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Original Article

Radiology Section

Evaluation of Intracranial Abnormalities by Transcranial Ultrasound in Neonates- An Observational Study

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ABSTRACT

Introduction: Intracranial abnormalities include hydrocephalus, intracranial haemorrhage and related hypoxic-ischemic damage, for which diagnosis can be confirmed by the transcranial ultrasound. Apart from this, transcranial ultrasound may also be helpful in screening of suspected intracranial infections and tumour. Various studies have demonstrated high sensitivity and specificity of transcranial ultrasound in detecting various intracranial abnormalities.

Aim: To evaluate the efficiency of ultrasonography in the diagnosis of intracranial abnormalities in neonates.

Materials and Methods: This observational cross-sectional study was conducted in the Department of Radiodiagnosis, SBKS MIRC Sumandeep Vidyapeeth, Piparia, Vadodara from February 2019 to August 2020. Forty neonates with abnormal neurological presentation were included in the study and detailed data regarding prenatal, perinatal and postnatal period was obtained from parents and entered in questionnaire. Length, weight was noted. Further, all the neonates were subjected to relevant blood investigations such as Complete Blood Count (CBC), blood glucose and other investigations depending upon the clinical findings. All the neonates were then subjected to transcranial ultrasonography.

Results: In present study, mean gestational age of 40 neonates was 35.38±3.59. Male preponderance was noted in present study with male:female ratio of 2.08:1. Mean birth weight of neonates was 2.11±0.60. Most common mode of delivery was vaginal in 57.5% cases followed by Lower (uterine) Segment Caesarean Section (LSCS) in 27.5% cases. Antenatally, steroids are given in only 25% of the cases in present study. Most common clinical manifestation was seizures and lethargy. Transcranial ultrasound revealed germinal matrix hemorrhage in majority of neonates.

Conclusion: Transcranial ultrasound is recommended in every high risk neonate as a first line modality to assess the presence of intracranial abnormalities and for timely referral to higher-centres. It is quick, inexpensive, portable, non invasive and free from ionising radiation.

Keywords: Anterior fontanelle, Germinal matrix haemorrhage, Neonatal brain, Neurosonography

INTRODUCTION

Brain development in fetus begins during third gestational week when neural progenitor cells start differentiating and the development continues throughout the life [1]. However, the brain development in fetal life is vulnerable to hemorrhagic and ischemic injuries especially during late second and third trimester. This insult may result from vascular, cellular, anatomical and physiological instability due to limited cerebral circulatory autoregulation [2].

Preterm neonates especially less than 32 weeks of gestation are at high risk of intracranial insults such as intraventricular haemorrhage and periventricular leucomalacia [3]. Apart from these, congenital anomalies such as disorder of neural tube closure, diverticulation, cleavage, sulcation, neuronal migration and posterior fossa developmental defects also affect intracranial component. As a result of cerebral injury, it has been estimated that approximately 5 to 10% of preterm neonates sustain permanent major motor impairment including Cerebral Palsy (CP) which may range from mild motor dyspraxia to severe spastic motor deficits [4,5]. Also, these insults are important cause of neonatal and infant mortality that are considered important indicator of health status of the community [4,5].

With the goal of reaching "EVERY NEWBORN", by 2030, various medical and technological advances have been made in neonatal care in India at community as well as facility levels [6]. Transcranial ultrasonogram plays an important role in neonatal care especially among preterm and unstable high risk neonates in screening of neonatal intracranial abnormalities. In modern neonatology, transcranial ultrasonogram has become an essential diagnostic tool for assessing the normal anatomy and pathological changes in neonatal brain [7,8].

As sutures and fontanelles are still open in neonates, these can be used as a window to look into the brain with the aid of ultrasonogram [8]. The use of brain imaging through anterior fontanelle was first reported by Dewbury KC and Aluwihare AP [9]. With further advancement i.e., with the development of high resolution transducers and doppler, the technique has gained importance and is being widely used for primary brain imaging among neonates.

Magnetic Resonance Imaging (MRI) and Computerised Tomography (CT) scan are helpful in assessing the intracranial anomalies among neonates. However, in resource poor setting like India, it is not possible to subject each child to MRI scan. Thus, ultrasound being available even at peripheral health centre is being used by radiologists for screening of intracranial abnormalities to evaluate the immediate risk and possible long-term neurological outcomes [10]. Transcranial Ultrasound (USG) has certain advantages over MRI and CT scan such as it is rapid, inexpensive, non invasive, portable, and free from risk of radiations. It can be performed in neonates without requiring sedation [7].

This modality is helpful in assessing the intraventricular volume and contents such as intraventricular septations. Also, transcranial USG may be helpful in follow-up of cases diagnosed by MRI [10].

Transcranial ultrasound helps in imaging of brain and intraventricular chambers through sound waves reflected from the Cerebrospinal Fluid (CSF). For the evaluation of extra-axial fluid space, meninges, sinuses, conventional markings and cerebral cortex, high frequency linear array transducers are used. Various studies have demonstrated

high sensitivity and specificity of transcranial ultrasound in detection of various intracranial abnormalities [10,11]. However, this technique is operator dependent and can be done in infants in whom anterior fontanelle or other acoustic window is patent [11].

Though accurate impact of cerebral insult can be done in childhood with the help of neurodevelopment assessment, there remains a critical need to identify as early as possible to implement potential therapies to prevent early injury or promote regeneration and repair of chronic lesions. Hence, present study was conducted to evaluate the accuracy of ultrasonography in diagnosis of intracranial abnormalities in neonates and also to classify various clinical presentations in neonates with neurosonographic observations of both gender, age of gestation and mode of delivery.

MATERIALS ANS METHODS

The present observational cross-sectional study was conducted in the Department of Radiodiagnosis, SBKS MIRC Sumandeep Vidyapeeth, Piparia, Vadodara, from February 2019 to August 2020. ethical clearence was obtained from Institutional Ethics Committee (IEC no. SVIEC/ON/MED1/BNPG281/D19031 of 1st Feb. 19'). Written consent was obtained from all the study participants after explaining them nature and purpose of study. They were ensured that confidentiality will be maintained and option to withdraw from the study was always kept open.

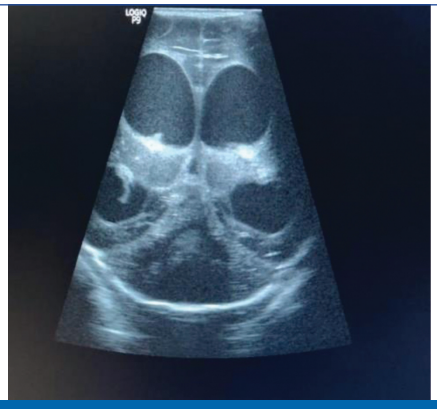
Inclusion criteria: All neonates referred to the Department of Radiodiagnosis with clinical presentation of intracranial pathologies such as seizures, lethargy, apnoea, sudden onset pallor, increase in muscle tone, bulging anterior fontanels and whose parents gave written informed consent were included

Exclusion criteria: Neonates, whose parents were not willing to participate in the study and refused to give consent, were excluded.

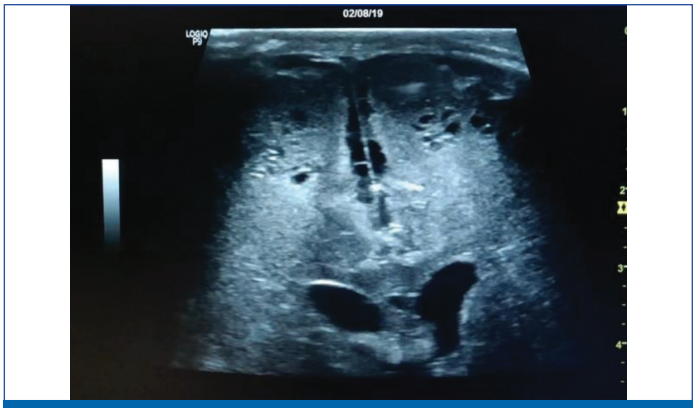
Sample size: Forty neonates, referred to the department of Radiodiagnosis, with clinical presentation of intracranial pathologies within the study duration were selected using purposive sampling method.

Data collection: Detailed data regarding sociodemographic variables such as age, gender etc., were obtained from all the parents. Detailed clinical history regarding prenatal, perinatal and postnatal period was obtained from the parents in a proforma. Length in cm, weight in kg was noted. Further, all the neonates were subjected to relevant blood investigations such as CBC, blood glucose and other investigation depending upon the clinical finding. All the neonates were then subjected to transcranial ultrasonography using USG machine (USG Machine- GE LOGIQ P9 and P5 machine.

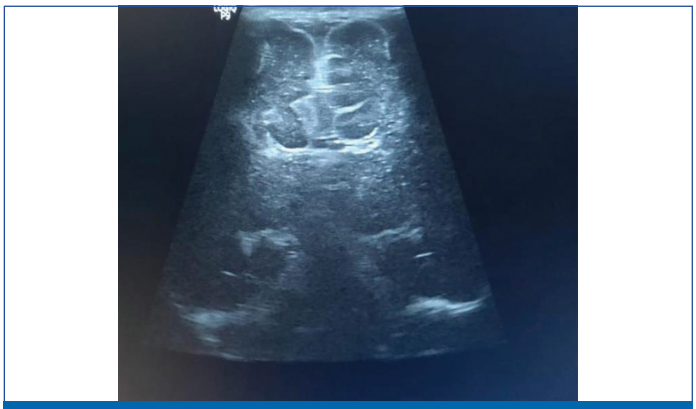
Probes- 7.5-10 MHz Curvilinear probe and 3.5-5 MHz sectoral probe. Initial USG was done as soon as possible following birth [Table/Fig-1-4] and repeat follow-up USG was done at the end of one month.



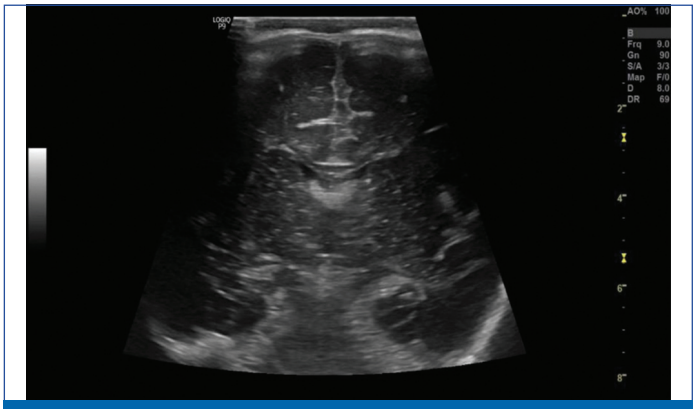
[Table/Fig-1]: Sonographic image of newborn shows bilateral lateral ventricles and third ventricle dilatation suggestive of communicating hydrocephalus.



[Table/Fig-2]: Sonographic image of neonatal brain showing multiple ill-defined anechoic cysts of varying sizes involving bilateral frontal deep white matter suggesting possibility of Grade-IV Periventricular Leukomalacia (PVL).



[Table/Fig-3]: Ultrasound of neonate showing widely separated, parellal and pointing frontal horns of lateral ventricles. Corpus callosum is not visualised. Suggest P/O agenesis of corpus callosum.



[Table/Fig-4]: Echogenic material anterior to bilateral caudothalamic groove suggest P/O germinal matrix haemorrhage Grade-I.

STATISTICAL ANALYSIS

Data was compiled using MS Excel and analysed using IBM SPSS software version 20. Data were grouped and expressed as frequency and percentage whereas numerical data was expressed as mean and standard deviation. Chi-square test was applied and p-value less than 0.05 were considered statistically significant.

RESULTS

In present study, mean gestational age was 35.38±3.59 weeks (range 27-40 weeks). About 19 (47.5%) neonates each belonged to 28 to 36 and more than 37 weeks. Majority of neonates in present study were males. Mean birth weight of neonates was 2.11±0.60 kg which ranged from 0.80-3.21 kg. Birthweight in majority of neonates was 2.1 to 2.5 kg (30%). Antenatally, steroids were given in one fourth i.e., 25% of the cases [Table/Fig-5].

Most common clinical manifestation was seizures and lethargy observed in 19 (47.5%) cases each, followed by absent sucking. Excessive cry and sudden onset pallor was noted in 5 (12.5%) and 4 (10%) cases,

Gestational age	Frequency (n=40)	Percent
<28 weeks	2	5.0
28-36 weeks	19	47.5
≥37 weeks	19	47.5
Gender		
Male	27	67.5
Female	13	32.5
Weight (kg)		
<1	2	5.0
1-1.5	6	15.0
1.5-2	9	22.5
2.1-2.5	12	30.0
>2.5	11	27.5
Parity		
Primipara	20	50.0
Multipara	20	50.0
Mode of delivery		
Vaginal delivery	23	57.5
LSCS	11	27.5
Outlet forceps	5	12.5
Preterm assisted breech	1	2.5
Steroid		
Given	10	25
Not given	30	75

[Table/Fig-5]: Distribution according to gestational age, gender, birth weight, parity, mode of delivery and antenatal use of steroids.

respectively. Least common clinical manifestation in present study was ear discharge observed in 1 (2.5%) case only [Table/Fig-6].

Clinical features	Frequency (n=40)	Percent
Seizures	19	47.5
Lethargy	19	47.5
Absent sucking	6	15
Excessive cry	5	12.5
Sudden onset pallor	4	10
Apnea	3	7.5
Flaccidity	3	7.5
Fever	3	7.5
Hypertonia	2	5.0
Bulging anterior fontanelle	2	5.0
Ear discharge	1	2.5

[Table/Fig-6]: Distribution according to clinical features.

Transcranial ultrasound revealed germinal matrix haemorrhage in majority of neonates followed by Periventricular Leukomalacia (PVL) [2,3] of various grades and meningitis. In about 9 (22.5%) cases, transcranial ultrasound revealed normal findings [Table/Fig-7].

In present study, out of 40 cases observed initially, 5 (12.5%) cases lost to follow-up whereas mortality was documented in 7 (17.5%) neonates. About 3 (7.5%) neonates were referred to higher centre for management. Findings were same in 16 (40%) cases. However, intracranial abnormalities worsened in 2 (5%) cases) [Table/Fig-8].

Out of 2 neonates with <28 weeks of gestation, seizures were observed in 2 (100%) cases whereas lethargy, absent sucking and excessive cry was observed in 1 (50%) case each. Similarly, out of 19 neonates between 28 to 36 weeks of gestation, lethargy was observed in 11 (57.9%) cases whereas seizures and apnea was documented in 8 (42.1%) and 3 (15.8%) cases, respectively. The observed association of gestational age with clinical features was statistically insignificant (p>0.05) [Table/Fig-9].

USG findings	Frequency (n=40)	Percent
Agenesis of corpus callosum	1	2.5
Choroid plexus cyst	1	2.5
Dandy walker malformation	1	2.5
Meningitis	5	12.5
Grade-I Germinal matrix haemorrhage [2]	7	17.5
Grade-II Germinal matrix haemorrhage	1	2.5
Grade-III Germinal matrix haemorrhage	4	10.0
Grade-IV Germinal matrix haemorrhage	1	2.5
Hydrocephalus	3	7.5
Persistent cavum septum pellucidum	1	2.5
PVL Grade-I [3]	4	10.0
PVL Grade-II	1	2.5
PVL Grade-IV	1	2.5
Normal	9	22.5

[Table/Fig-7]: Distribution according to findings of transcranial ultrasound.

USG findings at final follow-up	Frequency (n=40)	Percent
Resolved	7	17.5
Lost for follow-up	5	12.5
Referred	3	7.5
Expired	7	17.5
Worsened	2	5.0
Same findings	16	40.0

[Table/Fig-8]: Distribution according to USG findings on follow-up after one month.

Clinical features	Gestational age (weeks)			χ^2	p-value
	<28 (n=2)	28-36 (n=19)	≥37 (n=19)		
Seizures	2 (100)	8 (42.1)	9 (47.4)	2.43	0.29
Lethargy	1 (50)	11 (57.9)	7 (36.8)	1.69	0.53
Absent sucking	1 (50)	4 (21.1)	1 (5.3)	3.88	0.15
Excessive cry	1 (50)	1 (5.3)	3 (15.8)	3.67	0.16
Sudden onset pallor	0 (0)	2 (10.5)	2 (10.5)	0.23	0.89
Apnea	0 (0)	3 (15.8)	0 (0)	3.59	0.17
Flaccidity	0 (0)	2 (10.5)	1 (5.3)	0.55	0.76
Fever	0 (0)	1 (5.3)	2 (10.5)	0.55	0.76
Hypertonia	0 (0)	1 (5.3)	1 (5.3)	0.11	0.95
Bulging anterior fontanelle	0 (0)	0 (0)	2 (10.5)	2.33	0.31
Ear discharge	0 (0)	0 (0)	1 (5.3)	1.13	0.57

[Table/Fig-9]: Association between gestational age and clinical features.

In present study, hypertonia was observed in 2 (15.4%) females but in none of the males and the observed association between gender and hypertonia was statistically significant (p-value 0.04). However, no statistically significant association was observed between gender and other clinical features (p>0.05) [Table/Fig-10].

In present study, out of 23 neonates delivered vaginally, lethargy and seizures were the most common features observed in 13 (56.5%) and 12 (52.2%) neonates, respectively. Out of 11 neonates delivered via caesarean section, lethargy was observed in 5 (45.5%). Out of 6 cases with assisted delivery, seizure followed by excessive cry was the most common feature. There was no statistically significant association between mode of delivery and clinical features in present study [Table/Fig-11].

Out of 2 neonates with <28 weeks of gestation, Grade-III germinal matrix haemorrhage was observed in 2 (100%) cases. Out of 19 cases between 28 to 36 weeks of gestation, USG was suggestive of meningitis in majority 3 (15.8%) of cases and grade 1 germinal matrix haemorrhage in 6 (31.6%) cases. In neonates belonging to ≥37 weeks of gestation, USG revealed normal findings in 9 (47.4%) neonates. The

observed association between gestational age and USG findings was significantly significant (p-value 0.023) [Table/Fig-12].

Clinical features	Gender		χ^2	p-value
	Male (n=27)	Female (n=13)		
Seizures	13 (48.1)	6 (46.2)	0.014	0.91
Lethargy	15 (55.6)	4 (30.8)	2.16	0.14
Absent sucking	4 (14.8)	2 (15.4)	0.02	0.96
Excessive cry	4 (14.8)	1 (7.7)	0.41	0.52
Sudden onset pallor	2 (7.4)	2 (15.4)	0.62	0.43
Apnea	3 (11.1)	0 (0)	1.56	0.21
Flaccidity	2 (7.4)	1 (7.7)	0.001	0.974
Fever	3 (11.1)	0 (0)	1.56	0.21
Hypertonia	0 (0)	2 (15.4)	4.37	0.04
Bulging anterior fontanelle	2 (7.4)	0 (0)	1.01	0.31
Ear discharge	1 (4.3)	0 (0)	0.49	0.48

[Table/Fig-10]: Association between gender and clinical features.

Clinical features	Mode of delivery			χ^2	P-value
	Vaginal (n=23)	LSCS (n=11)	Assisted (n=6)		
Seizures	12 (52.2)	4 (36.4)	3 (50)	0.76	0.68
Lethargy	13 (56.5)	5 (45.5)	1 (16.7)	3.06	0.22
Absent sucking	4 (17.4)	1 (9.1)	1 (16.7)	0.42	0.81
Excessive cry	1 (4.3)	2 (18.2)	2 (33.3)	4.10	0.13
Sudden onset pallor	3 (13)	1 (9.1)	0 (0)	0.91	0.633
Apnea	1 (4.3)	1 (9.1)	1 (16.7)	1.09	0.58
Flaccidity	1 (4.3)	1 (9.1)	1 (16.7)	1.09	0.58
Fever	2 (8.7)	1 (9.1)	0 (0)	0.57	0.75
Hypertonia	1 (4.3)	0 (0)	1 (16.7)	2.32	0.31
Bulging anterior fontanelle	1 (4.3)	0 (0)	1 (16.7)	2.32	0.31
Ear discharge	1 (4.3)	0 (0)	0 (0)	0.76	0.69

[Table/Fig-11]: Association between mode of delivery and clinical features.

USG findings	Gestational age (weeks)		
	<28 (n=2)	28-36 (n=19)	≥37 (n=19)
Agenesis of corpus callosum	0 (0)	0 (0)	1 (5.3)
Choroid plexus cyst	0 (0)	1 (5.3)	0 (0)
Dandy walker malformation	0 (0)	0 (0)	1 (5.3)
Meningitis	0 (0)	3 (15.8)	2 (10.5)
Grade-I GMH	0 (0)	6 (31.6)	1 (5.3)
Grade-II GMH	0 (0)	1 (5.3)	0 (0)
Grade-III GMH	2 (100)	2 (10.5)	0 (0)
Grade-IV GMH	0 (0)	1 (5.3)	0 (0)
Hydrocephalus	0 (0)	1 (5.3)	2 (10.5)
Persistent cavum septum pellucidum	0 (0)	1 (5.3)	0 (0)
PVL Grade-I	0 (0)	2 (10.5)	2 (10.5)
PVL Grade-II	0 (0)	1 (5.3)	0 (0)
PVL Grade-IV	0 (0)	0 (0)	1 (5.3)
Normal	0 (0)	0 (0)	9 (47.4)

[Table/Fig-12]: Association between gestational age and USG findings.
χ^2=42.22; p=0.023

In present study, USG findings revealed germinal matrix haemorrhage in 9 (33.3%) males and 4 (30.8%) females, whereas meningitis was observed in 4 (14.8%) males and 1 (7.7%) female. Hydrocephalus was observed in 3 (11.1%) males but none in females. There was statistically insignificant association between USG findings and gender (p-value 0.31) [Table/Fig-13].

USG findings	Gender	
	Male (n=27)	Female (n=13)
Agenesis of corpus callosum	0 (0)	1 (7.7)
Choroid plexus cyst	1 (3.7)	0 (0)
Dandy walker malformation	0 (0)	1 (7.7)
Meningitis	4 (14.8)	1 (7.7)
Grade-I GMH	3 (11.1)	4 (30.8)
Grade-II GMH	1 (3.7)	0 (0)
Grade-III GMH	4 (14.8)	0 (0)
Grade-IV GMH	1 (3.7)	0 (0)
Hydrocephalus	3 (11.1)	0 (0)
Persistent cavum septum pellucidum	1 (3.7)	0 (0)
PVL Grade-I	3 (11.1)	1 (7.7)
PVL Grade-II	0 (0)	1 (7.7)
PVL Grade-IV	1 (3.7)	0 (0)
Normal	5 (18.5)	4 (13.8)

[Table/Fig-13]: Association between gender and USG findings.
χ^2=14.99; p=0.31

Grade-III germinal matrix haemorrhage was observed in 2 (100%) neonates with birth weight less than 1 kg, meningitis was observed in 2 (33.3%) neonates with birth weight of 1 to 1.5 kg. Majority of neonates [3 (33.3%)] with birth weight 1.5 to 2 kg were observed to have PVL Grade-I followed by hydrocephalus in 2 (22.2%) neonates [Table/Fig-14]. However, no statistically significant association was observed between USG findings and birth weight (p-value 0.055) [Table/Fig-14].

USG findings	Weight (kg)				
	<1 (n=2)	1-1.5 (n=6)	1.5-2 (n=9)	2-2.5 (n=12)	>2.5 (n=11)
Agenesis of corpus callosum	0 (0)	0 (0)	0 (0)	0 (0)	1 (9.1)
Choroid plexus cyst	0 (0)	1 (16.7)	0 (0)	0 (0)	0 (0)
Dandy walker malformation	0 (0)	0 (0)	0 (0)	0 (0)	1 (9.1)
Meningitis	0 (0)	2 (33.3)	0 (0)	2 (16.7)	1 (9.1)
Grade-I GMH	0 (0)	1 (16.7)	1 (11.1)	0 (0)	5 (45.5)
Grade-II GMH	0 (0)	0 (0)	0 (0)	1 (8.3)	0 (0)
Grade-III GMH	2 (100)	0 (0)	0 (0)	2 (16.7)	0 (0)
Grade-IV GMH	0 (0)	1 (16.7)	0 (0)	0 (0)	0 (0)
Hydrocephalus	0 (0)	0 (0)	2 (22.2)	1 (8.3)	0 (0)
Persistent cavum septum pellucidum	0 (0)	0 (0)	0 (0)	1 (8.3)	0 (0)
PVL Grade-I	0 (0)	0 (0)	3 (33.3)	1 (8.3)	0 (0)
PVL Grade-II	0 (0)	0 (0)	1 (11.1)	0 (0)	0 (0)
PVL Grade-IV	0 (0)	0 (0)	0 (0)	1 (8.3)	0 (0)
Normal	0 (0)	1 (16.7)	2 (22.2)	3 (25)	3 (27.3)

[Table/Fig-14]: Association between birthweight and USG findings.
χ^2=69.24; p=0.055

USG findings in majority of neonates born to primiparous females revealed meningitis and Grade-I germinal matrix haemorrhage 3 (15% each) whereas majority of neonates born to multiparous females had Grade-I germinal matrix haemorrhage 4 (20%) followed by Grade-III germinal matrix haemorrhage and PVL Grade-I 3 (15% cases each). Test of significance showed no statistically significant association between parity and USG (p-value 0.63) [Table/Fig-15].

Agenesis of corpus callosum [Table/Fig-3] was observed in 1 (4.3%) cases delivered vaginally. Grade-I, II and III germinal matrix haemorrhage was observed in 5 (21.7%), 1 (4.3%) and 2 (8.7%) cases respectively among neonates delivered via vaginal route. Out of 11 neonates delivered via caesarean section, USG findings revealed hydrocephalus in 2 (18.2%) cases. The present study

documented no statistically significant association between mode of delivery and USG findings (p-value 0.347) [Table/Fig-16].

USG findings	Parity	
	Primipara (n=20)	Multipara (n=20)
Agenesis of corpus callosum	1 (5)	0 (0)
Choroid plexus cyst	0 (0)	1 (5)
Dandy walker malformation	1 (5)	0 (0)
Meningitis	3 (15)	2 (10)
Grade-I GMH	3 (15)	4 (20)
Grade-II GMH	1 (5)	0 (0)
Grade-III GMH	1 (5)	3 (15)
Grade-IV GMH	0 (0)	1 (5)
Hydrocephalus	2 (10)	1 (5)
Persistent cavum septum pellucidum	0 (0)	1 (5)
PVL Grade-I	1 (5)	3 (15)
PVL Grade-II	1 (5)	0 (0)
PVL Grade-IV	1 (5)	0 (0)
Normal	5 (25)	4 (20)

[Table/Fig-15]: Association between parity and USG findings.
χ^2=10.79; p=0.63

USG findings	Mode of delivery		
	Vaginal (n=23)	LSCS (n=11)	Assisted (n=6)
Agenesis of corpus callosum	1 (4.3)	0 (0)	0 (0)
Choroid plexus cyst	0 (0)	0 (0)	1 (16.7)
Dandy walker malformation	0 (0)	1 (9.1)	0 (0)
Meningitis	3 (13)	1 (9.1)	1 (16.7)
Grade-I GMH	5 (21.7)	1 (9.1)	1 (16.7)
Grade-II GMH	1 (4.3)	0 (0)	0 (0)
Grade-III GMH	2 (8.7)	1 (9.1)	1 (16.7)
Grade-IV GMH	0 (0)	0 (0)	1 (16.7)
Hydrocephalus	1 (4.3)	2 (18.2)	0 (0)
Persistent cavum septum pellucidum	0 (0)	1 (9.1)	0 (0)
PVL Grade-I	4 (17.4)	0 (0)	0 (0)
PVL Grade-II	0 (0)	1 (9.1)	0 (0)
PVL Grade-IV	1 (4.3)	0 (0)	0 (0)
Normal	5 (21.7)	3 (27.3)	1 (16.7)

[Table/Fig-16]: Association between USG and mode of delivery.
χ^2=28.24; p=0.347

Out of 10 neonates whose mothers received steroids antenatally, USG findings in majority of them revealed Grade-III germinal matrix haemorrhage and PVL Grade-I in 2 (16.6%) cases each [Table/Fig-4]. There was no statistically significant association between USG findings and antenatal steroids (p-value 0.20) [Table/Fig-17].

Incidence of apnea was significantly higher in neonates with meningitis 2 (66.7%) and choroid plexus cyst 1 (33.3%) in present study [Table/Fig-18].

Out of three neonates who presented with fever, findings suggestive of meningitis were observed in USG in 3 (100%) cases. A statistically significant association was found between fever and USG findings (p-value 0.04) [Table/Fig-19].

Out of 40 cases, seven neonates succumbed to death. Of them, mortality was observed in 42.9% cases with Grade-I GMH [Table/Fig-4], 28.6% cases had meningitis whereas 14.3% neonates had Grade-II and IV GMH. About 5 neonates lost to follow-up and of them 60% had normal USG findings. USG findings worsened in two cases. Initially, one case each of PVL Grade-II and normal USG were diagnosed as Grade-III PVL on follow-up USG. Intracranial abnormalities resolved in 7 cases. Of them, 42.9% PVL and GMH Grade-I [Table/Fig-4] each showed resolution. However, test of significance showed no statistically significant association between USG finding at presentation and final follow-up (p>0.05) [Table/Fig-20].

USG findings	Antenatal steroids	
	No (n=28)	Yes (n=12)
Agenesis of corpus callosum	1 (3.3)	0 (0)
Choroid plexus cyst	0 (0)	1 (8.3)
Dandy walker malformation	1 (3.3)	0 (0)
Meningitis	4 (13.3)	1 (8.3)
Grade-I GMH	4 (13.3)	3 (25)
Grade-II GMH	1 (3.3)	0 (0)
Grade-III GMH	2 (6.7)	2 (16.6)
Grade-IV GMH	0 (0)	1 (8.3)
Hydrocephalus	2 (6.7)	1 (8.3)
Persistent cavum septum pellucidum	1 (3.3)	0 (0)
PVL Grade-I	2 (6.7)	2 (16.6)
PVL Grade-II	0 (0)	1 (8.3)
PVL Grade-IV	1 (3.3)	0 (0)
Normal	9 (30)	0 (0)

[Table/Fig-17]: Association between USG findings and antenatal steroids.
χ^2=16.94; p=0.20

USG findi ngs	Apnea	
	No (n=37)	Yes (n=3)
Agenesis of corpus callosum	1 (2.7)	0 (0)
Choroid plexus cyst	0 (0)	1 (33.3)
Dandy walker malformation	1 (2.7)	0 (0)
Meningitis	3 (8.1)	2 (66.7)
Grade-I GMH	7 (18.9)	0 (0)
Grade-II GMH	1 (2.7)	0 (0)
Grade-III GMH	4 (10.8)	0 (0)
Grade-IV GMH	1 (2.7)	0 (0)
Hydrocephalus	3 (8.1)	0 (0)
Persistent cavum septum pellucidum	1 (2.7)	0 (0)
PVL Grade-I	4 (10.8)	0 (0)
PVL Grade-II	1 (2.7)	0 (0)
PVL Grade-IV	1 (2.7)	0 (0)
Normal	9 (24.3)	0 (0)

[Table/Fig-18]: Association between USG findings and apnea.
χ^2=22.70; p=0.045

USG findings	Fever	
	No (n=37)	Yes (n=3)
Agenesis of corpus callosum	1 (2.7)	0 (0)
Choroid plexus cyst	1 (2.7)	0 (0)
Dandy walker malformation	1 (2.7)	0 (0)
Meningitis	2 (5.4)	3 (100)
Grade-I GMH	7 (18.9)	0 (0)
Grade-II GMH	1 (2.7)	0 (0)
Grade-III GMH	4 (10.8)	0 (0)
Grade-IV GMH	1 (2.7)	0 (0)
Hydrocephalus	3 (8.1)	0 (0)
Persistent cavum septum pellucidum	1 (2.7)	0 (0)
PVL Grade-I	4 (10.8)	0 (0)
PVL Grade-II	1 (2.7)	0 (0)
PVL Grade-IV	1 (2.7)	0 (0)
Normal	9 (24.3)	0 (0)

[Table/Fig-19]: Association between fever and USG.
χ^2=22.7; p=0.04

USG findings	Follow-up USG					
	Expired	LFU	Worsened	Referred	Resolved	Same
Agenesis of corpus callosum	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.2)
Choroid plexus cyst	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)
Dandy walker malformation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.2)
Meningitis	2 (28.6)	0 (0)	0 (0)	1 (33.3)	1 (14.3)	1 (6.2)
Grade-I GMH	0 (0)	0 (0)	0 (0)	0 (0)	3 (42.9)	4 (25)
Grade-II GMH	1 (14.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Grade-III GMH	3 (42.9)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.2)
Grade-IV GMH	1 (14.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hydrocephalus	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)
Persistent cavum septum pellucidum	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.2)
PVL Grade-I	0 (0)	0 (0)	0 (0)	1 (33.3)	3 (42.9)	0 (0)
PVL Grade-II	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)
PVL Grade-IV	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.2)
Normal	0 (0)	3 (60)	1 (50)	1 (3.3)	0 (0)	4 (25)

[Table/Fig-20]: Association between USG findings at the time of diagnosis and follow-up.
$\chi 2=83.19$; p=0.06

DISCUSSION

Transfontanellar ultrasonography of neonatal brain is one of the most important tools for diagnosis of intracranial abnormalities among neonates. It has advantage of being less expensive, non-invasive, portable, requires no sedation and is free from ionising radiation and thus, it is preferred diagnostic modality for evaluating neonates [10]. Barnes PD et al., documented that in neonates, when anterior and posterior fontanelle are open, transfonatnelle ultrasound is method of choice to detect CNS abnormalities whereas in neonates and infants, when fontanelle close, CT scan is the method of choice [12]. However, DeVries LS et al., suggested that MRI and ultrasound are complementary modalities and ultrasound is usually recommended in early days especially in unstable infants [13].

Mean gestational age of neonates was 35.38±3.59 weeks and maximum neonates were preterm (>50%). Neonates with intracranial anomalies may present with variable symptoms based upon underlying pathology. In present study, seizures and lethargy were the most common clinical features observed in 47.5% neonates.

Most common clinical presentation in a study by Nagaraj N et al., was tachypnea, poor activity and abnormal tone [14]. The incidence of transcranial abnormalities in high risk neonates was documented to be 38% in the study by Nagaraj N et al., which was much less than present study. The transcranial ultrasound revealed PVL (13%), intracranial bleed (12%), ventriculomegaly (7%), cerebral oedema (2%), simple cyst in middle cranial fossa, agenesis of corpus callosum, choroid plexus cyst [14].

Yasmin T et al., reported 61% preterm and 54% term neonates. Among preterm neonates, most common abnormality on transcranial ultrasound was PVL (29%), followed by germinal matrix haemorrhage (11%), intraventricular haemorrhage and cerebral oedema in 11% and 7% neonates respectively. However, among term neonates cerebral oedema was the most common finding of ultrasound (43%), followed by intracerebral haemorrhage, and focal cerebral infarct [15].

Yasmin T et al., in their study on 100 neonates observed respiratory distress to be the most common clinical findings (75%) followed by convulsions (42%), cyanosis (40%), apnoea (30%) and sepsis (12%) [15]. The observed difference in the clinical presentation between the reference and present study could be explained by difference in inclusion criteria.

Daneman A et al., concluded that transcranial ultrasound is an extremely useful modality for evaluation of neonatal brain [16]. However, various studies report variable diagnostic accuracy of USG in detection of intracranial abnormalities. Overall, the diagnostic accuracy, sensitivity and specificity of transcranial ultrasound was 78.9%, 81.8% and 60%, respectively when compared to MRI [16,17].

In present study, transcranial ultrasound revealed abnormal findings in 77.5% neonates whereas normal findings documented in only 22.5% neonates. Most common intracranial anomalies were germinal matrix haemorrhage in 32.5% neonates, PVL (15%), meningitis (12.5%) and hydrocephalus (7.5%) [Table/Fig-17]. Germinal matrix haemorrhage was divided into 4 grades i.e., I, II, III and IV based upon Papile's classification. In our study, Grade-I, II, III and IV germinal matrix haemorrhage was observed in 17.5%, 2.5%, 10% and 2.5%, respectively. Similar findings were documented in a study by Ramenghi La et al., in which incidence of Grade-I germinal matrix was observed in 57.5% neonates followed by Grade-III (24.15%), Grade-II (19.3) and Grade-IV (4.8%) [18].

In another study by Nazparveen LA et al., neonatal abnormalities were documented in 28.75% neonates admitted in NICU and of them, cerebral oedema and intraventricular haemorrhage were the most common intracranial abnormalities observed in at risk neonates [19].

Prematurity is a significant risk factor for various intracranial abnormalities. Our findings were similar to finding of Kumar N et al., in which most common sonographic finding in preterm neonates was Germinal Matrix haemorrhage in 67.56%, followed by hydrocephalus and peri-ventricular leukomalacia in 37.83% and 24.31%, respectively whereas most common sonography finding in term neonates was hydrocephalus in 76.19% followed by germinal matrix haemorrhage in 19.04% [20].

Gender of neonates play a major role in disease onset, course of disease especially in India where male preference is observed in almost all the communities and thus health seeking behaviour is good for males as compared to females. Apart from this, it has been established that in neonates, production of surfactant by fetal lung is gender dependent. It is well documented that incidence of respiratory distress is higher in males as compared to females [21].

In present study, about 67.5% neonates were males; however, clinical presentation was statistically similar in males and females except hypertonia which was significantly higher in females as compared to males ($p<0.05$).

O'Driscoll DN et al., in their study concluded consistently worse outcomes among male preterm neonate as compared to female preterm neonate. The aetiology of worse outcome among male preterm could be attributed to multiple factors such as hormonal, genetic and immunological factors [22].

In present study, majority of neonates were delivered vaginally (57.5%) followed by LSCS. Delivery with the help of outlet forcep and preterm assisted breach was conducted in 12.5% and 5% neonates, respectively.

These findings were contrasting to findings of Towner D et al., in which incidence of intracranial haemorrhage was documented in 1 in 664 neonates delivered with the use of forceps, 1 in 860 delivered by vacuum extraction, 1 in 1900 delivered spontaneously and 1 in 2750 delivered by caesarean section. They also reported that neonates delivered via vacuum extraction and forceps had higher incidence of intracranial haemorrhage as compared to normal delivery [23]. Mode of delivery especially vaccum extraction have been associated with increased risk of intracranial injury, however, data is inconclusive [24].

Breim MC et al., in their study observed statistically significant association of anoxia with mode of delivery ($p<0.01$). They documented that incidence of respiratory distress was significantly higher in neonates delivered via- caesarean section or forceps

as compared to vaginal delivery (p<0.05) [24]. However, no such association was documented in our study.

Low birth weight and very low birth weight neonates are independently one of the important risk factor for development of intracranial abnormalities [25]. In present study, mean birth weight of 40 neonates was 2.11±0.60 kg and about 77.5% neonates had either low birth weight or extremely low birth weight.

Tsimis MS et al., in their study observed incidence if PWMI in 9.4% of very low birth weight neonates [26]. As majority of neonates with low birth weight and very low birth weight neonate are preterm (which is an independent risk factor for increased risk of intracranial abnormalities), the incidence of intracranial abnormalities could be higher among neonates with low birth weight.

In present study, no statistically significant association was observed between parity of mother and transcranial ultrasound findings (p>0.05). These findings were supported by finding of Aberg K et al., the authors documented no significant association of parity with intracranial haemorrhage (p>0.05) [27].

Antenatal steroid is recommended in preterm neonates to reduce the adverse neonatal outcome such as respiratory distress syndrome, cerebroventricular haemorrhage as well as necrotising enterocolitis [28]. Out of 40 neonates, steroids were given in 10 neonates and among them, Grade-III germinal matrix haemorrhage and PVL Grade-I was documented in 20% cases each. Wei JC et al., concluded that use of antenatal steroid is associated with reduction in intracranial abnormalities across all gestational age [29].

The clinical features of various intracranial abnormalities among neonates depend upon underlying pathology and include seizures, lethargy, absent sucking, hypertonia, excessive cry etc. Neonatal seizures could be due to multiple aetiologies among neonates. Nemati H et al., in their study documented that neonatal seizures are associated with cerebrovascular causes such as HIE (23.9%) followed by hypoglycaemia (15.9%). Other causes of seizures in neonates include organic acidimia, inborn error of metabolism, maple syrup urine disease, CNS infections etc., [30].

In present study, seizures among neonates were associated with germinal matrix haemorrhage especially Grade-III and PVL especially Grade-I in 21.1% and 15.8% cases, respectively, the observed association between seizures and USG findings was not statistically significant (p>0.05).

The findings of present study were supported by finding of Nabavi N et al., in which the authors documented seizures to be due to haemorrhagic causes (12%) and hydrocephalus (7%) [Table/Fig-17] [31]. In another study by Mercuri E et al., seizures were documented in 16 neonates and of them, 11 neonates had pathologic lesions in brain which were mostly haemorrhagic in the initial weeks [32].

Eilers L et al., in their study documented that neonates with hypoglycaemia, intracerebral haemorrhage and HIE and meningitis may present with lethargy [33].

Differential diagnosis of lethargy in neonates include HIE, CNS infection, intraventricular haemorrhage, hyperbilirubinemia and neonates with lethargy usually present with poor feeding, absent sucking, and hypotonia [34]. In present study, lethargy was observed in 19 neonates and absent sucking in six neonates. USG in majority of them revealed Grade-III germinal matrix haemorrhage, but the observed association of lethargy and absent sucking in present study was not statistically significant.

Apnea in neonates may be due to apnea of prematurity and may be secondary to hypothermia, respiratory distress syndrome, intracranial infections, intracranial haemorrhage, and metabolic abnormalities [34].

Neonate with meningitis may present with nonspecific symptoms. Signs of meningitis in neonates may be convulsions, hypotonia, bulging anterior fontanelle etc., [35]. Fever was observed in three neonates of meningitis and the observed association of fever with USG findings was statistically significant (p<0.05). The present study documented no statistically significant association of excessive cry, hypertonia, bulging anterior fontanelle, flaccidity, ear discharge and sudden onset pallor (p>0.05). Neonatal hypertonia may be due to multiple causes such as HIE, secondary to tonic seizure, meningitis and metabolic causes [36].

Limitation(s)

There may be limitations due to misinterpretation of USG findings as it is operator dependent. Babies sometimes may not be cooperative in scanning as adults. There may be limitations to follow-up as they may never show-up for it.

CONCLUSION(S)

In present study, most common clinical manifestation were seizures and lethargy followed by absent sucking. Most common intracranial abnormalities among neonates were germinal matrix haemorrhage followed by PVL. Apnea was significantly higher in premature neonates as compared to term neonates. Hypertonia was significantly higher among female neonates. Though incidence of transcranial abnormalities was observed to be higher in low birth weight and preterm neonates but the observed difference was not statistically significant. Occurrence of apnea and fever was significantly higher in neonates with meningitis as compared to neonates with other findings. Screening by transcranial USG played a crucial and invincible role in the management of neonatal manifestations and abnormalities, so that the neonates requiring advanced care could be timely referred to higher centre.

Hence, Transcranial ultrasonography is recommended in every high risk neonates as a first line modality to assess the presence of intracranial abnormalities.

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