

Ultrasonographic Manifestations Of Germinal Matrix Haemorrhage And Periventricular Leukomalacia In Preterm Neonates At Teaching Hospital Peradeniya

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Abstract: Germinal Matrix Haemorrhage (GMH) and Periventricular Leukomalacia (PVL) are two common types of brain injuries seen in preterm neonates for which cerebral hypoxia and ischaemia are major contributory factors. The objective of this study was to determine the type and grade of GMH and PVL on cranial ultrasonography to predict the neuro-developmental outcome. This is a descriptive study. Two hundred and sixty four preterm neonates between 28-34 weeks of gestation with risk factors and clinical features of brain injuries admitted to Special Care Baby Unit (SBU), Teaching Hospital Peradeniya from January 2013 to December 2013 were included in the study. Neonates with congenital anomalies, traumatic birth injuries, recurrent hypoglycaemia and bleeding disorders were excluded. Cranial ultrasound scans were done by an experienced Medical Officer, Professor of Radiology and Consultant Radiologist using a dedicated neonatal head probe 4-10 MHz of Logic e portable ultrasound scanner. Measurements of the lesions and ventricles were documented. A series of ultrasound scans were done for all the neonates, within the first three days of life, on day 7 and thereafter once a week until one month of age. Clinical history of seizures, abnormal head growth (microcephaly or hydrocephalus) and developmental milestones were assessed and neurological examination was done monthly for all babies till the age of one year. Monthly ultrasound scans were done for neonates who had GMH and PVL. Informed written consent was obtained from the parents of the neonates. The results were analyzed by using SPSS version 14. GMH was seen in 76(75%) neonates. PVL was seen only in 11(11%) neonates. A combination of GMH and PVL was detected in 10(10%) neonates. All the neonates with Grade IV GMH succumbed. Among the live neonates 2 out of 3 with Grade III GMH had gross motor developmental delay and all the neonates with Grades 2 and 3 PVL had cerebral palsy. Neonates with Grades I and II GMH and Grade 1 PVL did not manifest any neurological defects till one year of age. When considering brain injuries of preterm neonates less severe brain injuries are more likely with Grades I and II GMH and Grade 1 PVL which have a good prognosis while severe brain injuries are more likely with Grades III and IV GMH and Grades 2 and 3 PVL which have poor outcomes such as neonatal deaths, cerebral palsy or gross motor developmental delay.

Index Terms: Preterm neonates, Hypoxic Ischaemic Brain damage (HIBD), cranial ultrasonography, Germinal Matrix Haemorrhage (GMH), Periventricular Leukomalacia (PVL), hydrocephalus, cerebral palsy

1 INTRODUCTION

Germinal Matrix Haemorrhage (GMH) and Periventricular Leukomalacia (PVL) or Hypoxic Ischaemic Encephalopathy (HIE) are two common types of brain injuries of preterm neonates for which cerebral hypoxia and ischaemia during the perinatal period are main aetiological factors. Maternal and fetal or neonatal, infections or inflammations are other most important aetiological factors. GMH and PVL may lead to neonatal deaths or severe neuro-developmental manifestations such as cerebral palsy, mental retardation, seizures, visual impairment and sensorineural hearing loss which are permanent neurological disabilities. It is a major health problem which requires additional expenses to the country and also a burden to the patient, family and society.

Real time cranial ultrasonography is a non-invasive imaging method which does not involve ionizing radiation, reproducible and can be performed at the patient's bedside. It has a sensitivity of 100% and specificity of 91% in detecting GMH lesions more than 5mm. [1] It has a sensitivity of 75% and specificity of 100% in detecting the cystic lesions of PVL. [2] The objective of this study was to determine the type and grade of GMH and PVL on cranial ultrasonography to predict the neuro-developmental outcome.

2 METHODOLOGY

This is a descriptive study. Two hundred and sixty four preterm neonates between 28-34 weeks of gestation admitted to Special Care Baby Unit (SBU) at Teaching Hospital Peradeniya from January 2013 to December 2013 were included in the study. Estimated gestational age (EGA) was used as the age of the neonate but not the period of amenorrhea (POA) as it is not quite accurate and the developmental milestones were assessed from 40 weeks of gestation (corrected age). Informed written consent was obtained from parents of the neonates before data collection.

2.1 Inclusion criteria

Neonates with risk factors and clinical features of brain injuries were included in the study. Risk factors are (A) Intrauterine hypoxia due to impaired utero-placental blood flow in pregnancy induced hypertension (PIH), intrauterine growth retardation (IUGR), placenta previa, abruption of the placenta and multiple pregnancies. (B) Intra-partum hypoxia in fetal distress with low Apgar score at birth (less than 5 at 5 min) and resuscitation at birth. (C) Post partum hypoxia in

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respiratory syndrome (RDS), recurrent apnoea, pneumothorax and Patent Ductus Arteriosus (PDA). (D) Infections due to prolonged Premature Rupture of Membranes (PROM) for more than 24 hours, chorioamnionitis and neonatal sepsis. The clinical features are nonspecific and those are altered consciousness, abnormal tone, abnormal cry, neonatal seizures, pallor or cyanosis, shock, stupor, coma and decerebrate posturing.

2.2 Exclusion criteria

Neonates with other causes for neurological manifestations were excluded and those are congenital anomalies including metabolic and genetic causes, congenital infections, meningitis or meningo-encephalitis, recurrent hypoglycaemia and hyperbilirubinaemia, other cause for intra-cranial haemorrhages in bleeding disorders and birth trauma and other causes for cerebral infarctions due to embolization.

2.3 Real time cranial ultrasonography

Scans were performed through the anterior fontanel of the neonatal head which acts as an acoustic window. A series of ultrasound scans were done for all the neonates, within the first 3 days of life, on day 7 and once a week until one month of age. The scans were done by an experienced Medical Officer, Professor of Radiology and Consultant Radiologist using a dedicated neonatal head probe 4-10 MHz of Logic e portable ultrasound scanner. Measurements of lesions and ventricles were documented.

2.4 Patient follow up

Clinical history of seizures, abnormal head growth (microcephaly or hydrocephalus) and developmental milestones were assessed and neurological examination was done monthly for all babies till the age of one year. Monthly ultrasound scans were done for the neonates who had GMH and PVL. Retinopathy of Prematurity (ROP) was excluded and special investigations like Visual Evoked Potential (VEP) and Brain Stem Auditory Evoked Potential (BAEP) were performed for the suspected cases which is the normal routine management. The study was approved by the Ethical Review Committee, Faculty of Medicine, University of Peradeniya. The results were analyzed by SPSS version 14.

3 RESULTS

In brain injuries of preterm neonates, two areas most commonly get damaged are Germinal Matrix and periventricular white matter giving rise to Germinal Matrix Haemorrhage (GMH) and Periventricular Leukomalacia (PVL).

Germinal Matrix Haemorrhage (GMH) grading system. [3]

Created by Papile et al in 1978.

- Grade I –bleeding confine to the caudothalamic groove.
- Grade II –bleeding extends into the ventricle but does not expand it.
- Grade III –blood fills and distends the adjacent ventricle.
- Grade IV –Grades I, II or III GMH with Parenchymal Haemorrhagic Venous Infarction (PHVI).

Periventricular Leukomalacia (PVL) grading system. [4]

- Grade 1 – increased periventricular echogenicity persisting for ≥ 7 days.

- Grade 2 – increased periventricular echogenicity developing into small periventricular cysts.
- Grade 3 – increased periventricular echogenicity developing into extensive occipital and fronto-parietal cysts.
- Grade 4 – increased periventricular echogenicity in deep white matter developing into extensive subcortical cysts. (Grade 4 PVL is seen mostly in full term neonates)

Among the total of 264 neonates 163 (62%) had normal cranial ultrasound and 101(38%) showed brain injuries. Germinal Matrix Haemorrhage (GMH) was common and it has manifested in 76 (75%) neonates. There were 20 (20%), 42 (42%), 4 (4%) and 4 (4%) neonates with unilateral or bilateral Grades I, II, III and IV GMH respectively and 6 (6%) neonates with combination of Grades I and II GMH. Periventricular Leukomalacia (PVL) was less common and it has manifested in 11(11%) neonates. There were 7(7%), 2 (2%) and 2 (2%) neonates with Grades 1, 2 and 3 PVL respectively. Neonates with both GMH and PVL has manifested in 10(10%) neonates. There were 6 (6%) neonates with PVL Grade 1 and GMH Grades I or II, 3 (3%) neonates with PVL Grade 2 and GMH Grades I, II or III and 1(1%) neonate with PVL Grade 3 and GMH Grade II. Diffuse brain injuries involving the white matter, grey matter and brain stem occurred in 4(4%) neonates. All the neonates who had Grade IV GMH and all the neonates who had diffused white matter, grey matter and brain stem lesions succumbed. Among the live neonates 2 out of 3 neonates with Grade III GMH had gross motor developmental delay. They had only partial head control and were unable to roll over at six months and were unable to sit without support or stand at one year of age. Vision, hearing and social development were normal. Clinical hydrocephalus occurred but progressively returned to normal. None of the neonates with Grade III GMH developed gross hydrocephalus which required Ventricular-Peritoneal shunts. (Table1) All the neonates with Grades 2 and 3 PVL had cerebral palsy. Cerebral palsy evolved with time and all the neonates (2) with Grade 3 PVL had cerebral palsy at six months of age and all the neonates (2) with Grade 2 PVL had cerebral palsy at one year of age. (Table 2) The cranial ultrasound of Grade 3 PVL showed some large periventricular cysts, ventriculomegaly and white matter volume loss due to the collapse of cysts which is called “End stage PVL” at six months of age and cerebral atrophy at one year of age. They clinically presented with microcephaly, developmental delay, spastic diplegia and vision and hearing impairment. Spasticity was associated with brisk deep tendon reflexes and extensor plantar response. Both neonates initially had hypotonia especially involving the head and trunk and delayed motor milestones. Reduced alertness and feeding difficulties like slow feeding, gagging and vomiting were associated. The cranial ultrasound of Grade 2 PVL showed mild fullness of the lateral ventricles at the end of six months and one year. All the neonates (2) with Grade 2 PVL showed regression of development from the age of six months. They had hemiparesis or quadriparesis without vision or hearing impairment at one year of age. None of the neonates with brain injuries manifested with seizures at one year of age.

Table 1
One year neurodevelopmental manifestations of GMH

Grade	Total number	Clinical manifestations
I	20 (20%)	Neonatal deaths 1 Normal 19
II	42 (42%)	Neonatal deaths 4 Normal 38
I and II	6 (6%)	Normal 6
III	4 (4%)	Neonatal deaths 1 Developmental delay 2 Normal 1
IV	4 (4%)	Neonatal deaths 4

GMH- Germinal Matrix Haemorrhage

Table 2
One year neurodevelopmental manifestations of PVL

Grade	Total number	Clinical manifestations
1	7 (7%)	Neonatal deaths 1 Normal 6
2	2 (2%)	Cerebral palsy 2
3	2 (2%)	Cerebral palsy 2

PVL- Periventricular Leukomalacia

Live neonates with Grades I and II GMH, Grade 1 PVL and combinations of GMH and PVL did not manifest with neurodevelopmental defects at one year of age. (Table 3)

Table 3
One year neurodevelopmental manifestations of combination of GMH and PVL

Grade	Total number	Clinical manifestations
PVL 1 and GMH	6 (6%)	Neonatal deaths 2 Normal 4
PVL 2 and GMH	3 (3%)	Normal 3
PVL 3 and GMH	1 (1%)	Neonatal deaths 1

GMH- Germinal Matrix Haemorrhage

PVL - Periventricular Leukomalacia

4 DISCUSSION

Preterm neonates less than 34 weeks of gestation are more prone to get brain injuries because of the immaturity of brain and lack of cerebral autoregulation which is inability to maintain cerebral perfusion with varying systemic blood pressure. [5] Neurodevelopmental manifestations are due to hydrocephalus which occurs as a complication of Grade III GMH and periventricular white matter cystic lesions which occur as a complication of Grade IV GMH and cystic PVL (Grades 1 and 2 PVL). Hydrocephalus may lead to degeneration of adjacent neurones due to the raised intracranial pressure. Tissue dissolution occurs in Grade IV GMH and in cystic PVL will damage the descending corticospinal motor tracts (pyramidal tracts), the visual

radiation and the auditory radiation. [6], [7]. Findings of our study at the end of six months were similar to the findings of a study titled "A preliminary study on diagnosis and grading of Hypoxic Ischaemic Brain Damage (HIBD) in preterm neonates." done in China by Chang L.W. and he has published an article in 2007 Aug. He has found Grades I and II GMH and Grades 1 and 2 PVL as less severe brain injuries and Grades III and IV GMH and Grades 3 PVL as severe brain injuries. [8] But at the end of one year neonates with Grade 2 PVL also manifested with cerebral palsy and the findings were similar to the literature titled Diagnostic Imaging in Paediatric Neuroradiology by James Barkovich A., Kevin Moore R., Blaise Jones V., et al where they have mentioned more than 50% live neonates with cystic PVL (Grades 2 and 3) manifest cerebral palsy. [3] In the study it was 50%. Real time cranial ultrasonography is an effective preliminary neuroimaging method and according to the type and grade of brain injury one can predict the neurodevelopmental outcome. Cranial ultrasonography is equivalent to Computer Topography (CT) in detecting GMH and superior to CT in detecting PVL. CT has a risk of exposure to the ionizing radiation. Cranial ultrasonography has a sensitivity of only 26% and a positive predictive value of only 36% in detecting noncystic PVL. Magnetic Resonance Imaging (MRI) is the most accurate imaging modality but it takes long data acquisition time which requires sedation and monitoring of the neonate. [2] Both CT and MRI need the sick preterm neonate to be transported to the fixed scan machine. [6], [7]. Cognitive disturbances occur during the early school age which manifests as Attention Deficit Hyperactivity Disorder (ADHD) and learning difficulties which require special educational services. [6] The study would have much more improved by follow up of the neonates till early school age to gather additional information and it would be a good future research.

5 CONCLUSION

When considering brain injuries of preterm neonates, less severe injuries are more likely with Grades I and II GMH and Grade 1 PVL which have a good prognosis while severe injuries are more likely with Grades III and IV GMH and Grades 2 and 3 PVL which have poor outcomes such as neonatal deaths, cerebral palsy or gross motor developmental delay.

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