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Role of Neurosonography in Preterm Infants in Prediction of Postnatal Mortality and Outcome in Nicu Setup.

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ABSTRACT:
Introduction: *ROLE OF NEUROSONOGRAPHY IN PRETERM INFANTS IN PREDICTION OF POSTNATAL MORTALITY AND OUTCOME IN NICU SETUP.*
Aims and objectives: *To assess the role of cranial ultrasound in preterm infants in NICU setup and to determine the correlation and significance between the mortality of the premature babies in NICU and the various abnormalities.*
Material and Methods: *100 preterm infants admitted in NICU ward in government medical college, Amritsar were included for neurosonographic examination in the department of Radio diagnosis and Imaging, Government Medical College, Amritsar. The abnormal findings were statistically tabulated.*
Results: *100 preterm infants were grouped on basis of birth weight and gestational age. 12 cases of GMH grade I were detected on first day of which one progressed to GMH II by the third day. 4 cases of GMH II were seen of which one progressed to GMH III on later scans. 5 cases with diagnosis of germinal matrix haemorrhage died during the stay in the hospital. 24 cases of PVL were detected on the first day of discharge, 2 new cases developed by the third day. 7 cases of PVL grade I progressed to grade II by the time of last scan. One neonate showed PVL grade III. 12 neonates who had PVL in the initial scans became normal. Significant association was found between abnormal ultrasonographic findings and low gestational age/ low birth weight. Abnormal ultrasonographic findings were also associated with mortality.*
Conclusion*: Cranial ultrasonography is an ideal investigation for diagnosing intracranial pathologies in preterm and term neonates, sensitive for the detection of the intracranial hemorrhage, periventricular leukomalacia and hydrocephalus. Of the various abnormalities seen, germinal matrix haemorrhage was associated with mortality. Low birth weight and gestational age was also associated with mortality.*
Keywords: *preterm infants, cranial ultrasonography, germinal matrix haemorrhage, periventricular leukomalacia.*

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I. Introduction :

Preterm birth is commonly defined as any birth before 37 weeks completed weeks of gestation. An estimated 15 million infants are born preterm globally, disproportionately affecting low and middle income countries (LMIC). It contributes directly to estimated one million neonatal deaths annually and is a significant contributor to childhood morbidities. [1]

The World Health Organisation (WHO)[2] defines preterm birth as any birth before 37 completed weeks of gestation and is further subdivided on the basis of gestational age (GA):

- Extremely preterm (<28 weeks);
- Very preterm (28–<32 weeks);
- Moderate or late preterm (32–<37 completed weeks of gestation).

The most common causes include: Antepartum haemorrhage or abruption; mechanical factors such as uterine over-distention and cervical incompetence; hormonal changes; and, bacterial infection and inflammation. [3]

Cranial ultrasonography provides a convenient, noninvasive, relatively low-cost screening examination of the hemodynamically unstable neonate at the bedside and is radiation free.

Unlike CT, there is no radiation exposure to the babies, so cranial ultrasound can be used for regular follow up if needed. For MRI examination, there is need for sedation considering the time taken for the study. This might cause adverse outcome in the babies.

So neurosonography is a safe, fast, inexpensive, repeatable, non invasive procedure better than CT and MRI in NICU setup.

It is useful in detecting various abnormalities like germinal matrix haemorrhage which appears as increased echogenicity at germinal matrix.[4] It can further be complicated by Intraventricular haemorrhage and periventricular hameorrhagic infarction. [5]

The characteristic ultrasonographic appearance of PHI is a triangular, "fan-shaped" hyperechogenicity in periventricular white matter, ipsilateral to GMH-IVH.[6]

Other main abnormality detected is periventricular leukomalacia which is categorized into 4 grades by de Vries et al.[7]

II. Materials And Methods:

Study was conducted after taking approval from Institutional Ethics Committee, Government Medical College, Amritsar.

Study design: Cross sectional, Observation study.

Study Setting:

The study was carried out in the department of Radio diagnosis and Imaging in collaboration with department of Paediatrics, Government Medical College, Amritsar.

Subject and Inclusion Criteria:

100 preterm infants in NICU ward were subjected to cranial ultrasonography on 1st day of admission, third day and at the day of discharge. Before recruitment in present study, written informed consent of mother/guardian was taken.

Exclusion Criteria:

The study excluded all cases suspected to have congenital malformations, severe infections failed resuscitation and more than 37 weeks gestational age.

Methodology:

All patients were subjected to cranial ultrasonography using American Institute of Ultrasound In Medicine (AIUM) and correlation was done with the mortality and morbidity data.

Ultrasound:

Ultrasound was performed using Samsung RS80 A.

III. Results:

Mean birth weight of the infants was 2215.5 grams and mean gestational age was 32.93 weeks. Male: Female ratio was 52: 48. 4 percent of the included infants were born below 28 weeks of gestation, 26 percent between 28-32 weeks, 44 percent between 32-35 weeks and 26 percent after 35 weeks of gestation. 24 percent of preterm infants weighed less than 2000 gms, 52 percent between 2000- 2500 gms and 24 percent above 2500 gms.

Out of 100 included preterm neonates, 56 neonates had normal neurosonogram findings on the first day of the scan, 54 neonates had normal neurosonogram findings at the second time of scan and 66 neonates had normal scan at the time of discharge. Total 12 cases of GMH I were detected on first day, one progressed to GMH II by the third day. 4 cases of GMH II were seen in initial scans, of which one progressed to GMH III. 24 cases of PVL were detected on the first day of discharge, 2 new cases developed by the third day. 7 cases of PVL grade I progressed to grade II by the time of last scan. One neonate developed extensive cyst formation in the periventricular region (PVL grade III). 6 neonates had increased periventricular echogenicity (PVL Grade I) till the last time of scan. Periventricular echogenicity disappeared in 12 neonated. 5 cases with diagnosis of germinal matrix haemorrhage, including 4 cases of GMH II and one case of GMH III, died during the stay in the hospital.

Significant association was found between abnormal ultrasonographic findings and lower gestational ages as well as birth weight (p value 0.00). no association between abnormal findings with sex of the infant was seen. (p value 0.97). Association between mortality and abnormal ultrasound findings was also significant (p value 0.04). Mortality was also associated with low gestational age and low birth weight (p value 0.00).

TABLE 1

FREQUENCY AND PERCENTAGE DISTRIBUTION OF SEX

Sex	Frequency	Percentage
Male	52	52.0%
Female	48	48.0%

Out of 100 preterm infants included in the study, 52 were males and 48 percent were females.

TABLE 2

FREQUENCY AND PERCENTAGE DISTRIBUTION OF GESTATION AGE

Gestational age	Frequency	Percentage
Less than 28 weeks	4	4.0%
28-32 weeks	26	26.0%
32-35 weeks	44	44.0%
>35 weeks	26	26.0%

4 percent of the infants under study were born before 28 weeks of gestation, 26 percent were born between 28-32 weeks, 44 percent were between 32-35 weeks and 26 percent were born after 35 weeks of gestation.

TABLE 3

FREQUENCY AND PERCENTAGE DISTRIBUTION OF BIRTH WEIGHT

Birth weight	Frequency	Percentage
Less than 2000 gms	24	24.0%
2000-2500 gms	52	52.0%
2500 & above	24	24.0%

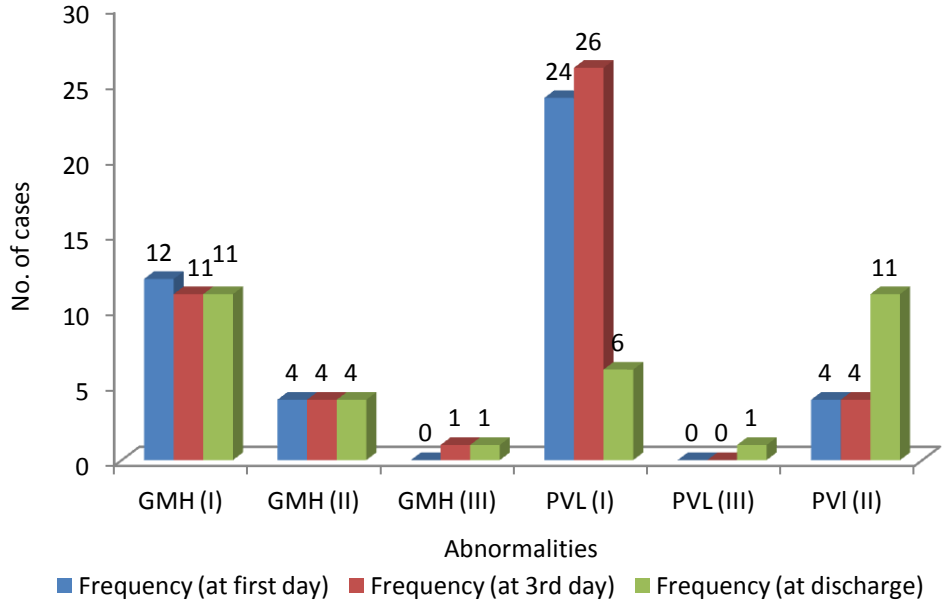
24 percent of preterm infants weighed less than 2000 grams, 52 percent weighed between 2000- 2500 grams and 24 percent weighed above 2500 grams.

TABLE 4

Frequency of ultrasound findings on 1^{ST}, 3^{rd} and day of discharge

More than 1 finding was observed in few infants at the time of ultrasound.

USG findings	Frequency 1^{st} day	Frequency 3^{rd} day	Frequency at day of discharge
CSP	19	19	19
CV	2	2	2
CVI	1	1	1
GMH (I)	12	11	11
GMH(II)	4	4	4
GMH(III)	0	1	1
PVL (I)	24	26	6
PVL(II)	4	4	11
PVL(III)	0	0	1



Graph 1: Bar diagram showing frequency distribution of abnormal ultrasonographic findings.

TABLE 5

FREQUENCY OF ABNORMAL ULTRASONOGRAPHIC FINDINGS AND ASSOCIATED MORTALITY

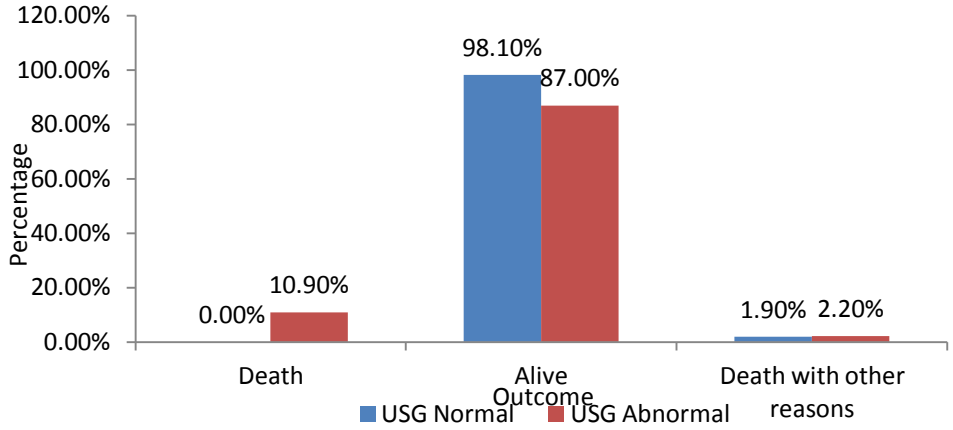
Abnormalities	Frequency (at first day)	Frequency (at 3rd day)	Frequency (at discharge)	Mortality (at discharge)
GMH(I)	12	11	11	0
GMH(II)	4	4	4	4
GMH(III)	0	1	1	1
PVL(I)	24	26	6	0
PVL(III)	0	0	1	0
PVL(II)	4	4	11	0
Total Abnormalities	44	46	34	5

TABLE 6

RELATIONSHIP BETWEEN POSTNATAL OUTCOME AND ABNORMAL ULTRASONOGRAPHIC FINDINGS

Outcome	USG		Total
	Normal	Abnormal	
Death	0 0.0%	5 10.9%	5 5.0%
Alive	53 98.1%	40 87.0%	93 93.0%
Death with Other Reasons	1 1.9%	1 2.2%	2 2.0%
Total	54 100.0%	46 100.0%	100 100.0%

'p' value=0.045

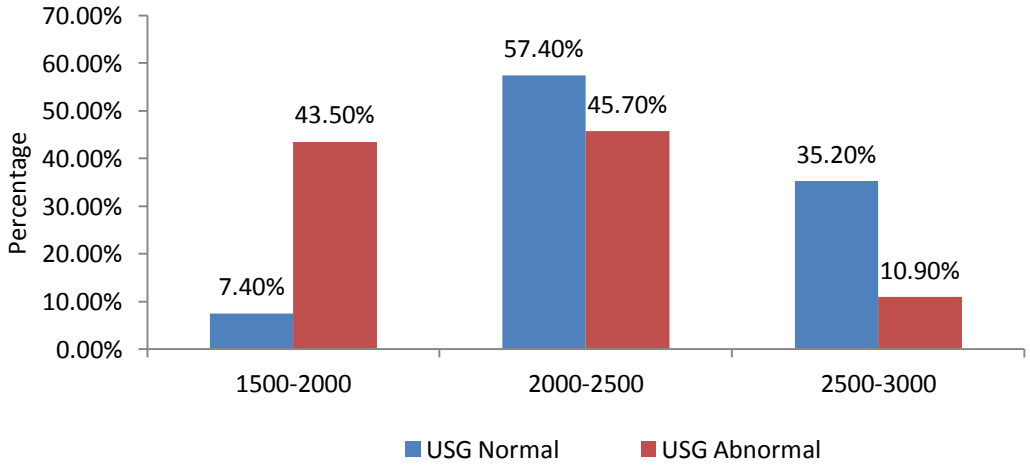


Graph 2: Bar diagram showing percentage distribution of postnatal outcome in relation to ultrasonographic findings.

TABLE 7
RELATIONSHIP BETWEEN ABNORMAL ULTRASONOGRAPHIC FINDINGS AND BIRTH WEIGHT OF THE INFANT

Birth weight	USG		Total
	Normal	Abnormal	
1500-2000	4 7.4%	20 43.5%	24 24.0%
2000-2500	31 57.4%	21 45.7%	52 52.0%
2500-3000	19 35.2%	5 10.9%	24 24.0%
Total	54 100.0%	46 100.0%	100 100.0%

'p' value=0.000



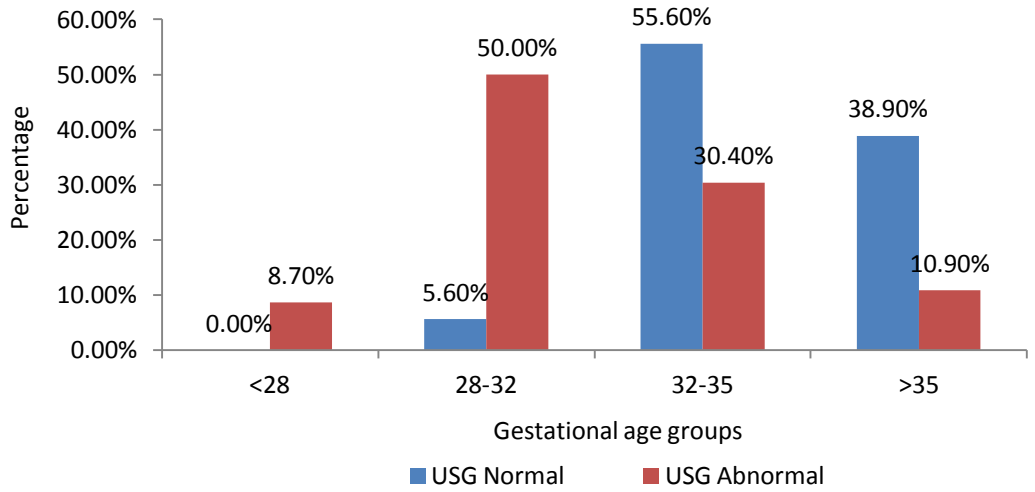
Graph 3: Bar diagram showing percentage distribution of ultrasonographic findings with birth weight.

TABLE 8
RELATIONSHIP BETWEEN ABNORMAL ULTRASONOGRAPHIC FINDINGS AND GESTATIONAL AGE GROUP

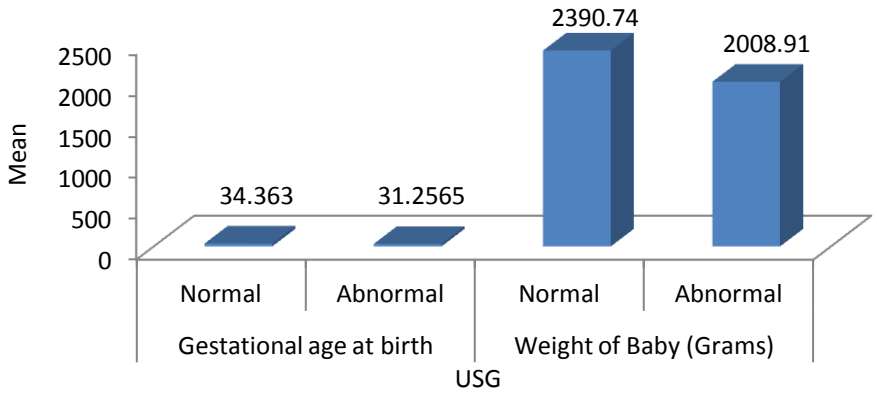
Gestational age groups	USG		Total
	Normal	Abnormal	
<28 weeks	0 0.0%	4 8.7%	4 4.0%
28-32 weeks	3 5.6%	23 50.0%	26 26.0%

32-35 weeks	30 55.6%	14 30.4%	44 44.0%
>35 weeks	21 38.9%	5 10.9%	26 26.0%
Total	54 100.0%	46 100.0%	100 100.0%

'p' value =0.000



Graph 4: Bar diagram showing percentage distribution of ultrasonographic findings with gestational age group.



Graph 5: Bar diagram showing mean birth weight and gestational age associated with sex of the infant.

TABLE 9

RELATIONSHIP BETWEEN POSTNATAL OUTCOME AND BIRTH WEIGHT

Birth weight Groups	OUTCOME			Total
	Death	Alive	Death with other reasons	
1500-2000 grams	5 100.0%	19 20.4%	0 0.0%	24 24.0%
2000-2500 grams	0 0.0%	50 53.8%	2 100.0%	52 52.0%
2500-3000 grams	0 0.0%	24 25.8%	0 0.0%	24 24.0%
Total	5 100.0%	93 100.0%	2 100.0%	100 100.0%

'p' value =0.001; degree of freedom= 4

TABLE 10
RELATIONSHIP BETWEEN POSTNATAL OUTCOME AND GESTATIONAL AGE

Gestational age groups (weeks)	OUTCOME			Total
	Death	Alive	Death with other reasons	
<28	3 60.0%	1 1.1%	0 0.0%	4 4.0%
28-32	2 40.0%	24 25.8%	0 0.0%	26 26.0%
32-35	0 0.0%	42 45.2%	2 100.0%	44 44.0%
>35	0 0.0%	26 28.0%	0 0.0%	26 26.0%
Total	5 100.0%	93 100.0%	2 100.0%	100 100.0%

'p' value=0.000

IV. Discussion :

Our study included 100 preterm neonates with varying gestational ages between 27 and 37 weeks. No term neonates were included in this study. Out of the included neonates, 4 neonates were born at gestational age less than 28 weeks, 26 neonates at gestational age between 28-32 weeks, 44 neonates between 32- 35 weeks and 26 neonates were born between 35-37 weeks of gestational age.

This study included 56 male and 44 female preterm neonates. Mean birth weight of the included neonates was 2215.1 grams with standard deviation of 354.8352726.

Neurosonogram findings observed during this study varied during the time of scans.

Out of the included preterm neonates, 56 neonates had normal neurosonogram findings at the first day of the scan, 54 neonates had normal neurosonogram findings at the second time of scan and 66 neonates had neurosonogram findings at the time of discharge. Normal neurosonograms also included normal variants.

Paul DA et al suggested the need for routine cranial ultrasonography for preterm infants.[8] Daneman A et al also found that CUS is an extremely useful modality for evaluation of the neonatal brain.[9]

In our study, 44 percent abnormalities were observed on the first day of neurosonogram, 46 percent on the second day and 34 percent on the day of discharge. Normal variants included cavum septum pellucidum in 19 percent of cases, cavum vergae in 2 percent and cavum velum interpositum in 1 percent of cases.

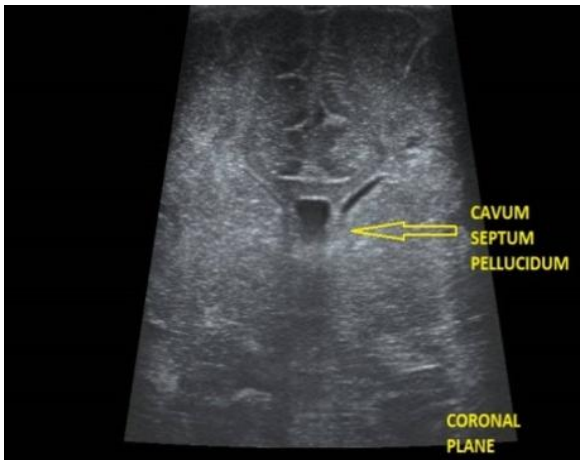


Figure 1: Coronal section showing cavum septum pellucidum

PVL is the most common intracranial abnormality in the preterm infants.

Goetz MC [10] et al performed screening cranial ultrasound on 115 preterm infants during the first week of life and found that few infants developed periventricular leukomalacia even after normal initial study thus emphasizing the need for late ultrasound screening. Our study also proves their conclusion as the ultrasonographic lesions of PVL went through dynamic evolution from time of first detection. These lesions either progressed to higher grades or regressed before discharge.

In our study, 24 cases of PVL were detected on the first day of discharge, 2 new cases developed by the third day.

On further screening of these neonates at discharge, 7 cases of PVL grade I progressed to grade II by the time of last scan. One neonate developed extensive cyst formation in the periventricular region (PVL grade

III). 6 neonates had persisting increased periventricular echoes (PVL Grade I). Neurosonogram of 12 neonates who had PVL on previous scans became normal by the last time of the scan s/o flaring. Flaring disappeared without causing any sequela in these neonates.

This emphasizes the need for follow up of the neonates in NICU with periventricular leukomalacia as:

- It can progress to cyst formation (Grade III) in the affected neonates.
- Neonates with initial normal scans can develop periventricular leukomalacia few days after birth.

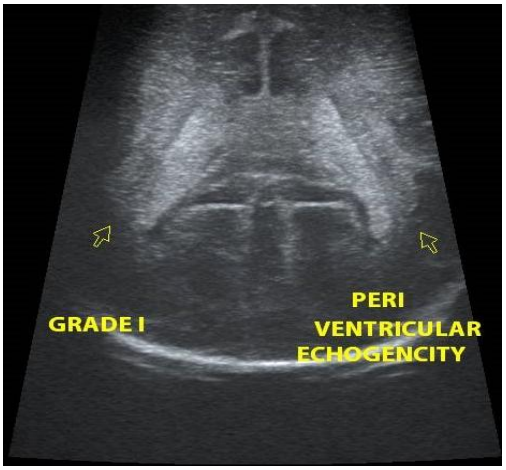


Figure 2: Coronal image obtained posteriorly showing Grade I Periventricular leukomalacia (Left>Right).

A study conducted by Ballardini E [11] showed that Babies born at gestational age less than 34 weeks were four times more likely to have an abnormal cranial ultrasonography than those at gestational age more than 35 weeks. In our study, most of the abnormalities (41 percent) were found in infants with GA 28-35 weeks and 5 were found in infants with GA more than 35 weeks, further supporting their conclusion.

Peacock JL et al[12] concluded that in very preterm infants, male sex is an important risk factor for poor neonatal outcome and poor neurological and respiratory outcome at follow-up. Our study also proves their conclusion as out of 7 total deaths, 6 included males and 1 included female.

In their study by Trounce JQ et al[13], intracranial haemorrhage was evident within the first 7 days of life in 78% of neonates and all neonates with grade II and III haemorrhages developed ventriculomegaly which was persisting till discharge.

In our study, of the total 12 cases of GMH I, one progressed to GMH II by the third day. Of the 4 GMH II cases seen on first day of the ultrasound, one case of GMH II progressed to GMH III by the second time of the scan during the hospital stay. 5 cases with diagnosis of germinal matrix haemorrhage, including 4 cases of GMH II and one case of GMH III, died during the stay in the hospital. Hydrocephalus was associated with grade III haemorrhages.

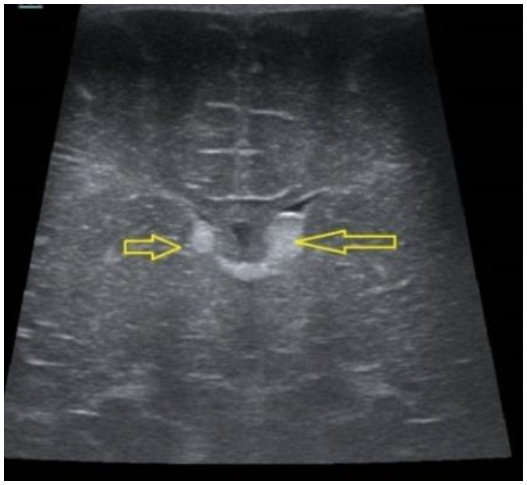


Figure 3: Coronal section showing bilateral germinal matrix haemorrhage

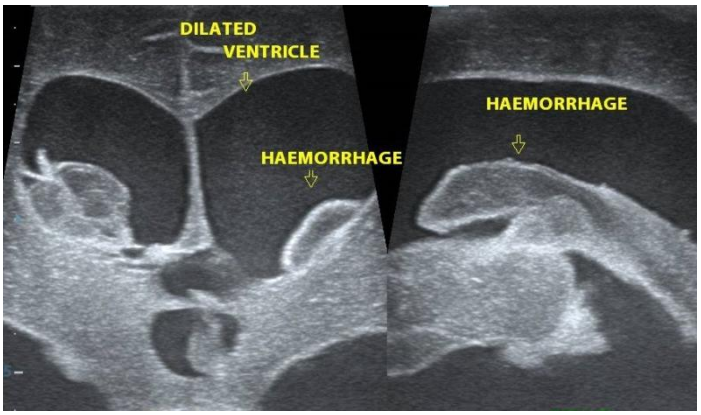


Figure 4: Coronal and sagittal image showing grade III GMH with hydrocephalus

Badrawy N et al[14] in their study concluded that 65 out of 175 (37%) of the preterm infants had abnormal cranial ultrasound findings. In our study, the maximum incidence of abnormal ultrasonographic findings was on the second day of the scan. Total abnormal findings were 44 neonates at the first day of the scan. On the second time of scan, 46 neonates with abnormal neurosonogram and at the time of discharge, the abnormal findings were observed in 34 neonates.

Mortality rate was 7 percent on the day of discharge. 5 of the deaths included infants with ultrasonographic findings of germinal matrix haemorrhage. No mortality was observed in the cases of the PVL.

2 of the 7 deaths were attributed to respiratory failure and were not related to abnormal neurosonographic findings.

The weights of the neonates with germinal matrix haemorrhage were less than 2000 g and gestational age was less than 30 weeks.

Enzmann D et al[15] conducted a study on 377 infants and found the mortality to be 40 percent in infants with higher grades of subependymal/ intraventricular Haemorrhage (III/ IV). In our study, out of 16 infants with GMH, 5 deaths were present which were of grade II/III.

Salih BK [16] in their study in 2019 proved that there was significant association between maternal risk factors and incidence of intracranial abnormalities ($P = 0.01$) as well as significant association between weight of the infant and gestational age at birth ($P = 0.001$). In our study, similar association was also present between abnormal ultrasonographic findings and low birth weights as well as lesser gestational age at birth.

Jha R et al[17] conducted a study on 75 preterm infants with incidence of cranial ultrasound abnormalities upto 25.4%. This incidence of abnormal cranial USG was significantly higher in males compared to females. Abnormal neurosonograms were also significantly related to gestational age and birth weight. In our study, statistically significant association was present between abnormal ultrasonographic findings and gestational age as well as birth weight. But there was no significant association between the sex of the infant and abnormal ultrasonographic findings.

Nagaraj N et al [18] in their study highlighted the convenience and diagnostic efficiency of cranial ultrasound in high-risk neonates in NICU. Our study also emphasizes the use of neurosonography as a screening modality for preterm neonates influencing their neurodevelopmental outcome.

Real time cranial ultrasonography of neonates was highly useful in detecting various abnormalities as well as their follow up.

V. Conclusion:

Cranial ultrasonography is widely accepted as a screening modality in the NICU set up as it is accurate, easy to perform and safe with no radiation exposure.

It is an ideal investigation for diagnosing intracranial pathologies in preterm and term neonates, sensitive for the detection of the intracranial haemorrhage, periventricular leukomalacia and hydrocephalus.

Several studies have been done previously to predict the neurodevelopmental outcomes based on cranial ultrasound abnormalities, but this study focused on predicting the mortality in NICU babies with identifiable brain abnormalities through neurosonogram.

This study emphasizes the need of doing routine neurosongram in all preterm babies and follow them up till they are discharged.

As we observed, there were dynamic changes in the intracranial abnormalities, more so in periventricular leukomalacia.

Thus, ultrasonography plays an important role in evaluation of these abnormalities and can alert the paediatrician at a very early stage.

5 percent mortality was observed in cases of germinal matrix haemorrhage.
Neurosonography can thus help in predicting the neonatal outcome in cases of higher grades of germinal matrix haemorrhage.

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