



ROLE OF TRANSCRANIAL DOPPLER PARAMETERS IN PRETERM NEONATES FOR PREDICTION OF INTRACEREBRAL HAEMORRHAGE.

Radio-Diagnosis

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ABSTRACT

Aims and Objectives: To assess the screening of intracerebral vessels in preterm newborns in early postnatal period by transcranial Doppler parameters; as a predictive method of identifying preterm infants at risk of intracerebral hemorrhage. **Materials and Methods:** The study is a prospective analytical observational study carried out on 50 preterm neonates; 23 male and 27 female, their gestational age (GA) ranged between 26 and 34 weeks, and their birth weights (BW) ranged from 1000 to 2500 g. Examination of the ACA and MCA were performed within the first two days of life measuring PSV, EDV, MV and Doppler indices RI and PI. Then repeated within 4 to 7 days (follow up study). The neonates are classified into hemorrhagic and non-hemorrhagic / control groups and comparison of the Doppler parameters. **Results:** The 50 preterm neonates showed no intracerebral hemorrhage by transcranial ultrasound at the initial examination. On the follow up study, 25 of them developed ICH - hemorrhagic group and 25 of them did not develop ICH - control group. There was statistically significant difference (P-value < 0.0001) between the two groups as regards; the gestational age <210 days, birth weight <1250 grams, mean value of EDV and RI in Doppler examination. **Conclusion:** The Doppler parameters were adequate enough to be used in the clinical practice to distinguish normal preterm neonates from those who might develop germinal matrix bleed / Intracerebral haemorrhage. The study showed that the most sensitive Doppler parameter which can be used as a predictor marker for intracerebral hemorrhage in preterm neonates during early postnatal period was RI < 0.64 and end diastolic velocity > 10.9 cm/s as a measurable screening predictor, when clinical symptoms of hemorrhage may be still silent and so preventive and therapeutic actions could be used.

KEYWORDS

Transcranial ultrasound Doppler; preterm neonates; germinal matrix bleed; intraventricular haemorrhage.

INTRODUCTION

Preterm babies born before 37 weeks of pregnancy are possibly the most vulnerable group of people on earth. An estimated 15 million infants are born prematurely each year. Preterm birth rates vary significantly between nations, ranging from 5% to 18% of all births.¹ Preterm births can occur naturally or when it is deemed medically necessary to induce labour or perform an early caesarean section. Intrauterine infections are the leading cause of spontaneously preterm newborns, followed by mother smoking, low socioeconomic status, and repeated gestations. In recent years, there has been a rise in the use of assisted reproductive procedures, which also causes multiple pregnancies and preterm birth.

Respiratory distress syndrome, necrotizing enterocolitis, and germinal matrix haemorrhage - intraventricular hemorrhages (GMH - IVH) are the morbidities that have a high mortality risk in preterm babies. These issues may result in morbidity that lasts from childhood into adulthood and places a significant financial and social burden on society.

GMH-IVH is one of the most important neurological problems in premature and very low birth weight (VLBW) infants. Its incidence is inversely related to the weight and the age of the newborn. The onset of bleeding coordinates with the occurrence of hypoxia and respiratory distress requiring mechanical ventilation. GMH-IVH is caused by the rupture of GM vessels. The majorities occur in the first 7 days of life.² Mortality of IVH is related to the extent of the injury as measured by grades I – IV (mortality of 4%, 10%, 18%, and 40% respectively). Since these infants are born at a crucial time of brain development, they can develop short term and long term neurological, sensory, cognitive and motor disabilities depending on the severity of the GM-IVH. Grade III-IV is associated with poor neurological outcome. Currently, Neurosonogram (NSG) is used to diagnose the condition.

This study is designed to assess the Doppler parameters of the anterior cerebral artery (ACA) and middle cerebral artery (MCA) in preterm neonates as a predictive method in identifying preterm infants at risk of intracerebral haemorrhage.

Advantages of transcranial Doppler can be performed at bedside of the neonate, with minimal to no sedation, scan can be initiated immediately after birth, safe, inexpensive and repeatability as for serial imaging.

AIMS AND OBJECTIVES

The aim of this study is to assess the screening of intracerebral vessels in preterm newborns in early postnatal period by transcranial Doppler parameters; as a predictive method of identifying preterm infants at risk of intracerebral hemorrhage.

METHODS AND MATERIALS

Source Of Data: Preterm neonates admitted to NICU at M. S. Ramaiah Hospitals, Bengaluru.

Inclusion Criteria

1. Neonates with gestational age ranging between 26 and 34 weeks.
2. Birth weights (BW) between 1000 to 2500 g.

Exclusion Criteria

1. Neonates with preexisting germinal matrix bleed.
2. Family history of bleeding disorders.

Methods Of Data Collection

Study Design: The study is a prospective analytical observational study carried out on preterm neonates admitted to NICU in MS Ramaiah hospitals, Bengaluru.

Study Methods: Prospective analytical observational study.

Data will be collected from preterm neonates admitted to NICU irrespective of their gender, background, socio-economic status in M.S. Ramaiah Hospitals. A detailed history of the patient will be entered in the proforma.

The study is a prospective analytical observational study carried out on 50 preterm neonates; 23 male and 27 females.

They all were considered clinically at risk of ICH due to their prematurity and low birth weight. Informed consent was obtained from one of the parents of each infant before the study.

Examination of cerebral vessels within the first two days of life with measurement of PSV, EDV, MV and Doppler indices RI and PI. Then repeated within 4 to 7 days (follow up study). The neonates are classified into hemorrhagic and non-hemorrhagic / control groups and comparison of the Doppler parameters.

Sample Size

50 (25 each in hemorrhagic and control group)

Transcranial US-Doppler technique: We transported the US-Doppler equipment to the NICU in the initial evaluation and in the follow up.

We took all the precautions specific for dealing with those risky newborns in NICU; like complete aseptic conditions, and not making the isolette open for prolonged time during Examination.

The newborn lay supine and head was gently held in a horizontal position by the nurse

We used 3.7-MHz convex transducer and 7.5-MHz linear transducer. The transducer was placed on the anterior fontanel and angled to produce images in coronal section and then rotated 90 and angled to produce sagittal images.

The ACA and MCA were visualized using color Doppler through the anterior fontanel; ACA was seen in the midline sagittal plane and blood flow velocity was determined at the proximal portion of it at its curve around the corpus callosum. The proximal part of MCA was seen in the coronal plane and its peripheral branches were examined in sylvian fissure in the sagittal plane.

All Doppler measures were taken from both vessels using an average from three cardiac cycles.



Figure 1: Voluson E8 and LOGIQ V2 / V1 ultrasound machines.

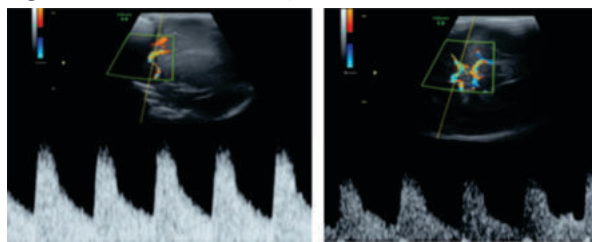


Figure 2: The ACA and MCA were visualized using color Doppler through the anterior fontanel; ACA was seen in the midline sagittal plane and blood flow velocity was determined at the proximal portion of it at its curve around the corpus callosum. The MCA was seen in the coronal or sagittal plane.

RESULTS

1. Gender distribution: There is no significant gender bias.

GENDER	CONTROL	CASES	TOTAL
MALES	14	9	23
FEMALES	11	16	27
TOTAL	25	25	50
M:F	1.27:1	0.56:1	0.85:1
CHI-SQUARE TEST	P = 0.15 (NOT SIGNIFICANT)		

2. Gestational age

Gestational age ≤ 210 days (30 weeks) is highly sensitive predictor of ICH with sensitivity of 76% and specificity of 92% ($p < 0.0001$).

GESTATIONAL AGE	CASES (DAYS)	CONTROLS (DAYS)
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MEAN	207.28	221.36
STANDARD DEVIATION	11.17	10.54
RANGE	186-236	200-237
T-TEST	0.00003 (SIGNIFICANT)	

3. Birth Weight

Table : distribution of subjects as per birth weight

BIRTH WEIGHT	CONTROLS	CASES
MEAN (gms)	1738	1404.4
STANDARD DEVIATION	333.88	295
T-TEST	0.000691 (SIGNIFICANT)	

CUTOFF: Birth weight of ≤ 1250 gms is a good predictor of ICH with sensitivity of 52% and specificity of 96% ($p < 0.0001$).

4. Mode of delivery distribution of subjects as per mode of delivery.

MODE OF DELIVERY	CONTROLS	CASES	TOTAL
LSCS	16	17	33
VAGINAL	9	8	17
TOTAL	25	25	50
CHI-SQUARE TEST	0.76 (NOT SIGNIFICANT)		

5. Laterality

LATERALITY	GRADE			TOTAL
	I	II	III	
RIGHT	1	0	1	2
LEFT	2	2	0	4
BILATERAL	10	9	0	19
TOTAL	13	11	1	25

Cutoff after comparison of Doppler indices of right ACA between two groups

RIGHT ACA	CUT-OFF	SENSITIVITY	SPECIFICITY	LEVEL OF SIGNIFICANCE
PSV	>34.4	76	56	0.04
EDV	>10.2	92	64	>0.0001
MV	>11.65	92	28	0.4
RI	<0.61	52	100	<0.0001
PI	≤ 1.5	76	44	0.56

Cutoff after comparison of Doppler indices of left ACA between two groups

LEFT ACA	CUT-OFF	SENSITIVITY	SPECIFICITY	LEVEL OF SIGNIFICANCE
PSV	>36.2	72	64	0.06
EDV	>10.4	96	60	<0.0001
MV	≤ 13.9	28	88	0.93
RI	≤ 0.66	84	72	<0.0001
PI	≤ 1.5	72	44	0.56

Cutoff after comparison of Doppler indices of right MCA between two groups

RIGHT MCA	CUT-OFF	SENSITIVITY	SPECIFICITY	LEVEL OF SIGNIFICANCE
PSV	>29.4	40	88	0.039
EDV	>10.5	96	64	<0.0001
MV	>15.07	76	40	0.82
RI	≤ 0.67	84	80	<0.0001
PI	>1.37	68	48	0.77

Cutoff after comparison of Doppler indices of left MCA between two groups

RIGHT MCA	CUT-OFF	SENSITIVITY	SPECIFICITY	LEVEL OF SIGNIFICANCE
PSV	>29.4	40	88	0.039
EDV	>10.5	96	64	<0.0001
MV	>15.07	76	40	0.82
RI	≤ 0.67	84	80	<0.0001
PI	>1.37	68	48	0.77



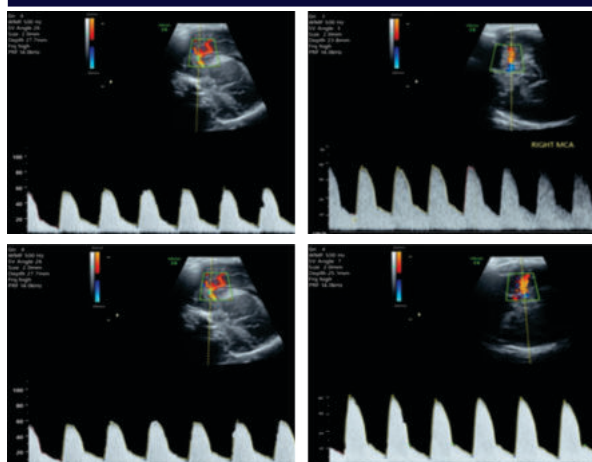


Figure 3: A day 1 neonate male born through Lower segment caesarean section (LSCS) developed bilateral grade I germinal matrix bleed detected after serial NSG imaging on day 5 of life. Coronal plane images (a) depict grade I germinal matrix bleed in both the caudothalamic groove (b,c,d,e) depict the Doppler assessment of the anterior and middle cerebral arteries.

DISCUSSION

Neurosonogram is the first modality of choice in preterm neonates for screening intracranial abnormalities however MRI has always been the gold standard. However, there is a necessity of non-invasive means of predicting the incidence of ICH. Transcranial Pulsed Doppler ultrasound is a non-invasive means of examining cerebral circulation at the bedside, even in sick preterm infants under intensive care. This information is of great value in a clinical setting for planning the management of the preterm neonates.

In a prospective study conducted by Elhameed et al.¹ on 39 preterm neonates showed that the most sensitive Doppler parameter which can be used as a predictor for intracerebral haemorrhage in preterm newborns in the early postnatal period was end diastolic velocity (EDV) of anterior cerebral artery > 9.2 cm/s and so offers a measurable screening predictor, when clinical symptoms of haemorrhage may be still silent and so preventive and therapeutic actions could be useful.

According to a study by Gabriel et al.³ conducted on 50 premature, very low birth weight neonates concluded that there is a correlation between the presence of cerebral hemodynamic changes demonstrated by resistance index measurements and the subsequent development of haemorrhage.

In another study by de Assis MC et al.⁴ concluded that the resistive index (RI) values of healthy preterm infants were always larger than the RI values of pre-term infants with intracranial haemorrhage.

In all the above-mentioned studies and many other studies concluded that the Doppler examination of the Intracerebral arteries in preterm neonates are helpful in identifying neonates at risk for subsequent development of haemorrhage.

The Present Study:

The study was conducted on 25 controls to establish a normal range of the Doppler parameters and 25 cases to screen for abnormal Doppler values. The study included 23 males and 27 female preterm neonates.

Gestational age ≤ 210 days (30 weeks) is highly sensitive predictor of ICH with sensitivity of 76% and specificity of 92% ($p < 0.0001$). The study was performed with subjects having their birth weights between 1000 to 2500g and birth weight of ≤ 1250 gms was found to be good predictor of ICH with sensitivity of 52% and specificity of 96% ($p < 0.0001$). The mode of delivery and laterality of the GMH-IVH showed weaker correlation.

The Doppler parameters from ACA and MCA were compared.

The PSV > 34.4 cm/sec of right ACA a moderately sensitive predictor of ICH with sensitivity of 76% and specificity of 56% ($p < 0.04$). The EDV > 10.2 cm/sec of right ACA was a highly sensitive predictor of ICH with sensitivity of 92% and specificity of 62% ($p < 0.0001$). The

RI < 0.61 of right ACA was a highly sensitive predictor of ICH with sensitivity of 92% and specificity of 62% ($p < 0.0001$).

The EDV > 10.4 cm/sec of left ACA was a highly sensitive predictor of ICH with sensitivity of 96% and specificity of 60% ($p < 0.0001$). The RI ≤ 0.66 of right ACA was a highly sensitive predictor of ICH with sensitivity of 84% and specificity of 72% ($p < 0.0001$).

The EDV > 10.5 cm/sec of right MCA was a highly sensitive predictor of ICH with sensitivity of 96% and specificity of 64% ($p < 0.0001$). The RI ≤ 0.67 of right ACA was a highly sensitive predictor of ICH with sensitivity of 84% and specificity of 80% ($p < 0.0001$).

The EDV > 12.7 cm/sec of left MCA was a highly sensitive predictor of ICH with sensitivity of 76% and specificity of 76% ($p < 0.0001$). The RI ≤ 0.64 of right ACA was a highly sensitive predictor of ICH with sensitivity of 72% and specificity of 100% ($p < 0.0001$).

The MV and PI values in both the ACA and MCA arteries did not have significant levels of correlation. The PSV values of the left ACA and both the MCA arteries did not show significant levels of correlation.

Limitations Of The Present Study:

1. The study was single center hospital study with a small sample size.
2. The study included only one observer in all the cases.
3. The study does not consider the effects of other systemic illnesses on the neonatal brain.

CONCLUSION

This study was conducted in 50 preterm neonates who had showed no intra cerebral hemorrhage by transcranial ultrasound at the initial examination. On the follow up US-Doppler study, 25 of them (9 males, 16 females) developed ICH and they are classified as hemorrhagic group and 25 of them (14 males, 11 females) did not develop ICH and they are classified as non hemorrhagic or control group.

Among the cases, majorities were in the gestational age group below 30 weeks. Out of the 25 cases, there were 13 cases of grade I, 11 cases of grade II and 1 case of Grade III germinal matrix bleed. There was statistically no significant difference (P-value of > 0.05) between the two groups as regards the mean value of PSV, MV and PI in Doppler examinations.

There was statistically highly significant difference (P-value of ≤ 0.0001) between the two groups as regards mean value of EDV ≥ 10.9 cm/s and RI ≤ 0.64 in Doppler examination.

The Doppler parameters were adequate enough to be used in the clinical practice to distinguish normal preterm neonates from those who might develop germinal matrix bleed / Intracerebral haemorrhage. The study showed that the most sensitive Doppler parameter which can be used as a predictor marker for intracerebral hemorrhage in preterm neonates during early postnatal period was RI ≤ 0.64 and end diastolic velocity ≥ 10.9 cm/s as a measurable screening predictor, when clinical symptoms of hemorrhage may be still silent and so preventive and therapeutic actions could be used. Further studies with a larger patient population may offer additional benefits.

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