Risk Factors for Germinal Matrix Haemorrhage-Intraventricular Haemorrhage in Very Low Birth Weight Infants

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Abstract- Germinal matrix hemorrhage-intraventricular hemorrhage (GMH-IVH) mainly occurs in preterm neonates and is an important cause of brain injury in them. In this retrospective cross-sectional study from march 2017 to march 2018 in our teaching hospitals, we investigated 250 newborns who were admitted to NICU with a birth weight under 1500 grams with ultrasonographic study for presence and grade of GMH-IVH in their first week of life. Risk factors for GMH-IVH were collected from their records and results been analyzed with SPSS software. From 250 neonates who had inclusion criteria of the study, 22 cases had GMH-IVH in ultrasonographic evaluation. 37.6% of all cases and 31.8% of newborns with GMH-IVH had a 5-minute APGAR score of less than six. 91 cases (39.9%) of the control group and 15 cases (68.1%) of the GMH-IVH group need resuscitation at birth. Of 250 cases 54 (21.6%) died, that 14 cases (63.6%) had GMH-IVH. Our study shows significant differences for birth weight, 5 minute APGAR score, and the need for resuscitation at birth as risk factors for the development of GMH-IVH in very low birth weight neonates, but we do not find a significant difference group in terms of gestational age, gender, route of delivery, fetal presentation, maternal parity, CBC parameters, sepsis, RDS, endotracheal tube suctioning and multiple pregnancies for them. In our study, the protective value for antenatal steroid therapy depends on the completion of the course of treatment for mothers.

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Introduction

Germinal matrix hemorrhage-intraventricular hemorrhage (GMH-IVH) mainly occurs in preterm neonates and is an important cause of brain injury in them. The negative impact of GMH-IVH on neurodevelopmental outcomes has caused concern (1).

Several risk factors have been proposed for developing GMH-IVH, such as prematurity, gender, low for gestational age, breech presentation, premature rupture of membranes, mode of delivery, sepsis, transport of infant, respiratory distress syndrome, recurrent endotracheal suctioning, pneumothorax, mechanical ventilation, metabolic acidosis, and rapid bicarbonate infusion. On the other hand, several conditions and pharmacological interventions have been reported to reduce the development of GMH-IVH, such as maternal pregnancy-induced hypertension, antenatal steroids, prenatal tocolytic, and postnatal surfactant and indomethacin therapy. However, there are many differences between the results of these studies, both in terms of the possibility and importance of these factors as important risk factors for GMH-IVH (2-6).

There are some contradictions in the fields of prenatal, intrapartum, and neonatal risk factors of GMH-IVH.

Determination of precise risk factors of GMH-IVH in lbw newborns will help clinicians to reduce the incidence of it, especially in this vulnerable group of patients.

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In this study, we investigate some of these risk factors for GMH- GMH-IVH in very low birth weight premature infants in our teaching hospital.

Materials and Methods

This study was conducted in Alieneabitaleb teaching hospital affiliated with Zahedan University of Medical Sciences.

In this cross-sectional study from march 2017 to march 2018, we investigate 250 newborns who were admitted to the NICU ward with a birth weight under 1500 grams and did not have congenital anomalies, central nervous system infection, and inborn errors of metabolism in their first week of life with ultrasonographic study for presence and grade if GMH-IVH. All sonographic studies were done by the same radiologist.

Other parameters include gestational age, neonatal sex, APGAR score, birth weight, mode of delivery and fetal presentation, neonatal sepsis (positive microbiological growth on bloodstream), respiratory distress syndrome (diagnosed in infants who need invasive or noninvasive respiratory support and have radiographic evidence of respiratory distress syndrome), mechanical ventilation and number of suctioning of the endotracheal tube and prenatal corticosteroid treatment collected using a checklist

The extracted data were analyzed using SPSS software package version 18.

Statistical significance was defined as $P \leq 0.05$.

Ethical clearance was obtained from the ethics committee of Zahedan University of Medical Sciences.

Results

From 250 neonates who had inclusion criteria of the study, 22 cases (8.8%) had GMH-IVH in their ultrasonographic evaluation.

In our 250 very low birth weight cases, 142 were male, and 108 were female. Their mean gestational age was 29.19 (±2.71) weeks, and their mean birth weight was 1146.76 (±295.64) grams.

Patients' characteristics of case and control groups are summarized in Table 1.

Table 1. Patients' characteristics

		IVH group	Control group	*P*
N		22	228	-
sex		10F:12M	98F:130M	0.823
Gestational age mean (SD)		29.81 (2.34)	29.13 (2.74)	0.274
Mode of delivery	**NVD**	16	137	0.36
	C/S	6	91	
Birth weight Mean (SD)		1054.09 (193.30)	1155.70 (302.50)	0.013
Number of deliveries	**1**	2	40	0.078
	2	4	55	
	3	3	56	
	4	3	35	
	5	4	23	
	6	3	12	
	More than 6	3	7	
CBC analysis	**WBC count Mean (SD)**	9759.09 (3947.1)	10015.96 (4424.71)	0.793
	Hb level Mean (SD)	12.24 (3.35)	13.43 (3.38)	0.106
	Plt count Mean (SD)	296181.81 (154602.6)	252228.07 (129176.96)	0.136
Fetal presentation	**cephalic**	13	93	0.437
	breech	2	27	
	other	7	108	
	Need to resuscitate at birth	15	91	0.01
	Have neonatal sepsis	8	87	0.868
	Have RDS	11	121	0.783
	endotracheal suctioning during intubation	12	111	0.599
	Received prenatal corticosteroid therapy	10	109	0.833
	Received one dose of bethamethasone	10	12	<0.001
	Mortality rate	14	40	<0.001
multiple pregnancy	**Single ton**	22	224	0.531
	twin	0	4	

From 119 patients whose mothers had received prenatal corticosteroid therapy, 10 cases developed GMH-IVH. 97 cases (81.5%) had received the full course of two doses of betamethasone 24 hours apart, and 22 cases (18.5%) only had received one dose of betamethasone less than 24 hours before delivery. The mothers of all 10 cases who developed GMH-IVH were in the latter group (had received an incomplete course of antenatal corticosteroid) (P<0.001).

37.6% of all neonates and 31.8% of newborns with GMH-IVH had 5 minute APGAR score of less than six that was statistically significant (P<0.001). 5 minute APGAR scores of the cases are summarized in Table 2.

From 250 cases 54 (21.6%) died, 14 cases (63.6%) had GMH-IVH. The prevalence of mortality in different grades of GMH-IVH has summarized in Table 3.

Table 2. Five minutes APGAR scores

5 minute APGAR score	3	4	5	6	7	8	9	total
IVH group	4	5	7	3	3	0	0	22
Control group	2	16	55	91	40	11	13	228

Table 3. Mortality in deferent grades of GMH-IVH

GMH-IVH grade	**Without IVH**	**1**	**2**	**3**	**4**
Expired	40	0	4	8	2
Alive	188	3	4	1	0
Total	228	3	8	9	2

Discussion

In our study, 250 very low birth weight neonates were investigated for GMH-IVH by ultrasonographic study. 22 cases had different grades of GMH-IVH, and others were considered as the control group.

According to several studies, antenatal corticosteroid therapy is the most important protective factor against developing GMH-IVH (7). As some previous studies (8) our study shows, this protective value for antenatal steroid therapy depends on the number of steroid doses received by the mother. In our study, protective effect for antenatal corticosteroid therapy was not observed in infants whose mothers did not receive the full course of treatment and mothers of all cases of GMH-IVH group had not received a complete course of antenatal corticosteroid treatment, while 12 cases in the control group were treated incompletely (P<0.001).

Also, previous studies have shown that the male gender can be associated with a higher incidence of GMH-IVH in neonates (9,10); this study fails to corroborate it.

The importance of the route of delivery and fetal presentation in the incidence of GMH-IVH is still uncertain (11). We did not find a statistically significant difference between cesarean section and vaginal deliveries or breech and cephalic presentation in our study, which is compatible with Herbst *et al.,* study (12) but incompatible with some population-based studies which have been done in this filed (13).

The role of respiratory distress syndrome, either a casual risk factor or due to its complications, especially during mechanical ventilation, has been recognized in some studies (14,15). We did not see this importance, perhaps due to the increased use of noninvasive continuous positive airway pressure therapy in our ward.

Due to previous studies, the risk of GMH-IVH and its severity increases with decreasing both GA and BW (16-18). In our study, Although lower birth weight was significantly associated with GMH-IVH (P=0.013), the gestational age of case and control groups was not significantly different (P=0.274) that would indicate the importance of birth weight, especially in small for gestational age newborns. Further case-control studies to omit confounding factors in this field seem necessary.

The need for Cardiopulmonary resuscitation (CPR) in the delivery room and low APGAR score, which have been shown as risk factors to increase GMH-IVH (19,20), were also significant risk factors in our study.

Also, singleton pregnancy (20) and early-onset neonatal sepsis (8), which have been mentioned in some studies as risk factors associated with GMH-IVH, were not significant risk factors in our patients.

The unimportance of maternal parity was as in previous studies (8).

In our study, the mean white blood cells count, and hemoglobin level was lower, and the mean platelet count was higher in the GMH-IVH group than the control group but, like previous studies (8), had no statistical significance.

Suctioning of the endotracheal tube by means of increasing intracranial pressure has been reported to increase developing GMH-IVH. Also, some studies even have shown an inverse relationship between the number of suctioning and incidence of GMH-IVH in very low birth weight newborns (8). Anyway, we do not find any significant role for the number of endotracheal tubes suctioning. Additional researches with controlling confounders seem necessary.

As the findings of previous studies (21), there was also a significant correlation between GMH-IVH presence and grade with the mortality rate of our patients.

From several risk factors which have been proposed as a risk factor for GMH-IVH, in our case-control prospective study, significant differences were shown for birth weight, 5-minute APGAR score, and the need for resuscitation at birth.

Our study shows the protective value for antenatal steroid therapy depends on the number of steroid doses received by the mother.

There was also a statistically significant correlation between GMH-IVH presence and grade with the mortality rate of these infants.

There was no statistical difference between the GMH-IVH group and control group in terms of gestational age, gender, route of delivery, fetal presentation, maternal parity, CBC parameters, sepsis, RDS, endotracheal tube suctioning, and multiple pregnancies.

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