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Role of Neurosonography in the Evaluation of Neonatal Hypoxic Brain Injury

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KEYWORDS

CNS injury, neonatal intensive care unit, ICH,Hypoxic ischemic injury.

ABSTRACT:

Introduction: Incomplete formation and maturation of the nervous system in preterm neonates makes them highly susceptible to CNS injury causing neurodevelopmental disabilities ranging from mild learning disabilities, gross motor delays to cerebral palsy and mental retardation.

Methodology: The present study is a non-interventional, prospective, cross-sectional observational study conducted over a period of 1.5 years at the Department of Radiodiagnosis, A.C.S Medical college and Hospital, Chennai. A total 60 preterm neonates who were admitted to neonatal intensive care unit (NICU) were selected as per the inclusion criteria on a non-randomized purposive sampling basis and were subjected to neurosonography on selected days.

Results: Out of 60 preterm neonates included in the study, 28 (46.7%) patients are female and 32(53.3%) are male. Out of 60 preterm neonates included in the study, 17 (28.3%) patients have a gestational age of 34-36weeks and a least number of neonates, 13 (21.7%) neonates have a gestational age of 28-30 weeks. In the study there was significant association between Abruptio placenta, IUGR, Preeclampsia with ICH. Among subjects with Abruptio Placenta 75% had ICH, among subjects with IUGR, 80% had ICH and among subjects with Preeclampsia, 72.7% had ICH.

Conclusion: Hypoxic-ischemic injury of the brain in preterm neonates is a devastating condition with significant morbidity and mortality. HIE and intracranial hemorrhage are two ends of the spectrum of hypoxic-ischemic events. Though MRI is considered as a gold standard, despite the limitations of the present study, neurosonography has reported high sensitivity and specificity in detection of hypoxic brain injury in preterm neonates.

Introduction

Incomplete formation and maturation of the nervous system in preterm neonates makes them highly susceptible to CNS injury causing neurodevelopmental disabilities ranging from mild learning disabilities, gross motor delays to cerebral palsy and mental retardation.

Hypoxic-Ischemic Injury (HII) is estimated to affect 2-4 infants per 1000 live births.[1–3.] The mortality rate in the neonatal period is around 15% and 20% for infants

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suffering from HII and an additional 25% develop permanent neurologic deficits.[4] The global incidence of GM-IVH among preterm infants ranges from 14.7% to 44.7% [5,6], with considerable variation across gestational age groups, neonatal intensive care units, and countries. [5,6,7,8]

Early identification and intervention is of utmost importance to prevent long-term neurological sequelae. This information can also be used for prognostication and counselling families.

Neurosonography (NSG) has become widely accepted as a primary imaging modality for screening of the neonatal brain as it detects most of the hemorrhagic, ischemic, cystic brain lesions, cerebral infections, and major structural abnormalities as early as the first week after birth. NSG is also used in determining the pattern, timing, and extent of the injury.

The advantage of NSG over computed tomography (CT) or magnetic resonance imaging (MRI) is its bedside portability, lesser duration of time for performing the procedure, the modality is widely available, low cost, it is devoid of ionizing radiation, no need for ant sedation and the procedure can be easily reproducible.

Hence the present study is undertaken to evaluate the role of neurosonography to detect typical findings of hypoxic brain injury in preterm neonates i.e. neuro Sonographic findings suggestive of intracranial hemorrhage (ICH) and hypoxic-ischemic encephalopathy (HIE).

AIM: To study the role of neurosonography in the evaluation of neonatal hypoxic brain injury.

Objectives

1. To study the neurosonography characteristics of hypoxic-ischemic encephalopathy (HIE) and intracranial hemorrhage (ICH), i.e. periventricular leukomalacia, periventricular cyst, germinal matrix hemorrhage (GMH), intraventricular hemorrhage (IVH), intraparenchymal hemorrhage (IPH), and ventricular dilatation
2. To evaluate the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of neurosonography for hypoxic-ischemic encephalopathy and intracranial hemorrhage in preterm neonates as isolated parameters in comparison to clinical diagnosis.

Methodology

Type of the Study	Prospective, cross-sectional study
Place of Study	Department of Radiodiagnosis, A.C.S Medical college and Hospital, Chennai.
Sample Size	60 preterm neonates
Duration of Study	October 2022 to March 2024
Ethics Committee Clearance	was obtained

The present study is a non-interventional, prospective, cross-sectional observational study conducted over a period of 1.5 years at Department of Radiodiagnosis, A.C.S Medical college and Hospital, Chennai. A total 60 preterm neonates who were admitted to neonatal intensive care unit (NICU) were selected as per the inclusion criteria on a non-randomized purposive sampling basis and were subjected to neurosonography on selected days.

Selection Criteria

Inclusion Criteria

The following criteria were included in the study:

1. Preterm neonates <37 weeks of gestation age admitted to NICU and referred to the department of radiodiagnosis for NSG
2. Patients having registration at this institute
3. Preterm neonates with clinically suspected HIE and intracranial hemorrhage

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Exclusion Criteria

The following criteria were excluded from the study:

1. Parents or guardians unwilling to give consent for the study
2. All suspected cases of congenital malformations, severe infection, and failed resuscitation.

Study Procedure

Informed consent was obtained from the parents/guardian regarding inclusion of the neonates in the study. Detailed maternal history was obtained by reviewing antenatal records. All demographic data, including the birth weight, gestational age, mode of delivery, vital parameters including the APGAR scores at the 1 min and 5 min, complete neurological examination findings, and baseline routine investigations were obtained. NSG of the preterm neonates fulfilling the inclusion criteria was performed on Day 1 of life. Follow-up NSG was done on day 0, day 3, day 7, day 15, and day 30 of life. The morphology of NSG findings of hypoxic-ischemic brain injury was studied and correlation with various clinical findings was done.

Data Collection

The data obtained was recorded onto a structured proforma for statistical analysis.

Statistical Analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test or Fischer's exact test** (for 2x2 tables only) was used as test of significance for qualitative data. **Yates correction** was applied were ever chi-square rules were not fulfilled (for 2x2 tables only). Continuous data was represented as mean and standard deviation. **P value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Results

Table 1: Gender wise distribution of Preterm Neonates (n=60)

Gender	**Number of Preterm Neonates**	**Percentage %**
Female	28	46.7
Male	32	53.3.%
Total	60	100%

Out of 60 preterm neonates included in the study, 28 (46.7%) patients are female and 32(53.3%) are male.

Table 2: Gestational Age wise distribution of Preterm Neonates (n=60)

Gestational Age (in weeks)	**Number of Preterm Neonates**	**Percentage (%)**
28 - 30	13	21.7%
31 - 32	15	25%
33 - 34	15	25%
34 - 36	17	28.3%
Total	60	100%

Out of 60 preterm neonates included in the study, 17 (28.3%) patients have a gestational age of 34-36weeks and a least number of neonates, 13 (21.7%) neonates have a gestational age of 28-30 weeks.

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Table 3: Distribution of preterm neonates with NSG findings based on Birth weight (n=60)

Birth weight (in grams)	**Number of Preterm Neonates**	**Percentage (%)**
<1500	**16**	**26.7%**
1500-2000	**14**	**23.3%**
2000-2500	**25**	**41.7%**
>2500	**5**	**8.3%**
Total	**60**	**100%**

Among 60 preterm neonates, 16 (26.7%) had a birth weight of <1500gms, 14 (23.3%) had 1500-2000gms, 25 (41.7%) had 2000-2500 gms and 5 (8.3%) had a birth weight of > 2500gms.

T**able 4:** Parity wise distribution of preterm neonates with NSG findings (n=60)

Gravida	**Number of Preterm Neonates**	**Percentage**
Primigravida	24	40%
Multigravida	36	60%
Total	60	100%

Out of 60 preterm neonates included in the study, 24 (40%) patients are born to a primigravida female and 36 (60%) are born to a multigravida female

Table 5: Distribution of Preterm Neonates based on mode of delivery (n=60)

Mode of Delivery	**Number**	**Percentage**
Cesarean	23	38.3%
Vaginal	37	61.7%
Total	60	100%

Out of 60 preterm neonates included in the study, 23 (38.3%) patients are born through cesarean delivery while 37(61.7%) through vaginal delivery.

Table 6: Distribution of preterm neonates based on APGAR Score at 1 minute (n=60)

Apgar at 1 min	**Number of Preterm Neonates**	**Percentage**
≤ 7	13	21.7%
>7	47	78.3%
Total	60	100%

Among 60 preterm neonates, 13 (21.7%) had a APGAR score of ≤ 7 and 47 (78.3%) had an Apgar score of <7.

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Table 7: Distribution of preterm neonates based on APGAR Score at 5 minutes.(n=60)

APGAR score at 5 min	Number of Preterm Neonates	Percentage
≤ 7	10	16.7%
>7	50	83.3%
Total	60	100%

Among 60 preterm neonates, 10 (16.7%) had an APGAR score of ≤ 7 and 50 (83.3%) had an Apgar score of <7.

Table 8: Distribution of Preterm Neonates based on Maternal Complications (n=60)

Maternal Risk Factors	Number of Preterm Neonates	Percentage
Placenta Previa	3	5%
Abruptio Placenta	4	6.7%
IUGR	5	8.3%
Preeclampsia	11	18.3%
Infection	2	3.3%
Prolonged Labour	4	6.7%
Breech	8	13.3%
PROM	1	1.66%
Total	38	63.33%

Among 60 preterm neonates, preeclampsia was the most common maternal complication affecting 18.3% neonates.

Table 9: Neurosonography (NSG) findings in preterm neonates (n=60)

NSG FINDINGS	NUMBER	PERCENTAGE (%)
NORMAL	34	56.67
ICH	16	26.67
HIE	10	16.67
Total	60	100

Among 60 preterm neonates who underwent NSG, Intracranial Hemorrhage (ICH) is seen in 26.7% and Hypoxic Ischemic Encephalopathy in 16.67%.

Table 10: Distribution of ICH in preterm neonates on Neurosonography (n=60)

NSG FINDINGS	NUMBER	PERCENTAGE (%)
Patients with ICH	16	26.7

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Patients without ICH	44	73.3
Total	60	100

Among 60 preterm neonates who underwent NSG, prevalence of Intracranial Hemorrhage (ICH) is 26.7% and 73.3% showed normal NSG

Table 11: Grading of the GMH on NSG as per the Papile classification [85] in Preterm Neonates (n=60)

GRADE	NUMBER	PERCENTAGE
I	6	37.5
II	5	31.2
III	4	25.0
IV	1	6.2
Total	16	100

Out if 16 preterm neonates with GMH on NSG, majority of them showed Grade I hemorrhage (37.5%) followed by Grade II (31.2%) , Grade III (25%) and Grade IV(6.2%) respectively

Table 12: Gender Wise distribution of NSG findings in Preterm Neonates with ICH (n=60)

Gender	ICH	No ICH	Total
Female	6 (21.4%)	22 (78.6%)	28 (46.7%)
Male	10 (31.2%)	22 (68.8%)	32 (53.3%)
Total	16 (47.4%)	44 (52.6%)	60 (100%)

Out of 16 neonates with intracranial hemorrhage, 10 (31.2%) were male and 6 (21.4%) were females.

Table 13: Gestational Age wise distribution of NSG findings in Preterm Neonates with ICH (n=60)

Gestational Age (in weeks)	ICH	No ICH	Total
28-30	6 (46.2%)	7 (53.8%)	13 (21.7%)
31-32	4 (26.7%)	11(73.3%)	15 (25%)
33-34	4(26.7%)	11 (73.3%)	15 (25%)
34-36	2 (11.8%)	15 (88.2%)	17 (28.3%)
Total	16 (26.7%)	44 (73.3%)	60 (100%)

Among 16 preterm neonates with ICH, 6(46.2%) had a gestational age of 28-30weeks, 4(26.7%) had 31-32 weeks,4 (26.7%) had 33-34weeks and 2(11.8%) had 34-36 weeks of gestational age respectively.

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Table 14: Distribution of preterm neonates with ICH on NSG based on Birth weight (in grams) n=60

Birth weight (in grams)	**ICH**	**No ICH**	**Total**
<1500	9 (56.2%)	7 (43.8%)	16 (26.7%)
1500-2000	4 (30.7%)	9 (69.3%)	13 (21.7%)
2000-2500	2 (8%)	23 (92%)	25 (41.7%)
>2500	1 (20%)	5 (80%)	6 (10%)
Total	16 (26.7%	44 (73.3%)	60 (100%)

Mean birth weight of neonates among subjects with ICH was 1515.62 ± 391.46 gms and among subjects without ICH was 2105.68 ± 444.63 gms.

Table 15: Gravida wise distribution of preterm neonates with ICH on NSG (n=60)

Gravida	**ICH**	**No ICH**	**Total**
Primi	10 (41.6%)	14 (58.4%)	24 (40%)
Multi	6 (16.67%)	30 (83.33%)	36 (60%)
Total	16 (58.26%)	44 (41.74)	60 (100%)

Among 16 preterm neonates with ICH, 10 (41.6%) were born to primi female and 6 (16.7%) were born to a multigravida female.

Table 16: Distribution of Preterm Neonates with ICH on NSG based on mode of delivery (n=60)

Mode of Delivery	**ICH**	**No ICH**	**Total**
Cesarean	6 (26.1%)	17 (73.9%)	23 (38.3%)
Vaginal	10 (27.0%)	27 (73.0%)	37 (61.7%)
Total	16 (53.1%)	44 (46.9%)	60 (100%)

Among16 preterm neonates with ICH, 6 (26.1%) were born through cesarean and 10(27%) through vaginal delivery.

Table 17: Distribution of preterm neonates with ICH in NSG based on APGAR Score at 1 min (n=60)

Apgar Score at 1 min	**ICH**	**No ICH**	**Total**
≤ 7	8 (61.5%)	5 (38.5%)	13 (21.66%)
>7	8 (17%)	39 (83%)	47 (78.34%)
Total	16 (26.66%)	44 (73.44%)	60 (100%)

Among 16 preterm neonates with ICH, 8 (61.5%) patients had an APGAR score of at ≤7 1 minute and 8(17%) patients had an APGAR score of >7. Significant association was observed between APGAR score at 1 minute and ICH.

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Table 18: Distribution of preterm neonates with ICH in NSG based on APGAR Score at 5 mins (n=60)

APGAR score at 5 min	**ICH**	**No ICH**	**Total**
≤ 7	8 (80.0%)	2 (20%)	10 (16.7%)
>7	8 (16.0%)	42 (84%)	50 (83.3%)
Total	16 (26.7%)	44 (73.3%)	60 (100%)

Significant association was observed between APGAR at 5 Min and ICH. Among neonates with APGAR score at 5min ≤ 7, 80% had ICH.

Table 19: Distribution of preterm neonates with ICH on NSG based on Maternal Complications (n=60)

Maternal Risk Factors	**ICH**	**No ICH**	**Chi Square - $\chi 2$**	**P value**	**Odd Ratio (95% CI)**
Placenta Previa	2 (66.7%)	1(33.3%)	2.584	0.108	6.143 (0.517-72.992)
Abruptio Placenta	3(75.0%)	1(25.0%)	5.120	0.204	9.923(0.950-103.70
IUGR	4(80.0%)	1(20.0%)	7.934	0.005*	14.333 (1.462-140.52)
Preeclampsia	8(72.7%)	3(27.3%)	11.709	0.006*	4.680(1.183-18.513)
Infection	0(0.0%)	2(100.0%)	0.752	0.386	-
Prolonged Labour	2(50.0%)	2(50.0%)	1.193	0.275	3.0 (0.396-23.33)
Breach	2(25.0%)	6(75.0%)	0.013	0.909	0.905(0.163 to 5.02)
PROM	0 (0.0%	1 (100%)	-	-	-

In the study there was significant association between Abruptio placenta, IUGR, Preeclampsia with ICH. Among subjects with Abruptio Placenta 75% had ICH, among subjects with IUGR, 80% had ICH and among subjects with Preeclampsia, 72.7% had ICH.

Table 20: Follow up NSG findings in preterm neonates with ICH (n=60)

Follow up NSG Scan	**ICH**
Expired	3(18.8%)
Lesion increased	1(6.2%)
Lesion Remains same	8 (62.5%)
Ventriculomegaly	2(12.5%)
Lost to Follow up	1 (0.0%

Among subjects with ICH, 18.8% (3) expired, 62.5% (8) had status quo and 12.5%(2) had Ventriculomegaly. Among 60 preterm neonates included in the study, 18 (30%) neonates had clinical findings suggestive of intracranial hemorrhage.

NSG diagnosis of ICH has Sensitivity of 93.75%, Specificity of 93.18%, Positive Predictive Value of

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83.33%, 97.62% had Negative Predictive Value and Diagnostic Accuracy of 93.33%. Kappa agreement between Clinical IVH and Final IVH diagnosis was 0.8361 (Almost perfect agreement).

Out of 60 preterm neonates (n=60), 10 (16.7%) neonates showed Periventricular Echogenicity (PVE) on NSG whilst 50 neonates (83.3%) showed no PVE. Among 10 neonates with HIE, 50% had PVE, 40% had PVE with periventricular cyst. PVL - Periventricular Leukomalacia. Out of 10 (32.6%) neonates with hypoxic ischemic encephalopathy, 7(21.9%) were male and 3(10.7%) were females.

Among 10 neonates with HIE, 2 (15.4%) had GA of 28-30 weeks, 7(46.7% with GA of 31-32 weeks, 1(5.9%) with GA of 34-36 weeks. There was a significant difference in mean gestational age with respect to HIE. Among 10 preterm neonates with HIE on NSG, the majority weighed between 1500-2000 grams at birth.

Among 10 preterm neonates with HIE, 6(20.0%) neonates were born to primi female and 4 (13.3%) were born to multigravida female. Among 10 preterm neonates with HIE, 3(25.0%) neonates have not received antenatal steroids and 7(14.6%) received steroids. Among 10 (16.7%) preterm neonates with HIE, 5 (38.5%) patients had an APGAR score <7 at 1 minute and 5 (10.6%) patients had an APGAR of >7. Among 10 (16.7%) preterm neonates with HIE, 2 (20%) patients had an APGAR score <7 at 1 minute and 8 (16%) patients had an APGAR of >7. Significant association was found between Preeclampsia with ICH. Among subjects with preeclampsia, 6 (46.1%) had HIE and 4 (53.9%) subjects with Preeclampsia had no HIE.

Among 60 preterm neonates included in the study, 9 (90%) neonates had clinical findings suggestive of HIE. In the study among 10 subjects with HIE, Clinically 90.0% had HIE and among 50 subjects without HIE, 2% had HIE. There was significant association between Clinical HIE and Final HIE diagnosis. Kappa agreement between Clinical HIE and Final HIE diagnosis was 0.880 (Almost perfect agreement).

Discussion

Severity dictates the treatment options, close surveillance, and often predicts motor and neurocognitive outcomes. Studies estimate a short therapeutic window of 2-6 hours during which interventions may be efficacious in reducing the severity of ultimate brain injury. Thus, early identification of a neonate who has sustained a hypoxic-ischemic insult is of paramount importance for optimal management and treatment.

Thus, the present study was undertaken at the department of radiodiagnosis at Kamineni Institute of Medical Sciences. A total of 60 preterm neonates (<36 weeks of gestational age) who were clinically diagnosed with hypoxic brain injury and admitted to NICU were included in the study. All the preterm neonates underwent neurosonography as per the standard protocol and results observations are tabulated as above.

Characteristics of the Study Population

Gender Predilection: In the present study, out of 60 preterm neonates, there were a total of 32 males (53.3%) and 28 females (46.7%). The total number of males was greater than that of females. However, it was not significantly higher statistically (p=0.14).

Gestational Age: In the study, 17 (28.3%) patients had a gestational age of 34-36weeks, followed by 25% with 31-32 weeks, 25% with 33-32 weeks, the least number of neonates, 13 (21.7%) neonates had a gestational age of 28-30 weeks. The mean gestational age of the neonates in the present study was 32.3 weeks with a standard deviation of 2.42 weeks with a range of 28-36 weeks and the median was 32 weeks.

Birth weight of the Neonates

In the present study involving 60 preterm neonates, 16 (26.7%) had a birth weight of <1500gms, 14 (23.3%) had 1500-2000 grams, 25 (41.7%) had 2000-2500 grams and 5 (8.3%) had a birth weight of > 2500 grams respectively. The mean birth weight of neonates was 1948.33 grams with a standard deviation of 502.280 grams. About 39 (60%) of the neonates were in the category of low-birth weight (LBW) and 16 (26.7%) of the preterm neonates were of very low birth weight (VLBW). LBW neonates were significantly higher than that of VLBW ($p < 0.001$).

Mode of delivery Among the study population of 60 preterm neonates, 23 (38.3%) neonates were delivered by cesarean section, and the remaining 37(61.7%) were

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born by vaginal delivery. Thus, the proportion of vaginal delivery (61.7%) was significantly higher than that of lower segment cesarean section (31.8%) ($p < 0.0001$).

APGAR score at 1 minute:

The mean Apgar score at 1 min was 7.70 with a standard deviation of 1.31, with a range of 5 –10. The median Apgar score at 1 min was 8. Most of the neonates (47, 78.3%) had an Apgar score at 1 min >7 which was significantly higher than score ≤7(21.7%) in 13 neonates.

APGAR score at 5 minutes:

The mean Apgar score at 5 min was 8.15 with a standard deviation of 1.37, with a range of 6–10. The median Apgar score at 5 min was 8. The majority of neonates, 50 (83.37%) had an APGAR score of >7 and 10 (16.7%) had an Apgar score of ≤ 7.

Maternal Parity:

In the present study, 40% (24) preterm neonates were born to a primi female while 60% (36) of them were born to a multigravida female.

Maternal Complications: A total of 38 (63.3%) preterm neonates had various maternal complications. Some neonates had more than one maternal complication. A total of 11 patients (18.3%) had preeclampsia as a maternal obstetric complication, followed by breech presentation (8 patients, 13.3%), IUGR (5 patients, 8.3%), abruptio placenta (4 patients, 6.7%), prolonged labour (4 patients,6.7%) placenta previa (3 patients, 5%), infection (2 patients, 3.3%), 1 patient (1.66%) with premature rupture of membranes. Prevalence of preeclampsia (18.3%) was the significantly highest of all.[6]

INTRACRANIAL HEMORRHAGE

In the present study, out of 60 preterm neonates, a total of 16 (26.7%) patients had neurosonography findings of intracranial hemorrhage, out of which Grade I hemorrhage was seen in the highest proportion (37.5%) of neonates. This result is consistent with study done by **Afsharkhas et al** in 2015.

However, in the study done by Kavya MK et al, an equal proportion (8%) of neonates showed Grade III and Grade IV hemorrhage.

Gender predilection for ICH

In the present study, out of 16 neonates with intracranial hemorrhage, 10 (31.2%) were male and 6 (21.4%) were females. The proportion of males with respect to females was high, however, there was no significant correlation. ($\chi 2 = 0.737$ $p = 0.391$). This finding was consistent with the study done by Thakker et al, which reported that about 66.7% of the neonates with ICH were male, which was higher than that of females (33.3%.5%), but it was not significantly higher ($Z = 1.27$; $P = 0.13$)

Gestational Age and ICH

Among 16 preterm neonates with ICH, 6(46.2%) had a gestational age of 28-30weeks, 4(26.7%) had 31-32 weeks,4 (26.7%) had 33-34weeks and 2(11.8%) had 34-36 weeks of gestational age respectively. Early gestational age was significantly associated with intracranial bleed in preterm neonates *($p = 0.001$)* The mean gestational age in patients with intracranial hemorrhage was 31.18 ± 2.20 weeks. Mean age is 32.75 weeks. There was a significant difference in mean weeks of Gestation with respect to intracranial hemorrhage.(t- test = -2.302, p = 0.025*). Early gestational age was significantly associated with intracranial bleeding in neonates.

Birth weight and ICH

Among 16 preterm neonates with ICH, 9 (56.2%) had a birth weight less than 1500 grams, 4 (30.7%) had 1500-2000 grams, 2 (8%) had 2000-2500 grams and 1 (8.3%) had a birth weight greater than 2500 grams. There were 6 preterm neonates with LBW and 9 neonates had VLBW. There was significant association of preterm neonates of LBW and VLBW with intracranial haemorrhage. Highest incidence of ICH was seen in babies with birth weight <1500 grams (56.2%). ($\chi 2 = 14.019$,p = 0.003*). Mean birth weight of neonates among subjects with ICH was 1515.62 ± 391.46 grams. There was a significant difference in mean birth weight with respect to intracranial haemorrhage. (t- test = 4.684, p <0.001*)

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Maternal Parity and ICH : In the present study, among 16 preterm neonates with ICH, 10 (41.6%) were born to primi females and 6 (16.7%) were born to multigravida females. The present study showed significant association with parity and intracranial haemorrhage. ($\chi 2 = 21.818$, $p < 0.001$*).

Mode of Delivery and ICH:

In the present study, a total of 6 (26.1%) neonates were born through caesarean and 10(27%) through vaginal delivery. There was no significant association between mode of delivery and intracranial haemorrhage in preterm neonates. ($\chi 2 = 0.06$, $p = 0.936$). The studies done by Gover A et al, Mercure E et al and Salih BK et al ($p = 0.61$) show no association with the mode of delivery and ICH

However, Koksal et al in 2002 also reported that cesarean section was a significant protective factor against intraventricular hemorrhage (IVH). Therefore, the effect of mode of delivery is controversial. The protective role of cesarean section is speculative and there was no significant difference in the present study.

APGAR scores at 1 min and ICH

A total of 8 (61.5%) neonates had an APGAR score of ≤ 7 at 1 minute and 8 (17%) patients had an APGAR score of >7. Significant association was observed between APGAR score at 1 minute and ICH. ($\chi 2 = 10.320$, $p = 0.001$*). Mean APGAR at 1 min among subjects with ICH was 7.25 ± 1.57.9 (t test = 1.616, $p = 0.012$).

In the study done by Thakker H et al in 2019**,** the mean Apgar score of preterm neonates with intracranial bleed at 1 min and 5 min was 7.05 ± 1.62 and 8.22 ± 0.74, respectively, which was statistically significant. Thus, cesarean section may probably diminish the injury due to the preterm vaginal delivery.

APGAR score at 5 min and ICH

Mean APGAR at 5 Min among subjects with ICH was 7.44 ± 1.82. Total of 8 (80%) neonates had an APGAR score of at ≤ 7 at 5 minute and 8 (16%) patients had an APGAR score of >7. Significant association was observed between APGAR score at 5 minute and ICH. ($\chi 2 = 10.320$, $p = 0.001$*).

Maternal Obstetric Complications and ICH

In the present study, among 16 neonates with intracranial haemorrhage, maternal obstetric complications; IUGR (4 patients, 80%), abruptio placenta (3 patients 75%), placenta previa (2 patients, 66.7%) preeclampsia (6 patients, 54.5%), prolonged labour (2 patients, 50%), Breech presentation (2 patients 25%) placenta previa were reported. In the study there was significant association between IUGR ($\chi 2 = 7.934$, $p = 0.005$*) and preeclampsia ($\chi 2 = 12.320$, $p = 0.001$*) with intracranial haemorrhage.

Clinical diagnosis of Intracranial Haemorrhage (ICH) vs NSG diagnosis of ICH

In the present study out of 16 preterm neonates with ICH on NSG, clinical diagnosis of ICH was made in 93.8% of preterm neonates. Out of 44 preterm neonates without ICH on NSG, 6.8% of preterm neonates were clinically diagnosed with ICH.

Gestational Age and HIE

Among 10 neonates with HIE, 2 patients (15.4%) had a gestational age (GA) of 28-30 weeks, 7 patients (46.7%) with 31-32 weeks, 1 (5.9%) with GA of 34-36 weeks. In the study there was significant association between gestational age and HIE. ($\chi 2 = 14.559$, $p = 0.003$*) and the highest incidence of HIE was seen among subjects in the gestational age 31 to 32 years (46.7%).

Birth weight and HIE

Mean birth weight of neonates among subjects with HIE was 1855.00 ± 293.31 grams. Among 10 preterm neonates with HIE, 3 patients (23.1%) had a birth weight less than 1500 grams, 4 (40%) patients had a birth weight between 1500-2000 grams, 2 (%) patients weighed 2000-2500 grams at birth and 1(3.2%) had a birth weight above 2500 grams.

Maternal Parity and HIE

In the present study, among 10 preterm neonates with HIE, 6(20%) were born to primi females and 4 (13.3%) of the neonates were born to multigravida females. The present study showed no significant association between maternal parity and HIE ($\chi 2 = 0.480$, $p < 0.488$*).

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Mode of Delivery and HIE

In the present study among 10 neonates with HIE, a total of 8 (34.8%) neonates were born by caesarean section and 2(5.4%) were born through vaginal delivery. There was an association between mode of delivery and HIE in preterm neonates. ($\chi 2 = 8.813$, $p = 0.003$*). The proportion of caesarean sections was significantly higher among patients with abnormal periventricular echogenicity (PVE) (34.8%) as compared to that of the patients without abnormal PVE.

APGAR score at 1 min and HIE

In the present study , out of 10 neonates with HIE, a total of 5 (38.5%) neonates had an APGAR score of ≤ 7 at 1 minute and 5 (10.6%) patients had an APGAR score of >7. There was a significant association. ($\chi 2 = 5.676$, $p = 0.017$*) Mean APGAR at 1 minute among subjects with HIE was 6.50 ± 1.18 There was significant difference in mean APGAR at 1 minute with respect to HIE. (t-test = -3.427 p value = 0.007*) consistent with the study done by Thakker et al.

APGAR score at 5 min and HIE

In the present study, the mean APGAR score at 5 minutes among subjects with HIE was 7.10 ± 0.74. There was a significant difference in mean APGAR at 5 min with respect to HIE. (t-test = -2.792 p value = 0.007*) Total of 2 (20%) neonates had an APGAR score of at ≤ 7 at 5 minute and 8 (16%) patients had an APGAR score of >7. Significant association was observed between APGAR score at 5 minute and HIE ($\chi 2 = 9.320$, $p = 0.003$*). The findings were consistent with the results of the study done by Ehrenstein et al, which shows that a low Apgar score of ≤ 7 at 5 min was associated with HIE.

Maternal Obstetric Complications and HIE

In the present study, among neonates with HIE, maternal obstetric complications; infection (50%), premature rupture of membranes (PROM) (50%), preeclampsia (46.1%), placenta previa (33.3%) abruptio placenta (25%) prolonged labour (25%), IUGR (20%) was reported. with intracranial haemorrhage. No association was found between the maternal risk factors and HIE for infection, IUGR, PROM, abruptio placenta, placenta previa and prolonged labour.[7]

In the present study, there was a strong association of HIE in preterm neonates with preeclampsia in the mother. ($\chi 2 = 10.389$, $p = 0.00126$*). The odds ratio was 9.213 with a 95% confidence interval from 2.063 - 41.141. The Z statistic is 2.909. This finding was consistent with the study done by Badawi et al and Putbrese et al that HIE is associated with maternal preeclampsia.

In the study done by Thakker et al, out of 14 patients of HIE, 8 patients had associated maternal preeclampsia. There was a strong association of HIE in preterm neonates with preeclampsia in the mother;.$\chi 2$=15.75 P<0.0001* OR-[12.53 with 95% CI 3.07- 51.01) which is consistent with the present study.[9]

Follow up changes of HIE on NSG

In the present study, on the follow up neurosonography which was performed on day 3, day 7, day 14 and day 30 which showed progression of the periventricular leukomalacia in 20% of the patients. Ventriculomegaly was found in 10% of the patients while 10% (1 patient) expired. Unfortunately, 10% of the patients with findings of HIE on initial NSG scan were lost to follow up.[10]

Conclusion

Hypoxic-ischemic injury of the brain in preterm neonates is a devastating condition with significant morbidity and mortality. HIE and intracranial hemorrhage is two ends of the spectrum of hypoxic-ischemic events. Though MRI is considered as a gold standard, despite the limitations of the present study, neurosonography has reported high sensitivity and specificity in detection of hypoxic brain injury in preterm neonates. Furthermore, NSG is a noninvasive, relatively safer, inexpensive modality that can be performed bedside without the hassle of transporting critically ill infants to MRI suite for evaluation. Thus, neurosonography should be used as first-line imaging modality for routine screening of all preterm neonates born before 37 weeks.

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