3	5
Apnoea	16	26.7
Total	60	100

Table 3: Distribution of various clinical presentations in HIE cases.

Shows majority of lesions found in GMH at 28 weeks - 32 weeks 7 babies and 33 weeks - 36 weeks were 13 babies found in 20 cases. PVL were equal 5 cases in 28 weeks - 32 weeks and 33 weeks - 36 weeks respectively where as 30 babies were found normal (Table 4).

Gestational Age(Weeks)	GMH	%	PVL	%	Normal	%
28-32	7	35	5	50	2	6.7
33-36	13	65	5	50	28	93.3
Total	20	100	10	100	30	100

Table 4: Distribution of various lesions in preterm neonates.

Shows most of HIE Stage 2 were GMH Grade 1 (Table 5).

HIE Stages	GMH 1	%	GMH 2	%	GMH 3	%	No. of Cases	%
Stage 1	0	0	0	0	0	0	0	0
Stage 2	13	86.6	2	13.34	0	0	15	75
Stage 3	2	40	2	40	1	20	5	25
Total	15	75	4	20	1	5	20	100

Table 5: GMH grading in HIE cases.

Out of total cases of GMH, 15 cases are of GMH1 corresponding 75% and 4 cases of GMH2 corresponding 20% and 1 cases were GMH 3 corresponding 5% (Table 6).

GMH Grades	No. of Cases	%
GMH I	15	75
GMH II	4	20
GMH III	1	5
GMH IV	0	0
Total	20	100

Table 6: Distribution of various grades of GMH in HIE cases.

DISCUSSION

Neurosonography is now being routinely performed in premature infants in many centers. This has produced a wealth of information about the central nervous system, abnormalities like GMH, PVL and ventriculomegaly, including the timing and evolution of these lesions and their eventual correlation with neurological outcome. Our study comprised of 60 preterm neonates who were sent for cranial ultrasound. Our study, there were a total of 46(76.7%) male and 14(23.3%) female and majority of babies were born to primigravida 33(55%) out of 60 preterm neonates. Sameera In Allu et al., reviewed 32(52%) male, and 30(48%) female out of 62 preterm neonates [8]. In our study, 44(73.3%) were born through vaginal, 14(23.3%) were born through LSCS and 2(3.4%) were born through assisted breech vaginal. Thakkar et al reviewed the proportion of cases that had vaginal delivery (68.2%) was significantly higher than that of those born through lower segment cesarean section (LSCS) (31.8%) in preterm neonates [9]. In our study, babies born between the gestational ages of 28 weeks to 36 weeks of which majority of them were between 33 weeks - 36 weeks of gestation comprising about 76.7% and birth weight was ranging from 0.935 kg to 2.91 kg of which most babies were >2 kg (50%). Kavya MK et al., reviewed preterm neonates with gestational age varying from 29 weeks to 37 weeks and the birth weight varying from 1.5 kg to 1.9 kg. The commonest clinical manifestation in preterm babies was

seizures (66.7%) followed by delayed cry and hypotonia (35%) and absent suckling (28.3%). Niranjan Nagaraj et al., reviewed most common clinical presentation was seizures followed by absent suckling and lethargy [10]. In our study, neurosonogram was performed within 7 days of birth which showed abnormal neurosonogram findings in 30 babies and rest of the 30 babies showed normal neurosonogram study. Gahlot A et al., reviewed first cranial neurosonography was done between first and third day, second between 7th and 10th day of birth. Out of 5 babies weighing <1.5 kg all babies showed abnormalities forming 100% and 55 babies weighing >1.5 kg 24 babies showed abnormality forming 43.6%. This study co-relates to numerous studies done previously. Abnormal neurosonogram findings in babies who have not received steroids were 15(about 25%). The most common abnormality found on neurosonogram was germinal-matrix haemorrhage. This result correlated with study done on preterm babies by Paneth N et al., [11] Germinal matrix haemorrhage was graded into I, II, III and IV. Grading was done according to Papile's classification. Grade I GMH was found in 75% babies, grade II was found in 20%, grade III in 5% and grade IV in 0% babies. This study is compared to previous studies as shown (Table 6). Our study showed periventricular leukomalacia in 10(16.6%) babies. This finding was in common with study done by Rezaie P et al., [12]. Studies done by Skullerud and Westre had also found mortality rate of 9.5% with grade I and II and mortality rate of 49% with grade III and IV GMH. Among the 10 cases of grade I GMH, all had resolved at the end of 8 weeks. All of the grade II hemorrhages resolved in subsequent studies. One babies with grade III GMH expired during follow-up. Most of the GMH is detected by Neurosonogram within first 72 hours of life. The 3 of the 4 cases of PVL persisted in the subsequent studies and developed cystic changes. In our study 14 babies were less than 32 weeks and 46 babies were more than 32 weeks' gestational age. Out of 14 babies born less than

32 weeks, 12 showed abnormal neurosonogram findings i.e. 85.7%. These findings were similar to findings in study done by Humsene et al which showed 75%. Out of 46 babies >32 wks gestational age 18 babies showed abnormalities (i.e. 39.1%) which co-relates with the study done by Amato M, Howald H Von Muralt [13]. Abnormal neurosonogram findings in babies who have not received steroids were about 63.6%. It co-relates with studies done by Singh Uma et al. (76%). The protective mechanism of it may be due to an increase in neonatal blood pressure which prevents blood pressure fluctuations or may result from enhanced maturation of the cardiopulmonary system and germinal matrix of the premature infant. In our study only full dose of corticosteroid therapy was considered positive for antenatal steroid therapy. All cases of germinal matrix hemorrhage were discovered in the initial study. In a study done by Tsiantos A et al. found that 60% of the hemorrhages took place between 15 hours to 48 hours of age with mean age of 38 hours. In another study done by Carol M Rumack MD et al., found that 64% of the hemorrhage took place within 24 hours. A study done by Leven MI et al. states that most hemorrhages occurred during first two days of life. Whereas TziporaDolfin et al., study shows 25% haemorrhage were diagnosed on first scan within first 6 hours. Neurosonogram remains the accurate, rapid imaging modality of choice for detecting GMH in preterm infants. This technique is both sensitive and specific for detecting germinal matrix

hemorrhage and periventricular leucomalacia. Neurosonogram helps in satisfactory grading of GMH. The advantages of neurosonogram includes easy to operate, noninvasiveness, accuracy, portability, lower cost, rapid diagnosis, wide availability, repeatability, lack of ionizing radiation, no need for sedation, bed side availability for unstable infants and suitable for screening. Neurosonography has now been routinely performed in premature infants. This has produced wealth of information about the central nervous system like GMH and PVL.

CONCLUSION

High efficacy of cranial ultrasound in detecting the presence of brain damage and its evolution on regular follow-up guides clinical decisions and prognosis. This is particularly important in the anticipation of potential preventive, protective, and rehabilitative strategies for the management of critically ill newborn infants. Cranial ultrasound mandatory screening for all preterm and low birth weight babies. It also emphasizes its use as a screening modality for preterm neonates influencing their neurodevelopmental outcome.

CONFLICT OF INTEREST

The authors not shows any conflict of interest.

ACKNOWLEDGEMENTS

We thanks the staff of the NICU and as well as Obstetrics and Gynaecology at UCMS for their assistance.

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