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Original Article

The Value of Routine Cranial Ultrasound in Preterm Neonates less than 37 weeks: A Prospective Analytical Study

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Abstract

Background: Cranial ultrasound is a safe imaging modality that does not require sedation and can be performed bedside in preterm.

Objective: To evaluate the value of routine cranial ultrasound as a routine screening in preterm neonates.

Patients and methods: This was a prospective observational comparative study conducted on 50 preterm infants less than 37 weeks gestational age admitted to the Neonatal Intensive Care Unit (NICU). The cranial ultrasound (CUS) was done to all neonates in the first 4 to7 days of life & repeated at 10 to 14 days of life for detection of any cranial ultrasound abnormality and follow up for these abnormalities if present. They were divided into two groups: group I included cases with normal cranial ultrasound and group II included cases with abnormal cranial ultrasound.

Results: Intraventricular hemorrhage was the most abnormal CUS findings (26.3%); followed by periventricular leukomalacia (15.8%) then intra cerebral hemorrhage, hydrocephalous & holoprosencephaly (10.5%). There was significant decrease of hemoglobin levels, significant increase in prothrombin time (P≤0.001 for all), partial thromboplastin time (P- 0.003), international normalized ratio levels (P-0.002) in neonates with abnormal CUS. There were significant increase in cases with apnea (P≤0.001), cyanosis (P- 0.017) and pallor (P-0.001) in cases with abnormal US.

Conclusions: Global routine cranial ultrasonography screening for all preterm neonates even if asymptomatic or not among at-risk population is highly valuable, cheap, and applicable tool investigation for detection of many neurological disorders like intraventricular hemorrhage, periventricular leukomalacia and intracerebral hemorrhages.

Key words: Preterm; cranial ultrasound; ventricular hemorrhage

Introduction

Preterm labor is an obstetrics emergency and a threat to population health. 75% of infant mortality is related to preterm labor. Preterm labor not only inflicts financial and emotional distress on the family, it may also lead to permanent disability (physical or neural damages) in infants. [1]

Cranial ultrasound is a safe imaging modality that does not require sedation and can be performed bedside. It can be repeated as often as necessary because of the lack of ionizing radiation. [2]

The importance of preterm screening by cranial ultrasound is sustained by the observation that in this vulnerable group, babies who are found to have abnormal brain scans are usually asymptomatic. Only occasionally these patients develop symptoms (seizures or other neurological symptoms) due to a massive intracranial hemorrhage (ICH).[3]

Intra Ventricular hemorrhage (IVH), defined as blood leakage into the ventricular space, is the main form of presentation with subsequent development of post hemorrhagic hydrocephalus (PHH) in 35% of cases. Approximately 20% of preterm newborns develop IVH. Higher-grade hemorrhages are more common as age and weight decrease. [4]

One of the major problems in preterm neonates is damage to white matter. This damage involves multifocal necrosis resulting in cystic periventricular leukomalacia (PVL) or a diffuse astrogliosis and loss of myelin-producing oligodendrocytes. [5]

Congenital brain anomalies could be seen during the cranial ultrasound screening, such as Dandy-Walker malformation (DWM), Chiari II malformation, agenesis of corpus callosum. [2]

The aim of this study was to evaluate the value of routine cranial ultrasound screening in preterm neonates.

Patients and methods

Study design: A prospective observational comparative study adopted to fulfill the purpose of the study.

Sample size: study conducted on 50 preterm whose age (<37 weeks) divided into cases with normal cranial ultrasound and cases with abnormal cranial ultrasound.

Cranial ultrasound done to all preterm babies admitted to the Neonatal Intensive Care Unit in the first 4 to7 days of life & repeated screening cranial ultrasound at 10 to 14 days of life.

Study population: The included study populations were preterm infants admitted to the Neonatal Intensive Care Unit (NICU) at Al-Azhar Assiut University Hospital and Samanoud General Hospital (Gharbia Governorate).

Inclusion criteria: Preterm babies less than 37 weeks gestational age of both genders were included in the study.

Exclusion criteria: Full term neonates.

Methods: The clinical data of patients fulfilling the inclusion criteria evaluated as follow

- Clinical data: Full history taking from parent and information, full maternal history, detailed prenatal history and Postnatal sign of respiratory distress, cyanosis, convulsion, and jaundice of the neonates.
- Clinical examination included meticulous general and systemic examinations with special emphasis on the birth weight, estimated gestational age, neonatal reflexes and vital signs (heart rate, respiratory rate and temperature & blood pressure).
- Laboratory and Radiological investigation: Complete blood count, C – reactive protein, serum urea, serum creatinine, Prothrombin time (PT), Partial thromboplastin time (PTT), International normalized ratio levels (INR), and cranial ultrasound.

Ethical approval

The study explained to all participants with oral consents of the parents of the patient after approval of the Faculty of Medicine, Al-Azhar University (Assiut), Egypt and written consent obtained from hospital administration.

Statistical analysis

Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows (Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test.

Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test while Fischer exact test and Monte Carlo test were used when expected cell count less than 5.

Continuous variables were presented as mean ± SD (standard deviation) for normally distributed data and the two groups were compared with Student t test. For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level.The results was considered significant when($p \leq 0.05$). The smaller the p-value obtained, the more significant are the results

Results

Table 1: IVH percentage (26.3%) was the most abnormal cranial US findings; PVL percentage (15.8%) was the second most common then intra cerebral hemorrhage, hydrocephalous, holoprosencephaly percentage (10.5%) for everyone and finally corpus agenesis percentage (5.3%).

Table 2: There was a statistically significant increase in in cases with abnormal US as regard maternal risk factor of premature rupture membrane (P-values=0.001) and multiple pregnancy (P-values = 0.047) compared to normal CUS cases.

Table 3: There was significant decrease of hemoglobin levels (P-values ≤0.001) in abnormal CUS cases and significant increase in Prothrombin time (P-values ≤0.001), Partial thromboplastin time (P-values =0.003), International normalized ratio levels (P-values =0.002) and serum creatinine (P-values= 0.017) as compared to normal CUS cases.

Table 4: There was significant decrease gestational age (P-values ≤0.001) in cases with abnormal US and significant increase cases with apnea (P-values ≤0.001), cyanosis (P-values= 0.017) and

pallor (P-values=0.001) as compared to normal cases.

Table 5: As regard neurological examination showing significant increase lethargic (P-values ≤0.001), hypo activity (P-values ≤0.001), plugging fontanel (P-values= 0.05), seizures P-values ≤0.001, abnormal muscle tone(P-values ≤0.001) and abnormal reflex (P-values ≤0.001) as compared to normal cases.

Table 6: There was a significance increases in cases with sepsis (P-values=0.001) in abnormal US cases as compared normal cases and significance increases in pneumothorax (P-values=0.049) in abnormal US cases as compared to normal cases

Table 7: There was significance increase in mortality rate (P-values= 0.002) in cases with abnormal US as compared to mortality in normal cases.

Figure (1): Ultrasound picture showed bilateral abnormal increase peri-ventricular hyper -echogenicity denoting grade I (periventricular leukomalacia). Normal size and shape of the ventricular system with bilateral germinal matrix hemorrhage.

Figure (2): Ultrasound picture showed left large periventricular area of abnormal hyper echogenic measuring about (2.68*1.58cm) denoting intra parenchymal hemorrhage of the left partial lobe, thalamus and intraventricular hyper- echogenic filling of the lateral ventricle denoting intraventricular hemorrhage with lateral ventricular dilatation.

Figure (3): Showed left intra parenchymal cerebral hematoma at thalamus with extension of hemorrhage to ventricular system these finding demonstrate picture of intra cerebral hemorrhage

Discussion

Our study's aim was to evaluate the importance of universal cranial ultrasound screening in all preterm neonates in the neonatal ICU with gestational age less than 37 weeks of gestational age even if clinically silent.

Our study included fifty premature, males represented (68%) of all patients while females represented (32%), with mean gestational age ranged from (32.50±2.37wk). Transcranial US examinations grey scale during their neonatal stay. Gray scale examination for morphological abnormalities detection.

These agree with study by Nadia et al., 2005[6] study included 175 preterm neonates (64%) were males and (36%) were females.

In our study, the first head ultrasound was performed between postnatal day 4 to 7 day table (1) and follow up at 10 to 14 day for follow up these agree with a study[7] for screening high risk preterm baby using trans fontanel sonography on days 1, 3, and 7 of life to identify the various cranial pathologies. Follow-up cranial USG was performed at 2 weeks.

As regard cranial US abnormality19 preterm with abnormal TCUS findings,11 cases represent (57,9%) with IVH divided as 5 cases (26.3%) having grade-I IVH, 2 cases (10.5%) with grade-II IVH, 2 cases (10.5%) with grade-III IVH, 2 cases (10.5%) with grade-IV IVH) and 8 cases with other cranial abnormality divided as 3 cases (15.8%) with PVL, 2 cases (10.5%) with intra cerebral hemorrhage, 2 cases with hydrocephalus, 1case (5.3 %) having congenital anomalies hollo pros encephala and corpus agenesis as shown in (Table 1).

This agree with a study done by Cizmeci et al., 2020[8] germinal matrix hemorrhage-intraventricular hemorrhage (GMH-IVH) remains a common form of brain injury in very preterm infants with an overall incidence of around (25%).

This slightly near to another study [9] among the abnormal CUS findings intraventricular hemorrhage was the most common (40.42%) followed by periventricular hyper-echogenicity (21.27%), cystic periventricular leukomalacia (8.51%), parenchymal bleed (8.51%), cysts (8.51%), cerebral edema (6.38%), ventriculomegaly (4.25%) and thalamic injury (2.12%).

Among our study, the mean gestational age (in weeks) in neonates with normal CUS was 33.52wk and with abnormal CUS was 30.84wk as shown in table (4). This finding was close to finding reported by Islam et al. 2016[10] in which mean gestational age (in weeks) in neonates with normal CUS was 31.9 wk. and with abnormal CUS was 31.8wk. which could be may be explained by that preterm with VLBW and low gestational age needed more care and well equipped unite to proper management of preterm neonates may lead to survival of large number of very preterm neonates with younger gestational age with less complication.

According to our study, most cases with birth weight less than > 1500mg mean wt. 1.32 and mean gestational age less than 32 wk. have abnormal US finding this result is also reported by Agha et al., 2012 [11] who stated that 32 GW and 1500 g BW should be considered alarming values, below which perinatal hypoxic insults are highly expected so expected preterm neonates are recommended to be conducted in well-equipped maternal hospitals with special baby care units.

According to our study the clinical data of abnormal cases by cranial ultrasonography the most common clinical manifestations of them were apnea, poor reflexes, pallor, cyanosis and convulsions. This agrees with reports stated that in presence of IVH there is often pallor, periods of apnea, cyanosis, failure to suck well, muscle twitching and convulsions. [12]

As regard percentage of clinical manifestation in cases with abnormal finding including anemia (57.9%), seizure (73,9%) cyanosis (47.9%) this higher than study do by Ou-Yang et al., [13] who stated that the clinical manifestations of IVH included anemia (54%), seizure (46%), cyanosis (29%), tachypnea (21%), fever (4%), hypothermia (4%) and poor feeding (4%) as shown in table (4,5).

Also, in our study there were certain maternal factors that were associated

with increased risk of abnormal cranial US including PROM (68.4 %), Multiple pregnancy (36,8%) as shown in table (2).

These finding were in agreement with the results of a studies reported the maternal risk factors which had significant association with SE-IVH were DM, antepartum hemorrhage and multiple pregnancies and found that the risk of PVL and grade-III IVH was higher in preterm born to mother with premature rupture of membranes (PROM). [6, 14]

In agreement with Ancel et al., 2005 [14] and (Lim et al., 2011) . [15] there were a significant lower hemoglobin, in the preterm with abnormal US finding as shown in table (3) compared to those without

As regarding PT and PTT, INR it was significant higher in the preterm with Abnormal cranial US as shown in table (3) compared to those without and it is in contrast with (Lim et al., 2011) [15] who found that There was no difference in the levels of prothrombin time or partial thromboplastin time between both groups in his case–control study.

In our study INR level was increased in cases with abnormal cranial us table (3) this agree with (Glover Williams et al., 2019) [16] an elevated INR in the first 48 hours of life may be useful to identify preterm infants at risk of severe IVH and may guide strategies to prevent the development, or limit the extension of IVH.

In our study serum creatinine level was higher in cases with abnormal us finding table (3) this agree with (Stoops et al., 2019) [17] this study expands our understanding of the association between AKI and IVH previously presented in a single-center cohort which demonstrated that infants with AKI had higher hazard ratios to develop grade II and III IVH.

As regard diagnosis with sepsis there is increase cranial us abnormality with cases associated with sepsis table (6) this agree with (Ghoor et al., 2017) [18] sepsis and mechanical ventilation showed a ~3-fold increase in IVH and

both of those factors can be modified by preventive measures.

In our study mortality rate was (20%) of cases as shown in table (7) and this agree with similar studies reported mortality rate (21.5%) of cases. [19] and [7] mortality (16%) and neurological symptoms were found in (20%) premature infants.

The follow up CUS was done after one week on 50 neonates and it was normal in 32 neonates (64.0%) of them and remains abnormal in 18 neonates (36.0%) and it not done in one neonate of abnormal cases as he was died before doing it.

There was a significant correlation between the first CUS and the follow up. All newborns that had a normal cranial ultrasound initially had no abnormal findings in the follow up sonar.

Conclusions

Global routine cranial ultrasonography screening for all preterm neonates even if asymptomatic or not among at-risk population is highly valuable, cheap and applicable tool investigation for detection of many neurological disorders like intraventricular hemorrhage, periventricular leukomalacia and intracerebral hemorrhages. Further studies should be done to study the relation of cranial ultrasound abnormalities to cognitive and neuro developmental outcome.

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Author's contributions

All of authors dhared equally in study design, interpretation of data, revision of draft critically for important intellectual content and final approval of the version to be published

Conflict of interest

The authors declare that they have no conflict of interest

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Table (1): Percentage distribution of the studied groups according to abnormal US finding (4 to 7 day).

Distribution Variables	NO (19)	Percentage (100%)
Intraventricular haemorrhage I	**5**	**(26.3%)**
Intraventricular haemorrhage II	**2**	**(10.5%)**
Intraventricular haemorrhage III	**2**	**(10.5%)**
Intraventricular haemorrhage IV	**2**	**(10.5%)**
Periventricular leukomalacia (PVL)	**3**	**(15.8%)**
Intracerebral haemorrhage	**2**	**(10.5%)**
Hydrocephalous	**2**	**(10.5%)**
Holoprosencephaly and corpus agenesis	**1**	**(5.3%)**

Table (2): Association between abnormal US and maternal risk factors

Demographic data	Normal US (n=31)	Abnormal US (n=19)	Test of significance	p value
Premature rupture membrane	6 (19.4%)	13 (68.4%)	χ^2=12.04	0.001*
Multiple pregnancy	4 (12.9%)	7 (36.8%)	χ^2=3.93	0.047*
History of abortion	5 (16.1%)	4 (21.1%)	χ^2=0.193	0.66
Pre-eclampsia	3 (9.7%)	2 (10.5%)	FET	1.0
Ante- partum hemorrhage	1 (3.2%)	2 (10.5%)	FET	0.549
Polyhydramnios	0 (0%)	2 (10.5%)	FET	1.0
Chorioamnionitis	0 (0%)	1 (5.3%)	FET	0.38
Urinary tract infection	1 (3.2%)	0 (0%)	FET	0.14

$\chi^{2:}$ Chi square test, FET: Fischer exact test, significant p ≤0.05

Table (3): Association between abnormal US and laboratory findings

Laboratory findings	Normal US (n=31)	Abnormal US (n=19)	Test of significance	p value
Hemoglobin (gm/dl)	14.16± 2.34	11.36± 2.77	t=3.82	≤0.001*
Total leukocytic count /mm^3	13.02± 4.35	15.30± 7.95	t=1.31	0.196
Platelet (*10/mm^3)	165.94± 66.75	130.79± 51.85	t=1.96	0.056
Hematocrit %	41.23± 7.68	37.27± 8.72	t=1.68	0.099
Prothrombin time (second)	14.32± 2.50	17.72± 3.91	t=3.75	≤0.001*
Partial thromboplastin time (second)	37.61± 4.13	42.37± 6.70	t=3.11	0.003*
International normalized ratio	1.19± 0.30	1.60± 0.56	t=3.32	0.002*
Serum creatinine (mg/dl)	0.667±0.19	0.816± 0.21	t=2.47	0.017*
C-Reactive protein (mg/l) **Positive** **Negative**	8 (25.8 %) 23 (74.2 %)	10 (52.6 %) 9 (47.4 %)	χ^2=3.68	0.055

T: t- test, $\chi^{2:}$ Chi square test, FET: Fischer exact test, significant p ≤0.05

Table (4): Association between abnormal US and neonatal characteristics

Neonatal characteristics	Normal US (n=31)	Abnormal US (n=19)	Test of significance	p value
Gender				
Male	20 (64.5%)	14 (73.7%)	χ^2=0.455	0.50
Female	11 (35.5%)	5 (26.3%)		
Mode of delivery				
CS	21 (67.7%)	12 (63.2%)	χ^2=0.11	0.74
NVD	10 (32.3%)	7 (36.8%)		
Gestational age (days) Mean ± SD	33.52± 1.74wk	30.84± 2.34wk	t=4.61	≤0.001*
Apnea				
Positive	5 (16.1%)	15 (78.9%)	χ^2=19.37	≤0.001*
Negative	26 (83.9%)	4 (21.1%)		
Cyanosis				
Positive	5 (16.1%)	9 (47.4%)	χ^2=5.70	0.017*
Negative	26 (83.9%)	10 (52.6%)		
Pallor				
Positive	4 (12.9%)	11 (57.9%)	χ^2=11.36	0.001*
Negative	27 (87.1%)	8 (42.1%)		

T: student t- test, $\chi^{2:}$ Chi square test, FET: Fischer exact test, significant p ≤0.05

Table (5): Association between abnormal US and neurological examination

Neurological examination	Normal US (n=31)	Abnormal US (n=19)	Test of significance	p value
Conscious level				
Conscious	29 (93.5%)	5 (26.3%)	χ^2=24.47	≤0.001*
Lethargic	2 (6.5%)	14 (73.7%)		
Activity				
Hypoactive	10 (32.3%)	18 (94.7%)	MC	≤0.001*
Active	13 (41.9%)	1 (5.3%)		
Moderate active	8 (25.8%)	0 (0%)		
Anterior fontanel				
AF at level	30 (96.8 %)	10 (52.6%)	MC	0.05*
bulging fontanel	0 ((%0	8 (42.1%)		
AF wide /full	1 (3.2%)	1 (5.3%)		
Seizures				
Positive	4 (12.9%)	14 (73.7%)	χ^2=18.89	≤0.001*
Negative	27 (87.1%)	5 (26.3%)		
Abnormal muscle tone				
Positive	5 (16.1%)	13 (68.4%)	χ^2=13.98	≤0.001*
Negative	26 (83.9%)	6 (31.6%)		
Abnormal reflex				
Positive	6 (19.4%)	16 (84.2%)	χ^2=20.11	≤0.001*
Negative	25 (80.6%)	3 (15.8%)		

MC: Monte carol test

T: student t- test, $\chi^{2:}$ Chi square test, FET: Fischer exact test, significant p ≤0.05

Table (6): Association between abnormal US and diagnosis

Diagnosis	Normal US (n=31)	Abnormal US (n=19)	p value
Respiratory distress syndrome	30 (63.8%)	17 (36.2%)	0.549
Sepsis	1 (11.1%)	8 (88.9%)	0.001*
Pneumothorax	0 (0%)	3 (100%)	0.049*
Pulmonary hemorrhage	2 (100%)	0 (0%)	0.519
Pneumonia	1 (100%)	0 (0%)	1.0
Hemorrhagic disease of newborn	0 (0%)	1 (100%)	0.38
Congenital brain mal formation	0 (0%)	1 (100%)	0.38
Neonatal sepsis meningitis	0 (0%)	1 (100%)	0.380

AF: Anterior fontanel p: p value for comparing between the studied groups, significant $p \leq 0.05$

Table (7): Association between abnormal US and mortality

Mortality	Normal US (n=31)	Abnormal US (n=19)	Test of significance	p value
Mortality				
Died	2 (6.5%)	8 (42.1%)	χ^2=9.36	0.002*
Survived	29 (93.5%)	11 (57.9%)		

$\chi^{2:}$ Chi square test

p: p value for comparing between the studied groups, significant $p \leq 0.05$

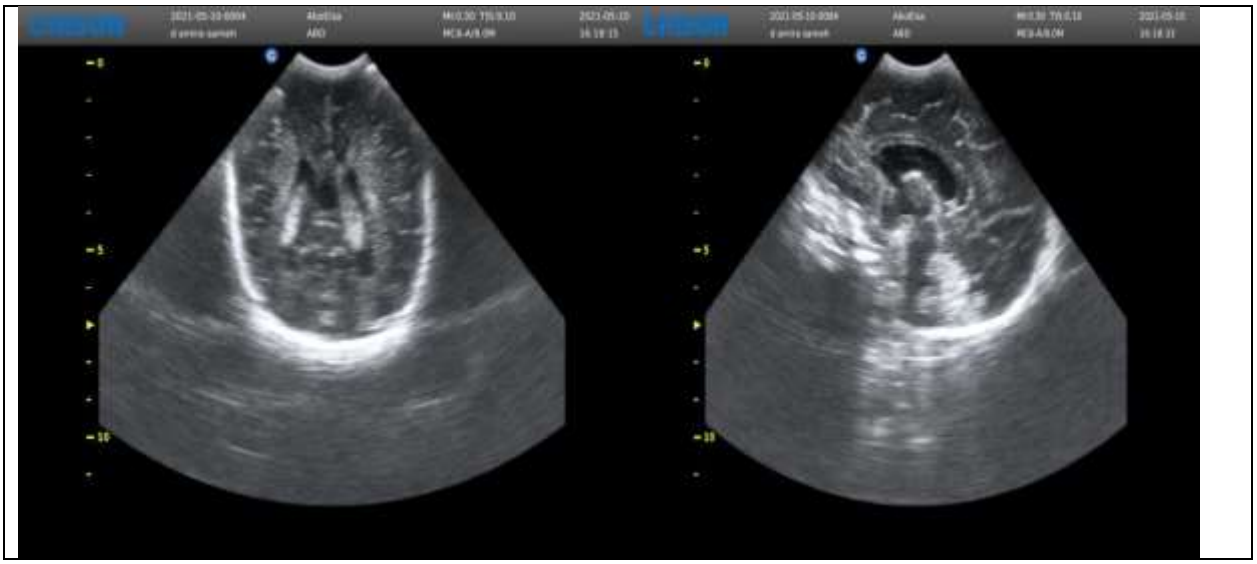

Figure (1): Germinal matrix hemorrhage (grade I) and PVL

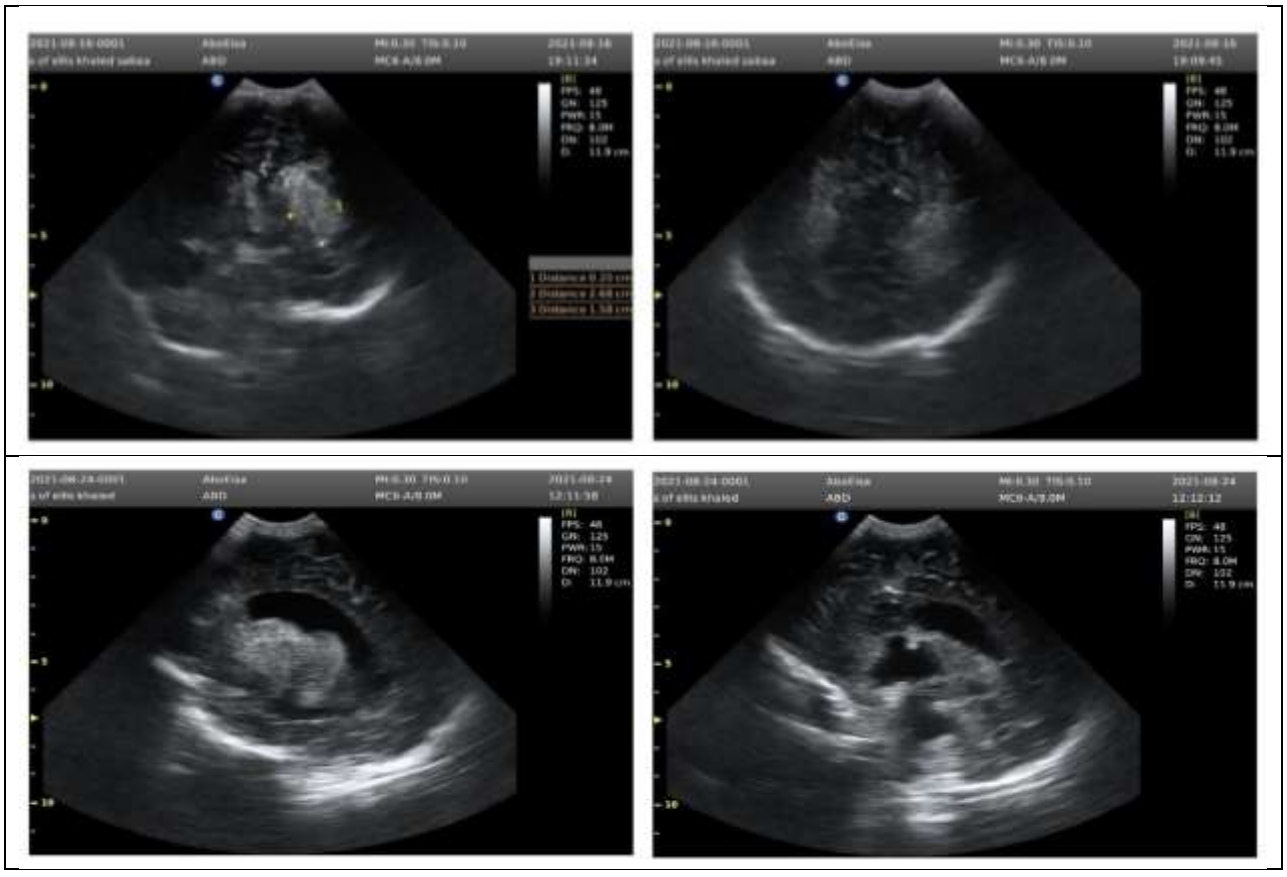

Figure (2): Ultrasound picture for grade IV intraventricular hemorrhage.

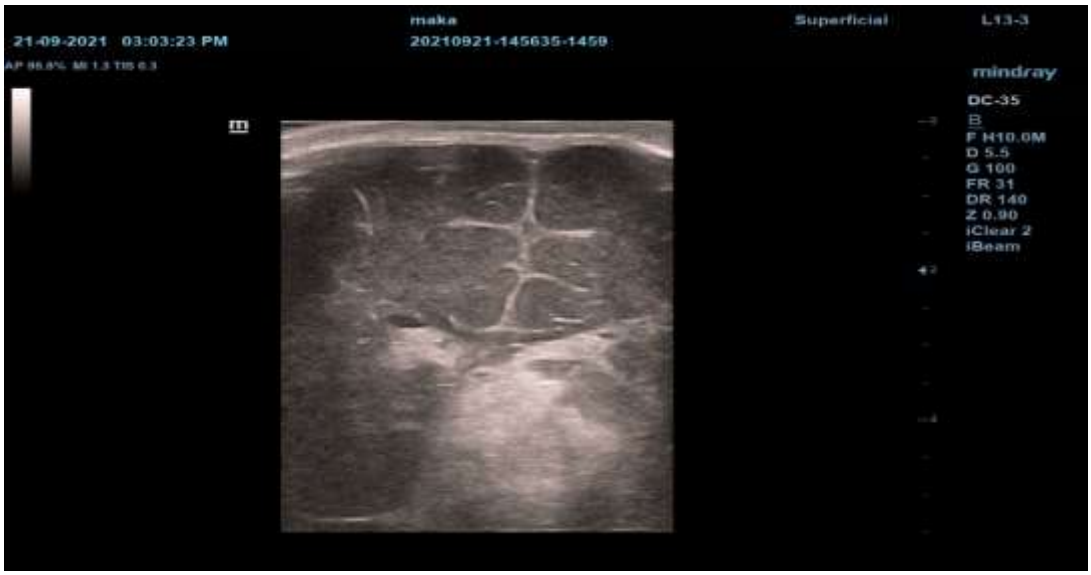

Figure (3): Left intra cerebral hemorrhage.

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