Association between Germinal Matrix Hemorrhage at the First Week of Life and Perinatal Factors of Preterm Neonates Born at St. Luke's Medical Center
(EP-007)

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Introduction

In the Philippines, 13 out of 100 live births are preterm with complications of prematurity being the leading cause of neonatal deaths (31%)[1]. Germinal matrix hemorrhage (GMH) is one of common pathologies associated with prematurity due to the inability of the germinal matrix to compensate for the hemodynamic and oxygen tension changes during and after childbirth[2].

GMH is associated with degree of prematurity and is therefore associated with low birthweight and low Ballard score. Studies also show an association between GMH and poor Apgar scores and reduction of GMH risk with use of antenatal corticosteroids. Premature rupture of membranes and mode of delivery did not have any association with GMH while there are varying results in the association of GMH with maternal hypertensive disorder, gestational diabetes mellitus and multiple gestation.

Determining the risk factors for GMH is important since early detection and prompt and appropriate treatment are key in decreasing morbidity, such as the long term neurologic deficits, including poor cognitive outcomes and cerebral palsy.

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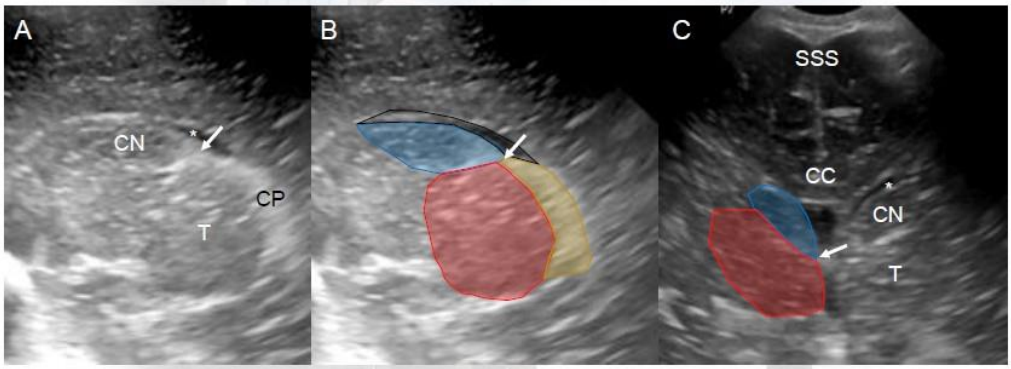

*Normal cranial ultrasound anatomy in sagittal (**A**,**B**) and coronal (**C**) planes showing the caudothalamic groove (→), caudate nucleus (CN), thalamus (T), lateral ventricle (*), choroid plexus (CP), corpus callosum (CC) and superior sagittal sinus (SSS)*

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Methodology

This is a retrospective, cross-sectional study involving all preterm neonates who underwent cranial ultrasound from 2017 to 2020 at St. Luke's Medical Center in their first week of life, excluding those with congenital malformations, metabolic disorders, central nervous system infection, unknown perinatal data and unavailable cranial ultrasound images.

The presence and grading of GMH was evaluated independently by two pediatric radiologists who were blinded to the perinatal factors. A third pediatric radiologist also evaluated the images in cases of incongruent findings. The researcher, who is blinded to the cranial ultrasound findings, also determined the patient's sex, gestational age, birthweight, Ballard score, Apgar score in the 1st and 5th minute, mode of delivery, multiple gestation, presence of maternal hypertensive disorder, gestational diabetes mellitus, preterm premature rupture of membranes (PPROM) and use of antenatal corticosteroids through the medical records.

Determination of the association between GMH and perinatal factors was analyzed using univariate and multivariate statistics.

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Operational Definitions

Germinal matrix hemorrhage grading by Papile, et al.

- Grade I: hemorrhage confined in the caudothalamic groove
- Grade II: hemorrhage extending to the ventricle without dilatation
- Grade III: hemorrhage extending to the dilated ventricle
- Grade IV: parenchymal hemorrhage secondary to venous infarction

Preterm: Birth before 37 weeks age of gestation

Maternal hypertensive disorder: blood pressure higher than 140/90 mmHg after 20 weeks of gestation

Gestational diabetes mellitus: fasting blood sugar > 92 mg/dL or 2 hour 75 gram oral glucose tolerance test > 140 mg/dL

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Neonatal and Maternal Characteristics

Perinatal Factor		n (%) / Mean ± SD
GMH	Present	140 (37.6)
	Grade I	111 (29.8)
	Grade II	24 (6.5)
	Grade III	3 (0.8)
	Grade IV	2 (0.5)
	Absent	232 (62.4)
Sex	Male	195 (52.4)
	Female	177 (47.6)
GA (weeks)		33.1 ± 2.79
	Below 28	21 (5.6)
	28 to 31 6/7	74 (19.9)
	32 to 33 6/7	90 (24.2)
	34 to 36 6/7	187 (50.3)
BW (grams)		1829.1 ± 553.81
	Below 2,500	331 (89.0)
	2,500 and above	41 (11.0)
BS (weeks)		33.0 ± 2.84
	Below 28	20 (5.4)
	28 and above	352 (94.6)
APGAR 1'		7.9 ± 1.75
	0-3 (Concerning)	18 (4.8)
	4-6 (Moderately Abnormal)	31 (8.3)
	7-10 (Reassuring)	323 (86.8)
APGAR 5'		8.7 ± 0.94
	0-3 (Concerning)	2 (0.5)
	4-6 (Moderately Abnormal)	14 (3.8)
	7-10 (Reassuring)	356 (95.7)
Mode of Delivery	Vaginal	80 (21.5)
	Emergency CS	285 (76.6)
	Elective CS	7 (1.9)
Multiple Gestation	Singleton	268 (72.0)
	Multiple	104 (28.0)
Maternal Hypertension		105 (28.2)
GDM		127 (34.1)
PPROM		67 (18.0)
Antenatal Corticosteroids		159 (42.7)

Univariate Analysis in the Relationship between Perinatal Factors and Presence of GMH

Perinatal Factor	GMH Present n (%) / β coefficient	Odds Ratio (95% Confidence Interval)	p-value
Sex		0.98 (0.65 – 1.50)	0.934
Male, n=195	73 (37.4)		
Female, n=177	67 (37.9)		
GA	0.038	1.04 (0.96 – 1.12)	0.326
BW	0.000	1.00 (1.00 – 1.00)	0.307
BS	0.053	1.06 (0.98 – 1.14)	0.169
APGAR 1'		0.96 (0.51 – 1.78)	0.889
0 – 6, n=49	18 (36.7)		
7 – 10, n=323	122 (37.8)		
APGAR 5'		1.30 (0.48 – 3.58)	0.606
0 – 6, n=16	7 (43.8)		
7 - 10, n=356	133 (37.4)		
Mode of Delivery		1.00 (0.60 – 1.65)	0.978
Vaginal, n=80	30 (37.5)		
CS, n=292	110 (37.7)		
Multiple Gestation		1.05 (0.66 – 1.67)	0.837
Multiple, n=104	40 (38.5)		
Singleton, n=268	100 (37.3)		
Maternal Hypertension		1.03 (0.65 – 1.64)	0.908
Present, n=105	40 (38.1)		
Absent, n=267	100 (37.5)		
GDM		1.24 (0.80 – 1.92)	0.343
Present, n=127	52 (40.9)		
Absent, n=245	88 (35.9)		
PPROM		1.06 (0.62 – 1.83)	0.827
Present, n=67	26 (38.8)		
Absent, n=305	114 (37.4)		
Antenatal Corticosteroids		0.84 (0.55 – 1.28)	0.406
Given, n=159	56 (35.2)		
Not Given, n=213	84 (39.4)		

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Results

140 out of the 372 subjects (37.6%) had germinal matrix hemorrhage, of which, 29.8% had grade I, 6.5% had grade II, 0.8% had grade III and 0.5% had grade IV GMH.

Univariate and multivariate analyses showed no statistically significant association between the presence of GMH and sex, gestational age, birthweight, Ballard score, Apgar score, mode of delivery, multiple gestation, maternal hypertensive disorder, gestational diabetes mellitus, PPROM, and use of antenatal corticosteroids.

Multivariate Analysis in the Relationship between the Perinatal Factors and Presence of GMH

Perinatal Factor	Odds Ratio (95% Confidence Interval)	p-value
Male Sex	0.95 (0.62 – 1.46)	0.831
Multiple Gestation	1.16 (0.69 – 1.93)	0.574
With Maternal Hypertension	1.16 (0.69 – 1.94)	0.581
With GDM	1.22 (0.78 – 1.91)	0.386
With PPROM	1.11 (0.63 – 1.96)	0.725
Given Antenatal Corticosteroids	0.81 (0.53 – 1.25)	0.348
APGAR 5' of 0-6	1.59 (0.55 – 4.55)	0.392
Vaginal Delivery	1.04 (0.60 – 1.78)	0.900
Birthweight less than 2,500 grams	1.00 (1.00 – 1.00)	0.215

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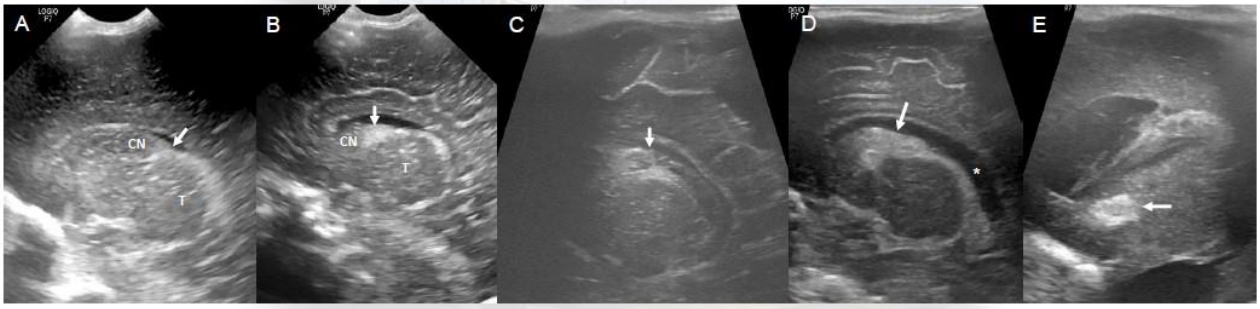

***A**. Normal sagittal cranial ultrasound showing the caudothalamic groove (→) between the caudate nucleus (CN) and thalamus (T); **B**. Grade I GMH showing hyperechoic focus localized in the caudothalamic groove (→); **C**. Grade II GMH showing extension of the hemorrhage (→) into the non-dilated ventricle; **D**. Grade III GMH showing intraventricular hemorrhagic extension (→) with ventricular dilatation (*); **E**. Grade IV GMH showing parenchymal hemorrhage at the caudate nucleus (→)*

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Conclusion

Germinal matrix hemorrhage did not show any association with the various perinatal factors in this study.

Recommendations

We recommend further studies with a higher sample size and to consider evaluation of grades I and II versus the clinically significant grade III and IV GMH, as well as to look into the timing of and follow-up cranial ultrasound scans. The association between GMH and maternal COVID-19 infection during the perinatal period may also be a potential point of interest.

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