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Original Article

Early Detection of Central Nervous System Abnormalities by Neurosonography in Critically Ill Neonates

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ABSTRACT

Background: Neurosonography has been widely used for screening and early detection of Central Nervous System (CNS) defects, such as intraventricular hemorrhage, hydrocephalus, cerebral edema, or any structural anomalies in the neonatal brain in the neonatal intensive care unit (NICU) of a tertiary level hospital. The present study aimed to assess the detection of CNS abnormalities by neurosonography in critically ill neonates.

Methods: This prospective cross-sectional study at the Neonatology Unit of the Paediatric Department of Acharya Vinoba Bhave Rural Hospital (AVBRH). A neonate was described as "critically ill" based on detailed maternal history and clinical examination. These neonates were subjected to neurosonography according to the inclusion and exclusion criteria in accordance with the noted protocols and various anomalies. Gestational age, birth weight, clinical examination, investigation, neurosonography finding, and outcomes were evaluated.

Results: Neurosonography was performed in 105 critically ill neonates, out of whom 21 cases had abnormal neurosonography findings. Abnormal neurosonography was not significantly correlated with birth weight and gestational age of high-risk neonates (P=0.538 &P=0.130). The most frequent clinical manifestation was respiratory distress syndrome, followed by a neonatal seizure. The mean scores of heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation were obtained at 140±19.81, 54.08±13.07, 90.96±8.66, 54.13±8.39, and 94.39±6.93, respectively. There was no statistically significant correlation between the vital parameters and the presence of abnormalities on neurosonography. On neurosonography, 20% of neonates had abnormal findings, including hydrocephalus (8.57%), Intraventricular hemorrhage (6.6%) periventricular echogenicity (1.90%), cerebral edema (0.95%), germinal matrix hemorrhage (0.95%), and brain abscess (1%). Furthermore, 72 (68.57%) neonates had positive outcomes at the time of NICU discharge, and 19(18.10%) cases died.

Conclusion: Neurosonography is a useful tool in NICU. It is an acceptable and reliable modality to screen critically ill neonates, assisting the early detection and management of these ill neonates.

Keywords: Critically ill neonates, Hydrocephalus, Intra-ventricular hemorrhage, Neurosonography

Introduction

Neurosonography (NUSG) is a reliable cost-effective modality which can be performed at neonates' bedside to detect their intracranial changes with little disturbance to neonates. It can be also used whenever appropriate for the visualization of continuous brain maturation and development of lesions. Moreover, it resolves the transportation problem of critically ill neonates to the computed tomography or Magnetic resonance Imaging room. In neonates, fontanels and many other sutures are remained open, allowing us to observe inside the brain for any maturation and development of pathological abnormality.

Fontanel, which is also known as "window to the brain" can be used to detect most pathological changes occurring in the brains of critically ill

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neonates (1-3). The NUSG plays a peculiar role in the regular assessment of the brains of high-risk neonates. It can detect most of the hemorrhagic, ischemic, and cystic brain, as well as calcification lesion, infection in the brain, and significant anatomical anomalies. It can be also used for early detection of many etiological factors of neonatal encephalopathy and epilepsy in term neonates and continuous progress monitoring of hypoxic-ischemic brain damages (2-4). Neurosonogram helps in the assessment of the gravity of neurodevelopment and its outcome in neonates with hypoxic-ischemic encephalopathy (HIE) and critically ill neonates with congenital or acquired brain anomalies (3-6). Immediately after birth, a neurosonogram can be used as many times as possible for screening of neonatal brain without any side effects. In light of the aforementioned issues, the present study aimed to assess the early detection of central *nervous system* (CNS) abnormalities by neurosonography in critically ill neonates.

Methods

This prospective cross-sectional study at the Neonatology Unit of Paediatric Department of Acharya Vinoba Bhave Rural Hospital (AVBRH) between June 2019 and Aug 2020. It has a 1525-bedded medical college in SawangiMeghe, Wardha, India, with state-of-the-art facilities. The inclusion criteria entailed admission to neonatal intensive care unit (NICU) due to a serious illness. On the other hand, the exclusion criteria were as follows: term neonates with hyperbilirubinemia, transient tachypnoea of newborns, neonates admitted to NICU for observation, and neonatal death within 24 h. The Ethical Committees of the Datta Meghe Institute of Medical Sciences (DMIMS) approved the study protocol.

After taking the consent from parents, neonates were included in the research. Irrespective of the birth weight, size, and gestational age, all the neonates at higher risk of morbidity or mortality due to maternal, fetal, or placental abnormalities, mainly in the first 28 days of life were regarded as critically ill. This comprised critically ill neonates with neonatal seizures, birth asphyxia, HIE, respiratory difficulty, neonatal Septicaemia, premature birth, traumatic/instrumental labor neonate, metabolic abnormalities with seizure, congenital CNS malformation, and neural tube disorders. All seriously ill neonates admitted to NICU were selected via non-random sampling and subjected to neurosonogram. Clinical examinations, including anthropometric measurements, were performed. Vital parameters were recorded within 24-48 hours of admission, and a complete neurological examination was performed during neonates' stay in NICU. Gestational age was assessed as the last menstrual period and modified Ballard's scoring method for all preterm neonates.

In case of neonatal convulsions and sepsis, evaluation was performed with baseline routine investigations (septic and metabolic workup) and lumbar puncture; moreover, the cases with respiratory distress underwent chest X-ray. The morphology of neurosonogram findings was analyzed and collected, followed by clinical association with different studies on neurosonography. The GE ultrasound system was used for performing a neurosonogram. Sequelae were monitored in case of any abnormal neurosonography results. Neonates were supervised until recovery and discharge.

Sample Size Calculation

The sample size of the present study was calculated at 997 newborns admitted to the NICU during the study period. Finally, by considering the population size of 5,000 with 95% confidence level, and ±5% margin of error, 99 subjects entered the study to determine CNS abnormalities by neurosonography in critically ill neonates admitted to the NICU using the following formula:

$n = [DEFF*Np(1-p)]/ [(d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)]$

where N=population size, P= anticipated prevalence rate, d= confidence limit, and DEFF: design effect.

Statistical analysis

Descriptive statistical analysis was carried out in the present study. The results of continuous measurements were presented as mean±standard deviation (SD), while those of categorical measurements were presented in number (%). Chi-square ($\chi 2$) test was conducted to compare the categorical data. Nevertheless, when the expected frequency was less than 5, Fisher's exact test was used instead. For parametric data, Student's t-test was employed to compare the two groups. A p-value less than 0.05 was considered statistically significant.

Results

From July 2019 to August 2020, a total of 1,109 neonates were born, 105 (9.46%) of whom were critically ill and admitted to NICU. Out of these

105 ill neonates, 21 (20%) cases had abnormal neurosonography findings. In terms of gender, the majority of neonates (60.95%) were male with no significant association with abnormal neurosonography findings (P=0.368). The mean weight score of very low birth weight (VLBW), low birth weight (LBW), and normal weight neonates were reported as 1.24±0.32, 1.99±0.29, and 1.99±0.29 gr, respectively (Table 1). There was no significant association between birth weight and abnormal neurosonography (P=0.538). It was found that 44(81.48%) and 10(18.52%) of cases had normal and abnormal cranial ultrasound results(Table 2) in critically ill neonates with preterm gestation. There was no significant association between the gestational age of high-risk neonates and abnormal neurosonography (P=0.130). Regarding delivery mode, 40 (38.10%), 64(60.95%), and 1 (0.95%) neonates were born via normal labor, lower segment cesarean section, and instrumental delivery, respectively. There was a statistically significant association between mode of delivery and abnormal neurosonography (P=0.00).

Table 1. Distribution of the cases according to weight

Weight (gm)	Normal Neurosonography cases		Abnormal Neurosonography		Total	
	Number of cases (n=84)	Mean±SD	Number of cases (n=21)	Mean±SD	Number of cases (n=105)	Mean±SD
<1500	16 (76.19%)	1.30±0.34	5 (23.81%)	1.05±0.17	21	1.24±0.32
1500-2500	49 (84.48%)	1.98±0.28	9 (15.52%)	2.06±0.33	58	1.99±0.29
2501-3500	18 (72.00%)	2.78±0.34	7 (28.00%)	2.82±0.38	25	2.79±0.34
>3501	1 (100%)	4.0	00 (0.0%)	00	01	4.00
	84	2.05±0.60	21	2.07±0.74	105	2.05±0.63

Table 2. Distribution of the according to gestational age

Gestational Age (weeks)	Number of Normal Neurosonography	Number of Abnormal Neurosonography	Total
<36	44 (81.48%)	10 (18.52%)	54 (100%)
37-42	40 (80%)	10 (20%)	50 (100%)
>42	0.00 (0.00%)	01 (100%)	01 (100%)

Table 3. Association of Neurosonography with Maternal Risk factors and Neonatal comorbidities

	Normal Neurosonography N=84		Abnormal Neurosonography N=21		P-value
	Number	Percentage	Number	Percentage	
Maternal Risk Factors					
• Pregnancy-induced hypertension	12	14.29	2	9.52	0.731
• Premature Rupture of Membrane	4	4.76	1	4.76	1.000
• Antepartum hemorrhage	4	4.76	0	0.00	0.581
• Others	28	33.33	4	19.05	0.291
Neonatal Comorbidities					
• Respiratory distress syndrome	37	44.05	8	38.10	0.622
• Neonatal Sepsis	34	40.48	11	52.38	0.324
• Birth Asphyxia	15	17.86	5	23.81	0.534
• Neonatal Seizure	28	33.33	9	42.86	0.414
• Necrotizing enterocolitis	0	0.00	1	4.76	0.200
• Birth trauma	1	1.19	2	9.52	0.101
• Other comorbities	37	44.05	10	47.62	0.768

Table 4. Association between Neurosonography and abnormal clinical examination finding in critically ill neonates

Clinical Examination	Normal Neurosonography N=84		Abnormal Neurosonography N=21		P-value
	Number	Percentage	Number	Percentage	
Abnormal cry	19	22.62	5	23.81	0.907
Poor Activity	30	35.71	10	47.62	0.315
Poor abnormal tone	17	20.24	7	33.33	0.201
Poor reflexes	15	17.86	4	19.05	0.899
Abnormal posture	17	20.24	5	23.81	0.719
Pallor presence	13	15.48	5	23.81	0.365
Cyanosis presence	8	9.52	2	9.52	1.000
Tachycardia	11	13.10	8	38.10	0.008
Tachypnoea	37	44.05	10	47.62	0.768

Abnormal CFT	14	16.67	2	9.52	0.415
Abnormal temperature	3	3.57	1	4.76	0.799
Presence of *congenital heart disease*	13	15.48	3	14.29	0.892
RS abnormality	50	59.52	14	70	0.387
Hepatosplenomegaly	3	3.57	00	00	--

Table 5. Vital parameter of the critically ill neonates on admission in neonatal intensive care unit

Vital Parameter	Number of Normal Neurosonography N= 84 (Mean±SD)	Number of Abnormal Neurosonography N=21 (Mean±SD)	P-value
Heart Rate	138±2.08	145.90±4.81	0.142
Respiratory rate	53.98±1.46	54.47±2.59	0.879
Systolic Blood Pressure	91.03±0.84	90.66±2.56	0.862
Diastolic Blood Pressure	54.35±0.88	53.23±2.05	0.587
oxygen saturation	94.54±0.69	93.76±1.95	0.644

Table 6. Association of Neurosonography with abnormal investigation in critically ill neonates

Investigation	Normal Neurosonography		Abnormal Neurosonography		P-value
	Number	Percentage	Number	Percentage	
Hemoglobin (<13gm%)	14	16.67	5	23.81	0.447
PCV (<40%)	17	20.24	4	20	0.903
TLC (<5000 or >30,000)	9	10.71	4	19.05	0.300
Platelet (<1.5lakh)	44	52.38	7	33.33	0.118
Positive CRP	22	26.19	7	33	0.513
Positive C/S	33	39.29	11	52.38	0.277
Hypoglycaemia	11	13.10	3	14.29	0.886
Hypocalcemia	7	8.33	1	4.76	0.581
Abnormal electrolyte	23	27.38	6	28.57	0.913
Abnormal bilirubin	20	23.81	4	19.05	0.642

Table 7. Neurosonography abnormalities in critically ill neonates

Neurosonography	Number	Percentage
Normal Neurosonography	84	80
Abnormal Neurosonography	21	20
• Hydrocephalus	09	8.57
• Intraventricular haemorrhage	07	6.66
• Periventricular echogenicity	02	1.90
• Germinal matrix haemorrhage	01	0.95
• Cerebral edema	01	0.95
• Brain abscess	01	0.95

Table 8. Association of Neurosonography with clinical outcome in critically ill neonates

Outcome	Normal Neurosonography		Abnormal Neurosonography		P-value
	Number	Percentage	Number	Percentage	
Discharge	60	71.43	12	57.14	
Death	14	16.67	5	23.81	0.446
Discharge against *medical* advice	10	11.90	4	13.33	
Total	81	100	21	100	

Regarding the relationship between maternal risk factors and abnormal cranial ultrasound findings, abnormal cranial ultrasound was not significantly correlated with pregnancy-induced hypertension (PIH) (P=0.731), premature rupture of membranes (P=1.00), and antepartum hemorrhage (P=0.581). In addition, neurosonography showed no significant association with respiratory distress syndrome (RDS), sepsis, birth asphyxia, neonatal seizure, Necrotizing enterocolitis (NEC), and birth trauma (Table 3). There was no significant association between abnormal neurosonography and the day of life it was performed. The RDS was the most common clinical presentation, followed by neonatal seizures in symptomatic children.

The most common clinical feature in critically ill neonates was tachypnoea, followed by poor activity on clinical examination (Table 4). There was no statistically significant association between clinical examination and the presence of abnormalities on neurosonography. There was no case of congenital malformations or neural tube defects. The mean scores of heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, and SpO2 were reported as 140±19.81, 54.08±13.07, 90.96±8.66, 54.13±8.39, and 94.39±6.93, respectively. There was no

statistically significant association between the vital parameters and the presence of abnormal findings in NUSG (Table 5).

In the present study, 27.62%, 41.90%, 13.33%, 7.62%, of cases had C-reactive protein (CRP) positive, positive blood culture, hypoglycemia, and hypocalcemia on investigatory record, respectively (Table 6). There was no statistically significant association between the investigation and the presence of abnormalities on neurosonography. Cerebrospinal fluid (CSF) analysis was performed on 29 neonates, out of whom 22 cases had normal NUSG, 7 neonates showed abnormal NUSG, and meningitis was observed in 15 neonates. On neurosonography, 20% of neonates had abnormal findings: hydrocephalus (8.57%), Intraventricular hemorrhage (IVH)(6.6%), periventricular echogenicity (1.90%), cerebral edema (0.95%), germinal matrix hemorrhage (0.95%), and brain abscess (1%) (Table 7). Furthermore, 72 (68.57%) neonates had good outcomes at the time of discharge from NICU, 19(18.10%) died, and 14(13.33%) of cases were discharged from NICU for various reasons before clinical recovery (discharge against medical advice) (Table 8). There was no association between the outcome and neurosonography abnormalities (P=0.446).

Discussion

Neurosonography can be used as a general screening procedure for critically ill neonates admitted to NICU. It is of great help in routine serial scanning in high-risk neonates and further treatment of critically ill neonates. The early detection of CNS abnormalities by neurosonography will help in early therapeutic interventions. It is now regularly performed in preterm neonates in many hospitals in India. Neurosonography provides a wealth of information about CNS anomalies, such as Germinal matrix hemorrhage, periventricular leukomalacia, and ventriculomegaly, and their subsequent association with neurological outcome. It is also useful in the diagnosis of certain significant congenital CNS abnormalities, such as cyst-like lesions (e.g., hydrocephalus, porencephalic cysts, Dandy-Walker cysts complex, and arachnoid cysts), corpus callosal agenesis, and vein of Galen aneurysm (7-9). Mercuri et al. (10) reported that the incidence of abnormal neurosonogram findings in apparently well neonates was 20%, whereas Badrawy et al. (11) pointed out that 37% of preterm neonates had abnormal cranial ultrasound findings. In a similar vein, De Vries et al. (12) reported that 79% of neonates with cerebral palsy (CP) had major cranial ultrasound findings.

Maternal risk factors were found in 55 neonates, with PIH being the most common one. Nonetheless, the association between maternal risk factors and abnormal neurosonogram was not statistically significant in the present study. However, no neurological abnormality was found in neonates born to diabetic mothers. Moreover, 12 neonates were born to mothers who suffered from PIH. Out of critically ill preterm neonates, 44(81.48%) and 10(18.52%) cases had normal and abnormal neurosonography, respectively. Due to vascular, cellular, and anatomical features of developing brain and physiological instability owing to limited cerebral circulatory autoregulation, the brain of premature neonates is vulnerable to both hemorrhagic and ischemic injury during the late second and early third trimesters (9-12). In these studies, abnormal neurosonogram showed no significant association with neonatal comorbidities, such as RDS and birth asphyxia. The most common abnormality was RDS, followed by neonatal sepsis and birth asphyxia. Fumagalli et al. (13) also observed an increased risk of brain injury, especially IVH, in preterm neonates with RDS since it has been associated with alteration of blood flow to the brain in the first few days of life. In their study, Vermeulen et al. (14) reported early-onset neonatal infectious disease as an independent risk factor for abnormal cranial USG.

In the current study, out of all high-risk neonates, 8.57%, 6.6%, and 1.90% of cases had hydrocephalus, IVH, and periventricular echogenicity, respectively. Along the same lines, in their study, Glass et al. (15) reported that 47.6% and 52.4% of all high-risk neonates presenting with seizures had normal and abnormal cranial ultrasound results, with thalamic periventricular echogenicity being the most commonly detected abnormality (30.9%). In the same context, Van Houten et al. (16) found that 59% of neonates with congenital heart diseases had a higher incidence of cranial ultrasound abnormalities. In the present study, 14.29% of high-risk neonates with abnormal findings on neurosonography had congenital heart diseases. In this study, abnormal cranial ultrasound findings showed no statistically significant association with neonates demonstrating positive CRP and low platelet. Furthermore, abnormal neurosonography findings were not significantly correlated with hemoglobin, packed cell volume, total leukocyte count, positive culture, serum electrolytes, serum

bilirubin, and cerebrospinal fluid analysis. The NUSG findings in cases with HIE included increased echogenicity in white matter and resultant increased grey matter-white matter differentiation (17). These findings could be focal or diffuse and are assumed to reflect edema or necrosis. Neurosonography can be also used to detect dilatation of ventricles and hydrocephalus. In a related study, it was found that coronal measurements of the diameters of both ventricles are similar when obtained by sonography and MRI (18). Mortality was reported as 23.81% in the abnormal neurosonography group, while 16.67% of cases died in the normal neurosonography group. The IVH was the most common cause of mortality in the present study. This result is consistent with those reported by Ghoor et al. (18). The findings of the studies conducted by Ballabh P et al. (19) and Mulindwa MJ et al. (20) pointed out that birth asphyxia, sepsis, mechanical ventilation, and patent ductus arteriosus were associated with increased risk of IVH. They also reported higher mortality in neonates with IVH.

Conclusion

Neurosonography is an excellent instrument for the initial screening of neonatal brain. As evidenced by the results of the present study, neurosonography assumes great importance as an analysis tool which efficiently records the anatomy of brain injury in neonates. It is a mandatory screening for only preterm and LBW neonates. Our studies also demonstrated abnormalities in term neonates. Neurosonography should be mandatory for all NICU high-risk neonates. The most common abnormalities were hydrocephalus and IVH, leading to the highest rate of mortality. Early neurosonography could help in prognosticating immediate outcomes and early interventions.

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Conflicts of interest

The authors declare that they no conflict of interest regarding the publication of this article.

References

1. Nagaraj N, Berwal PK, Srinivas A, Sehra R, Swami S, Jeevaji P, et al. A study of neurosonogram abnormalities, clinical correlation with neurosonogram findings, and immediate outcome of high-risk neonates in Neonatal Intensive Care Unit. J Pediatr Neurosci. 2016; 11(3):200-5.
2. Kinikar U, Dhanawade S. Study of cranial ultrasound its correlation with perinatal risk factors and its outcome in preterm neonates admitted to Neonatal intensive care unit. Int J Pediatr Res. 2018; 5(4):169-74.
3. Gahlot A, Joshi A. Role of neurosonography in neonates with clinically suspected intracranial pathology. Int J Res Med Sci. 2019; 7(6):2302.
4. Pape KE, Bennett-Britton S, Szymonowicz W, Martin DJ, Fitz CR, Becker L. Diagnostic accuracy of neonatal brain imaging: A postmortem correlation of computed tomography and ultrasound scans. J Pediatr. 1983; 102(2):275-80.
5. Stark JE, Seibert JJ. Cerebral artery Doppler ultrasonography for prediction of outcome after perinatal asphyxia. J Ultrasound Med. 1994; 13(8):595-600.
6. Bracci R, Perrone SN. Hypoxic-ischemic encephalopathy: clinical aspects. In: Volpe J, editor. Neurology of the newborn. 5th ed. Philadelphia, PA: WB Saunders; 2001. P. 218-80.
7. de Vries LS, Groenendaal F. Neuroimaging in preterm infants. Ment Retard Dev Disabil Res Rev. 2002; 8(4):273-80.
8. Daneman A, Epelman M, Blaser S, Jarrin JR. Imaging of the brain in full-term neonates: does sonography still play a role? Pediatr Radiol. 2006; 36(7):636-46.
9. Van Wezel-Meijler G. Cranial ultrasonography: advantages and aims. Neonatal cranial ultrasonography. 1st ed. Berlin: Springer; 2007. P. 3-4.
10. Mercuri E, Dubowitz L, Brown SP, Cowan F. Incidence of cranial ultrasound abnormalities in apparently well neonates on a postnatal ward: correlation with antenatal and perinatal factors and neurological status. Arch Dis Child Fetal Neonatal Ed. 1998; 79(3):F185-9.
11. Badrawy N, Edrees A, Sebaie DE, El-Ghawas M. Cranial ultrasonographic screening of the preterm newborn. Alex J Pediatr. 2005; 19(2):347-56.
12. De Vries LS, Wigglesworth JS, Regev R, Dubowitz LM. Evolution of periventricular leukomalacia during the neonatal period and infancy: correlation of imaging and postmortem findings. Early Hum Dev. 1988; 17(2-3):205-19.
13. Fumagalli M, Ramenghi LA, De Carli A, Bassi L, Farè P, Dessimone F, et al. Cranial ultrasound findings in late preterm infants and correlation with perinatal risk factors. Ital J Pediatr. 2015; 41:65.
14. Vermeulen GM, Bruinse HW, Gerards LJ, de Vries LS. Perinatal risk factors for cranial ultrasound abnormalities in neonates born after spontaneous labour before 34 weeks. Eur J Obstet Gynecol Reprod Biol. 2001; 94(2):290-5.
15. Glass HC, Bonifacio SL, Sullivan J, Rogers E, Ferriero DM, Goldstein R, et al. Magnetic resonance imaging and ultrasound injury in preterm infants with seizures. J Child Neurol. 2009; 24(9):1105-11.
16. van Houten JP, Rothman A, Bejar R. High incidence of cranial ultrasound abnormalities in full-term infants with congenital heart disease. Am J

Perinatol. 1996; 13(1):47-53.
17. Levene MI. Measurement of the growth of the lateral ventricles in preterm infants with real time ultrasound. Arch Dis Child. 1981; 56(12):900-4.
18. Ghoor A, Scher G, Ballot DE. Prevalence of and risk factors for cranial ultrasound abnormalities in very-low-birth-weight infants at Charlotte Maxeke Johannesburg Academic Hospital. South Afr J Child Health. 2017; 11(2):66-70.
19. Ballabh P. Pathogenesis and prevention of intraventricular hemorrhage. Clin Perinatol. 2014; 41(1):47-67.
20. Mulindwa MJ, Sinyangwe S, Chomba E. The prevalence of intraventricular hemorrhage and associated risk factors in preterm neonates in the neonatal intensive care unit at the University teaching hospital, Lusaka, Zambia. Med J Zambia. 2012; 39(1):16-21.