FREQUENCY AND GRADING OF INTRAVENTRICULAR HEMORRHAGE IN PRETERM BABIES ADMITTED IN NATIONAL INSTITUTE OF CHILD HEALTH, KARACHI, PAKISTAN

Deepak Kumar✉, Mashal Khan, Mehmood Sheikh, Muhammad Hanif

Department of Pediatrics, National Institute of Child Health, Jinnah Sindh Medical University, Karachi - Pakistan

Address for correspondence:
Deepak Kumar
Department of Pediatrics, National Institute of Child Health, Jinnah Sindh Medical University, Karachi - Pakistan

E-mail:
drdeepakkumar6778@gmail.com

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ABSTRACT

Objective: To report the frequency of IVH in preterm neonates and IVH grading on cranial ultrasound.

Methodology: This prospective cross-sectional study was carried out at NICH. All preterm infants of either gender were consecutively enrolled. Detailed history of the infant regarding the clinical examination and socio-demographic characteristics of the infants were noted. IVH was observed in all preterm neonates, and all infants were categorized according to the Papile grading.

Results: Of 144 neonates, the mean age was 2.34 ±0.97 days. There were 93 (64.6%) males and 51 (35.4%) females. IVH was observed in 144 (37.6%) neonates. A significant mean difference of age (p: <0.001), gestational age (p: <0.001), birth weight (p: <0.001), APGAR score at 1 min (p; <0.001), APGAR score at 5 min (p: <0.001) was observed in between IVH and non IVH neonates. Furthermore, a significant association of place of admission (p: <0.001), mode of delivery (p: 0.038), need of invasive/non-invasive ventilator (p: 0.002), and preterm status (p: <0.001) was observed with IVH. IVH grade I was observed in 75 (52.1%), grade II in 45 (31.3%), grade III in 18 (12.5%), and grade IV in 6 (4.2%) neonates.

Conclusion: A notably higher number of preterm neonates had IVH. While grade I was most common, a majority exhibited severe grades (III and IV). Extremely early preterm births carried increased risk of spontaneous delivery and greater reliance on invasive/non-invasive ventilator support.

Keywords: Intravenous Hemorrhage; Preterm Neonates; Ultrasound

INTRODUCTION

Preterm birth also known as premature birth is one of the important issues in neonates worldwide. Preterm newborns are more susceptible than term babies to illnesses in the early neonatal period. When compared to term-born controls, the mortality rate is increased by thrice, and the morbidity rate almost doubles for each extra week of gestation before 38 weeks.[1-5] Studies reported that preterm births are expected to afflict 15 million babies worldwide, primarily in low- and middle-income nations.[2,3]

In high-risk preterm infants, cranial ultrasounds are a helpful technique for finding intracranial abnormalities.[6,7] Given that they are a group at high risk for developing brain lesions, regular screening tests are advised for all neonates delivered before 30 weeks of pregnancy.[8] Near-term neonates typically have brain abnormalities indicative of preterm delivery, including intraventricular hemorrhage (IVH).[9-12]

The diagnostic tool has the extra benefits of being substantially less costly, radiation-free, not requiring anaesthesia, and portable enough to allow for bedside examination of critically sick patients. However, there aren't many studies in the literature right now particularly from Pakistan about how effective cranial ultrasonography is for preterm neonates. The current study objective is to report the frequency of IVH in preterm neonates and IVH grading on cranial ultrasound.

METHODOLOGY

This was a cross sectional descriptive study conducted at National Institute of Child Health, Karachi, Pakistan for a period of one year from August 2021 to July 2022. The study was initiated after approval from the Institutional Review Board and obtaining informed consent from the parents/guardian.

Epi Info sample size calculator is used for the estimation of sample size taking confidence interval 95%, margin of error 5%, IVH in previous study 47.5%.[13]

The estimated sample size came out to be 383.

The inclusion criteria were all preterm infants of either gender was consecutively enrolled. Those who had ultrasound abnormalities other than IVH, had culture proven meningitis, or who lost to follow up were excluded.

Preterm was defined as infants born less than 37 weeks. Whereas Aneurysmal and arteriovenous malformation rupture, as well as spontaneous intracerebral haemorrhage, are the most common secondary causes of IVH, which is defined as the eruption of blood in the cerebral ventricular system.[14]

Information regarding history and examination was collected on specially designed pro forma. Ultrasound was performed by consultant radiologist at the department of neonatology, NICH. cranial ultrasound technique was undertaken, and scanning was done through the anterior fontanelle while the baby was in an incubator or cot.[15,16]

Intraventricular Hemorrhage was observed in all preterm neonates, and they were categorized according to the Papile grading. Grade I was assigned to those who had isolated germinal matrix hemorrhage, grade II to those who had less than 50% of their ventricles filled with blood and no ventricular dilatation, grade III to those who had more than 50% of their ventricles filled with blood and ventricular distension, and grade IV to those who had parenchymal haemorrhage.[17]

Ultrasound finding along with other variables like age of the infants, gestational age, birth weight, mode of delivery, date of admission, need for invasive or non-invasive mechanical ventilation was noted.

SPSS version 24 was used for the purpose of statistical analysis. Mean and standard deviation was calculated for age, birth weight at 34, 35 and 36 weeks, APGAR score at 1 min and 5 minutes. Frequency and percentages were calculated for gender, twin pregnancy, abnormal head circumference, mode of delivery, need of invasive or non-invasive mechanical ventilation, and ultrasound finding. Chi-square test was be applied to see the association of ultrasound findings with predictor variables. Whereas one-way ANOVA test was applied to see the mean score of quantitative variables among different ultrasound gradings. The p-value of ≤0.05 was taken as significant

RESULTS

Of 144 preterm neonates, the mean age of the neonates was 2.34 ±0.97 days. Most of the neonates were males compared to females, i.e., 93 (64.6%) and 51 (35.4%) respectively. The mean gestational age and birth weight were 30.71 ±2.67 weeks and 1.40 ±0.30 kg. Moreover, the weight at 34 weeks was 2.22 ±0.14 kg that increases to 2.42 ±0.14 kg at 35 weeks, and 2.67 ±0.16 kg and 36 weeks.

The mean APGAR score at 1 min was 3.41 ±1.14 whereas at 5 min was 4.45 ±1.18. Twin birth was observed in 5 (3.5%) neonates. Most of the neonates were hospitalized in ward, i.e., 114 (79.2%) whereas 30 (20.8%) were admitted in neonatal intensive care unit. SGA at birth was observed in 44 (30.6%) patients while abnormal head circumference in 7 (4.9%). The majority of the neonates had elective mode of delivery 101 (70.1%) while spontaneous delivery was observed in 43 (29.9%) neonates. Need of invasive/non-invasive ventilator was observed in 6 (4.2%) neonates.

IVH was observed in 144 (37.6%) neonates. A significant mean difference of age (p: <0.001), gestational age (p: <0.001), birth weight (p: <0.001), APGAR score at 1 min (p: <0.001), APGAR score at 5 min (p: <0.001) was observed in between IVH and non IVH neonates. Furthermore, a significant association of place of admission (p: <0.001), mode of delivery (p: 0.038), need of invasive/non-invasive ventilator (p: 0.002), and preterm status (p: <0.001) was observed with Intraventricular Hemorrhage (Table 1).

Ultrasound findings revealed that grade I was observed in almost half of the neonates, i.e., 75 (52.1%), followed by grade II in 45 (31.3%), grade III in 18 (12.5%), and grade IV in 6 (4.2%) neonates. A significant mean difference of age (p: <0.001), gestational age (p: <0.001), birth weight (p: <0.001), APGAR score at 1 min (p: <0.001), and APGAR score at 5 min (p: <0.001) was observed among four ultrasound gradings. Moreover, a significant association was also observed for twin birth (p: 0.010), place of admission (p: <0.001), SGA at birth (p: 0.008), abnormal head circumference (p: 0.006), mode of delivery (p: 0.036), need of invasive/non-invasive ventilation (p: 0.013), and preterm status (p: <0.001) (Table 2).

Stratification based on the preterm status showed that of 99 neonates with IVH who were presented with early preterm, a significant mean difference of APGAR score at 1 min (p: <0.001) and 5 min (p: <0.001) was observed with respect to different ultrasound gradings. Moreover, a significant association of ultrasound findings was observed with gender (p: 0.033), place of admission (p: <0.001), SGA at birth (p: 0.021), and mode of delivery (p: 0.008) (Table 3).

However, of 45 neonates with IVH who were presented with late preterm status, only mean APGAR score at 5 min (p: <0.001) was found significantly different among different ultrasound groups. In addition, a significant association was observed for place of admission (p: <0.001) and abnormal head circumference (p: <0.001) (Table 4).

Table 1: Comparison of Intravenous Hemorrhage with baseline and clinical characteristics of the neonates (n=383)

Intraventricular Hemorrhage					
Preterm neonates		Yes (n=144)	No (n=239)	t-value	p-value
		mean ±SD	mean ±SD		
Age, days		2.34 ±0.97	2.77 ±1.01	-4.060	<0.001
Gestational age, weeks		30.71 ±2.66	32.05 ±2.71	-4.691	<0.001
Birth Weight, kg		1.40 ±0.30	1.56 ±0.32	-4.823	<0.001
Weight at 34 weeks		2.22 ±0.14	2.22 ±0.12	-0.432	0.666
Weight at 35 weeks		2.42 ±0.14	2.41 ±0.13	0.621	0.535
Weight at 36 weeks		2.67 ±0.16	2.66 ±0.16	0.873	0.383
APGAR at 1 min		3.42 ±1.13	2.98 ±1.12	3.595	<0.001
APGAR at 5 min		4.45 ±1.17	3.91 ±1.24	4.235	<0.001
		n (%)	n (%)	p-value	
Gender	Male	93 (36.5)	162 (63.5)	0.576	
	Female	51 (39.8)	77 (60.2)		
Twin birth	Yes	5 (50.0)	5 (50.0)	0.512	
	No	139 (37.3)	234 (62.7)		
Place of admission	Ward	114 (34.9)	213 (65.1)	0.001	
	Neonatal ICU	30 (53.6)	26 (46.4)		
SGA at birth	Yes	44 (33.8)	86 (66.2)	0.316	
	No	100 (39.5)	153 (60.5)		
Abnormal head circumference	Yes	7 (29.2)	17 (70.8)	0.515	
	No	137 (38.2)	222 (61.8)		
Mode of delivery	Spontaneous	43 (46.7)	49 (53.3)	0.038	
	Elective	101 (34.7)	190 (65.3)		
Need of invasive/non-invasive ventilator (n=105)*	Yes	12 (54.5)	10 (45.5)	0.002	
	No	18 (21.7)	65 (78.3)		
Preterm Status	Early Preterm	99 (50.0)	99 (50.0)	<0.001	
	Late Preterm	45 (24.3)	140 (75.7)		

*need of invasive/non-invasive ventilator was calculated in those neonates who were admitted in neonatal ICU

DISCUSSION

The findings of the current study revealed that cranial ultrasonography has reported IVH in 37.6% of the preterm neonates. A somewhat higher frequency was reported in a previous study from Pakistan in which the IVH among premature neonates were observed in almost half, i.e., 47.5% of the premature neonates.[13] The prevalence of IVH is dependent on gestational age, according to the author. With advancing age, its gradually grows. The same finding that the frequency of IVH is negatively associated to gestational age was reached by Egwu et al in their investigation.[18] A meta-analysis revealed that 48% of IVH occurred during 0 to 6 hours of life and 38% after 24 hours of life.[15]

In the current study, a significantly higher number of neonates with IVH had early preterm and were admitted in neonatal ICU. Spontaneous mode of delivery and need of invasive/non-invasive ventilator support was also higher in these individuals. Moreover, according to the current study findings, grade I was observed in almost half of the neonates, followed by grade II, grade III, and grade IV neonates. The risk of hospitalization in neonatal ICU is significantly higher than ward admission in neonates who had III and IV grading of IVH. Moreover, need of invasive/non-invasive ventilatory support was also higher among early preterm neonates who had III and IV grading of IVH. In his study, Linder N. discovered an inverse relationship between gestational age and birth weight and the likelihood of IVH. According to published research, preterm babies with extremely low birth weights had a greater risk of grade III and grade IV haemorrhage.[19]

Neonates with IVH who were presented with early preterm in the current study had a significant mean difference of APGAR score at 1 min and 5 min with respect to different ultrasound gradings. Moreover, a significant association of ultrasound findings was observed with gender, place of admission, SGA at birth, and mode of delivery. However, neonates with IVH who were presented with

Table 2: Comparison of ultrasound grading with baseline and clinical characteristics of preterm neonates with IVH (n=144)

Ultrasound Grading							
Preterm Neonates		Ultrasound Grading				F-Value	p-value
		I (n=75)	II (n=45)	III (n=18)	IV (n=6)		
		mean ±SD	mean ±SD	mean ±SD	mean ±SD		
Age, days		2.60 ±1.09	1.89 ±0.74	2.22 ±0.43	3.01 ±0.63	6.782	<0.001
Gestational age, weeks		31.53 ±2.81	29.13 ±2.04	30.56 ±1.72	32.83 ±1.33	10.730	<0.001
Birth Weight, kg		1.47 ±0.33	1.25 ±0.23	1.44 ±0.18	1.63 ±0.15	7.355	<0.001
Weight at 34 weeks		2.22 ±0.14	2.21 ±0.14	2.21 ±0.14	2.22 ±0.07	0.011	0.998
Weight at 35 weeks		2.42 ±0.14	2.41 ±0.13	2.42 ±0.15	2.35 ±0.05	0.567	0.638
Weight at 36 weeks		2.68 ±0.16	2.67 ±0.16	2.69 ±0.17	2.60 ±0.18	0.543	0.654
APGAR at 1 min		3.21 ±1.15	4.26 ±0.72	2.55 ±0.51	2.16 ±0.40	21.492	<0.001
APGAR at 5 min		4.28 ±1.08	5.31 ±0.76	3.77 ±0.73	2.17 ±0.41	25.504	<0.001
		n (%)	n (%)	n (%)	n (%)	p-value	
Gender	Male	42 (45.2)	36 (38.7)	11 (11.8)	4 (4.3)	0.066	
	Female	33 (64.7)	9 (17.6)	7 (13.7)	2 (3.9)		
Twin birth	Yes	0 (0)	5 (100)	0 (0)	0 (0)	0.010	
	No	75 (54.0)	40 (28.8)	18 (12.9)	6 (4.3)		
Place of admission	Ward	75 (65.8)	39 (34.2)	0 (0)	0 (0)	<0.001	
	Neonatal ICU	0 (0)	6 (20.0)	18 (60.0)	6 (20.0)		
SGA at birth	Yes	16 (36.4)	21 (47.7)	7 (15.9)	0 (0)	0.008	
	No	59 (59.0)	24 (24.0)	11 (11.0)	6 (6.0)		
Abnormal head circumference	Yes	2 (28.6)	3 (42.9)	0 (0)	2 (28.6)	0.006	
	No	73 (53.3)	42 (30.7)	18 (13.1)	4 (2.9)		
Mode of delivery	Spontaneous	29 (67.4)	12 (27.9)	1 (2.3)	1 (2.3)	0.036	
	Elective	46 (45.5)	33 (32.7)	17 (16.8)	5 (5.0)		
Need of invasive/ non-invasive ventilator*	Yes	0 (0)	0 (0)	7 (58.3)	5 (41.7)	0.013	
	No	0 (0)	6 (33.3)	11 (61.1)	1 (5.6)		
Preterm Status	Early Preterm	39 (39.4)	44 (44.4)	14 (14.1)	2 (2.0)	<0.001	
	Late Preterm	36 (80.0)	1 (2.2)	4 (8.9)	4 (8.9)		

*need of invasive/non-invasive ventilator was calculated in those neonates who were admitted in neonatal ICU

late preterm status, only mean APGAR score at 5 min was found significantly different among different ultrasound groups. In addition, a significant association was observed for place of admission and abnormal head circumference.

The study is of importance as it has reported the prevalence of IVH from a large cohort of preterm neonates who were suspected to have IVH. This study has reported findings from a large public sector children hospital of metropolitan city Karachi which is facilitating not only the children living in Karachi but children from other part of Sindh and Baluchistan as well. As morbidity and mortality in preterm infants due to IVH are increasing, there is dire need to diagnose the disease in its early state. In our part of world, due to limited availability of health-care resources and financial constraints, a cost-effective and easily available diagnostic modality for the determination of disease like IVH is of utmost importance. As ultrasound is undoubtedly a cost-effective and readily available diagnostic modality which is also recommended in various literature and in the current study too for diagnosis of IVH in preterm. However, dearth of literature on this topic is highlighting the need of further studies on this topic to get the deepest insight of the problem. The study has certain limitations such as important maternal characteristics such as presence of any comorbidities, prepartum hemorrhage, antenatal antibiotics or steroids and neonatal characteristics such as cord pH, base deficit, and other medical condition like occurrence of sepsis, meningitis or chorioamnionitis are not reported in the current study.

CONCLUSION

A significantly higher number of preterm neonates experienced intraventricular hemorrhage (IVH) in this particular cohort. Furthermore, while grade I was the most prevalent, a greater severity of IVH (grades

Table 3: Comparison of ultrasound grading with baseline and clinical characteristics of early preterm neonates with IVH (n=99)

Ultrasound Grading							
Early Preterm Neonates		I (n=39)	II (n=44)	III (n=14)	IV (n=2)	F-Value	p-value
		mean ±SD	mean ±SD	mean ±SD	mean ±SD		
Age, days		1.82 ±0.68	1.86 ±0.73	2.01 ±0.01	2.50 ±0.71	0.856	0.467
Gestational age, weeks		29.25 ±1.80	29.02 ±1.92	29.71 ±0.61	31.50 ±0.71	1.695	0.173
Birth Weight, kg		1.21 ±0.23	1.23 ±0.22	1.35 ±0.05	1.50 ±0.01	2.593	0.057
Weight at 34 weeks		2.22 ±0.14	2.21 ±0.14	2.21 ±0.15	2.25 ±0.07	0.043	0.988
Weight at 35 weeks		2.43 ±0.13	2.41 ±0.14	2.44 ±0.17	2.35 ±0.07	0.358	0.783
Weight at 36 weeks		2.71 ±0.16	2.66 ±0.16	2.70 ±0.19	2.60 ±0.14	0.662	0.578
APGAR at 1 min		3.10 ±1.07	4.25 ±0.72	2.50 ±0.52	2.50 ±0.70	21.260	<0.001
APGAR at 5 min		4.23 ±1.20	5.32 ±0.77	4.01 ±0.68	2.50 ±0.71	15.168	<0.001
		n (%)	n (%)	n (%)	n (%)	p-value	
Gender	Male	21 (32.3)	35 (53.8)	7 (10.8)	2 (3.1)	0.033	
	Female	18 (52.9)	9 (26.5)	7 (20.6)	0 (0)		
Twin birth	Yes	0 (0)	5 (100)	0 (0)	0 (0)	0.086	
	No	39 (41.5)	39 (41.5)	14 (14.9)	2 (2.1)		
Place of admission	Ward	39 (50.6)	38 (49.4)	0 (0)	0 (0)	<0.001	
	Neonatal ICU	0 (0)	6 (27.3)	14 (63.6)	2 (9.1)		
SGA at birth	Yes	6 (19.4)	20 (64.5)	5 (16.1)	0 (0)	0.021	
	No	33 (48.5)	24 (35.3)	9 (13.2)	2 (2.9)		
Abnormal head circumference	Yes	2 (40.0)	3 (60.0)	0 (0)	0 (0)	0.768	
	No	37 (39.4)	41 (43.6)	14 (14.9)	2 (2.1)		
Mode of delivery	Spontaneous	20 (60.6)	12 (36.4)	1 (3.0)	0 (0)	0.008	
	Elective	19 (28.8)	32 (48.5)	13 (19.7)	2 (3.0)		
Need of invasive/ non-invasive ventilator*	Yes	0 (0)	0 (0)	4 (80.0)	1 (20.0)	0.236	
	No	0 (0)	6 (35.3)	10 (58.8)	1 (5.9)		

*need of invasive/non-invasive ventilator was calculated in those neonates who were admitted in neonatal ICU

III and IV) was observed in a majority of the preterm neonates. Among these neonates, those who were born extremely early faced a heightened risk of spontaneous delivery and demonstrated a higher need for invasive or non-invasive ventilator support.

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Table 4: Comparison of ultrasound grading with baseline and clinical characteristics of late preterm neonates with IVH (n=45)

Ultrasound Grading							
Late Preterm Neonates		I (n=36)	II (n=1)	III (n=4)	IV (n=4)	F-Value	p-value
		mean ±SD	mean ±SD	mean ±SD	mean ±SD		
Age, days		3.44 ±0.77	3.01 ±0.0	3.01 ±0.01	3.25 ±0.50	0.593	0.623
Gestational age, weeks		34.01 ±1.06	34.00 ±0.0	33.50 ±0.58	33.50 ±1.01	0.511	0.677
Birth Weight, kg		1.75 ±0.14	1.80 ±0.0	1.75 ±0.05	1.70 ±0.14	0.207	0.891
Weight at 34 weeks		2.21 ±0.14	2.30 ±0.00	2.20 ±0.08	2.20 ±0.08	0.149	0.93
Weight at 35 weeks		2.42 ±0.15	2.30 ±0.00	2.35 ±0.06	2.35 ±0.06	0.688	0.564
Weight at 36 weeks		2.65 ±0.17	2.90 ±0.00	2.68 ±0.15	2.60 ±0.22	0.838	0.481
APGAR at 1 min		3.33 ±1.24	2.75 ±0.50	2.01 ±0.00	3.20 ±1.22	2.609	0.064
APGAR at 5 min		4.33 ±0.95	5.00 ±0.00	3.00 ±0.01	2.00 ±0.01	10.668	<0.001
Gender	Male	21 (75.0)	1 (3.6)	4 (14.3)	2 (7.1)	0.318	
	Female	15 (88.2)	0 (0)	0 (0)	2 (11.8)		
Twin birth	Yes	0 (0)	0 (0)	0 (0)	0 (0)	-	
	No	36 (80.0)	1 (2.2)	4 (8.9)	4 (8.9)		
Place of admission	Ward	36 (97.3)	1 (2.7)	0 (0)	0 (0)	<0.001	
	Neonatal ICU	0 (0)	0 (0)	4 (50.0)	4 (50.0)		
SGA at birth	Yes	10 (76.9)	1 (7.7)	2 (15.4)	0 (0)	0.174	
	No	26 (81.3)	0 (0)	2 (6.3)	4 (12.5)		
Abnormal head circumference	Yes	0 (0)	0 (0)	0 (0)	2 (100)	<0.001	
	No	36 (83.7)	1 (2.3)	4 (9.3)	2 (4.7)		
Mode of delivery	Spontaneous	9 (90.0)	0 (0)	0 (0)	1 (10.0)	0.658	
	Elective	27 (77.1)	1 (2.9)	4 (11.4)	3 (8.6)		
Need of invasive/ non-invasive ventilator	Yes	0 (0)	0 (0)	3 (42.9)	4 (57.1)	>0.999	
	No	0 (0)	0 (0)	1 (100)	0 (0)		

*need of invasive/non-invasive ventilator was calculated in those neonates who were admitted in neonatal ICU

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Author's Contribution

DK conceived the idea, collected the data and write up of the manuscript. MS performed and contributed in data analysis and write up of the manuscript. MK, and MH helped in collection of data and write up of the manuscript. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.