

## *Factors Associated With Intraventricular Hemorrhage in Very Low Birth Weight Neonates in Mousavi Hospital in Zanjan in 2012-2013*

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### **Abstract**

**Background:** Intraventricular hemorrhage (IVH) is one of the most important causes of cognitive and motor disorder in children with very low birth weight and is associated with high mortality and disability rate.

**Objectives:** The aim of this study was to determine IVH risk factors in the first days of life in neonates weighing less than 1500g (VLBW) so that the results can contribute to the improvement of the therapeutic function of the delivery room and ultimately IVH risk prevention.

**Methods:** This descriptive study was conducted on 110 VLBW neonates who were admitted to the hospital affiliated to Zanjan University of Medical Sciences during the years 2012-2013 Zanjan-Iran. Parameters including gender, birth weight, birth Apgar, regimens, and type of delivery were recorded in the questionnaire and data analysis was conducted using Chi-square test in SPSS.

**Results:** From 110 studied neonates, 21(19%) had IVH, of which 11(52%), 5(23.8%) and 5(23.8%) suffered from Grade I, II and III IVH, respectively. Meanwhile, among the studied variables, recovery steps were taken in the delivery room in the IVH group. The cranial ultrasonography was carried out for these neonates in the first 72 h of birth and they were categorized as Grade one to four, based on evidence of brain hemorrhage. There was a significant difference between maternity and infant information and without IVH; but it was not statistically significant.

**Conclusion:** According to the present study, the recovery process seemed to be a risk factor for the incidence of IVH in neonates; therefore, the health level of neonates can be improved by optimizing the mentioned process and reducing this risk factor.

**Key words:** *Intraventricular hemorrhage, very low birth weight, recovery steps, APGAR, Znan, Iran*

### **Introduction**

Intraventricular hemorrhage (IVH) is one of the major causes of cognitive and motor disorders in children with very low birth weight (VLBW) and can be associated with high rates of mortality and disability [1]. This hemorrhage occurs in the germline matrix of premature neonates and

immature blood vessels and weak tissue support from the vessels make them highly susceptible to hemorrhage. High-grade IVH can lead to cerebral palsy and neurodevelopmental-functional and neurological complications in neonates [2-4]. The overall incidence of IVH has reduced in recent decades, due to the development of prenatal care

and the use of corticosteroids, however, the hemorrhage occurs in about 25-30% of neonates under 1500g [5]. The risk factors for IVH development include low birth weight, gestational age, low Apgar score, intubation and post-partum recovery, vaginal delivery, acidosis, infection, premature rupture of amniotic membrane, respiratory distress syndrome, pneumothorax, maternal anticoagulation drug use and maternal coagulation, endotracheal continuous suction and mechanical ventilation [6,7]. IVH severity is divided into four grades on the basis of ultrasound, [4,8,9].

Grade I: Hemorrhage is limited to the germinal matrix or less than 10% of the ventricles

Grade II: IVH is accompanied by 10 to 50% ventricular filling.

Grade III: More than 50% IVH is associated with ventricular dilatation.

Grade IV: IVH is evaluable based on CT scan, and hemorrhage is accompanied by parenchymal involvement in the brain. Given that the clinical symptoms of IVH are non-specific or there exists no clinical symptoms at all, it is recommended that neonates with a gestational age of less than 34 weeks be routinely screened by cranial ultrasonography through anterior fontanelle [4]. This issue occurs most often in the first 3 days of life and 7 days after birth in more than 90% of cases. Identification and grading of IVH in neonates and subsequent therapeutic measures are effective on the outcome and health status of the patients. Therefore, considering that IVH is one of the most important factors in the development of neurodevelopmental disabilities in premature neonates, and because the quality of services varies from time to time and from center to center, no study has been carried out on the frequency and severity of intracerebral hemorrhage in neonates, this research was conducted in Zanjan in 2012-2013.

### Methods

This descriptive-analytical study was carried out in the neonatal intensive care unit (NICU) in Zanjan. All neonates weighing less than 1500 grams who were born in this center during the years 2012-2013 were studied. The convenient

sampling method was also employed and neonates were serially entered into the study. Nevertheless, there were also no confounding factors, such as very bad conditions, and even infant death, due to which they were not enrolled in the study. All neonates were examined by an ultrasound sonographer using a Siemens G55 and 10-5 L probes during the second and third day of birth for IVH and cranial ultrasound. The following variables were then recorded in the pre-set data collection form. The variables included: birth weight, newborn's gender, 5-min Apgar score, recovery steps in the delivery room, delivery method (vaginal delivery or cesarean delivery). Inclusion criteria included all neonates weighing less than 1500 g. Exclusion criteria included neonates who died prior to any action (ultrasound), and those who were discharged to other centers with parental consent, neonates with significant CNS anomalies, neonates with positive family history in terms of hemorrhagic diseases, such as hemophilia, neonates whose mothers took medication at the end of pregnancy, neonates whose sepsis was confirmed using positive blood culture. Data analysis was carried out using chi-square test in SPSS. Given that parents' consent was obtained at the time of admission and cerebral hemorrhage screening is one of the most important issues for neonatal care, and the treatment steps and related complications were fully explained to the parents by the physician, there was no ethical restrictions. Data were later analyzed using frequency distribution tables, central indicators and dispersion and Chi-square test in SPSS.

### Results

Of the 110 studied neonates, 21 (19%) had IVH, of which 11(52%), 5(23.8%) and 5(23.8%) suffered from Grade I, II and III IVH, respectively. Twenty neonates weighed less than 1000 grams, of which 30% suffered from brain hemorrhage, while 16.6% of neonates weighing between 1.000 and 1.500 g had brain hemorrhage (Table 1). The mean weight of brain hemorrhage and non-hemorrhage groups was  $1128\pm195$  g and  $1260\pm160$  g, respectively. This difference was not statistically significant ( $P=0.45$ ).

*Table 1: Distribution of IVH relative frequency based on birth weight*

Birth weight in grams	IVH positive	IVH negative	Total
Less than 1000	6(30%)	14(70%)	20(100%)
1500 - 1000	15(16.6%)	75(83.4%)	90(100%)
<b>Total</b>	21(19%)	89(81%)	110(100%)

According to Table 2, the results of the present study regarding the severity of brain hemorrhage indicate that the number of Grade I,II,III brain

hemorrhage cases is 11 (52%), 5 (23.8%), and 5 people (23.8%), respectively.

*Table 2: Frequency distribution of IVH severity (grade) based on birth weight in neonates*

	Grade (severity IVH)			Total
	Grade I	Grade II	Grade III	
Less than 1000	1(16.7%)	2(33.3%)	3(50.0%)	6(100%)
1500 - 1000	10(66.7%)	3(20.0%)	2(13.3%)	15(100%)
<b>Total</b>	11(52.4%)	5(23.8%)	5(23.8%)	21(100%)

As shown in Table 3, the results of the present study on the frequency of brain hemorrhage showed that there were 7 (33.3%) girls among IVH neonates, while non-IVH girl neonates accounted for 47.1% of neonates and that was not statistically significant ( $P=0.39$ ). With regard to the IVH-group, 11 neonates (52.4%) were born with vaginal delivery, while in the non-IVH group, 31 neonates (34.8%) were born using vaginal delivery, which was not statistically significant. A total of 42.9 and 22.4% of IVH and non-IVH neonates had Apgar score less than 7,

respectively and this difference was not statistically significant ( $P=0.18$ ). Among IVH and non-IVH neonates, 100 and 77.5% were recovered in the delivery room, respectively, which was not statistically significant ( $P=0.61$ ). A total of 61.9% of IVH neonates and 31.4% of IVH-free neonates underwent advanced recovery (recovery with ambu bag or with chest compression or drug use), which was not statistically significant except for significant differences ( $P=0.24$ ).

*Table 3: Frequency distribution of neonatal IVH based on studied variables*

Studied variable	IVH positive	IVH negative	Total	
	<b>Infant gender</b>			
	female	7(33.3%)	42(47.1%)	49(44.5%)
	male	14(66.7%)	47(52.8%)	61(55.5%)
<b>Type of delivery</b>				
	Normal	11(52.4%)	31(34.8%)	42(38.2%)
	Cesarean section	10(47.6%)	58(65.2%)	68(61.8%)
<b>Apgar 5 minutes</b>				
	Below 7	9(42.9%)	20(22.4%)	29(26.4%)
	Above 7	12(57.1%)	69(77.5%)	81(73.6%)
<b>Recovery from birth</b>				
	Done	21(100%)	69(77.5%)	90(81.8%)
	It's not done	0(0%)	20(22.4%)	20(18.2%)
	Initial Recovery	8(38.1%)	61(68.5%)	69(62.7%)
<b>Recovery steps</b>				
	Recovery with ambu bag	7(33.3%)	23(25.8%)	30(27.3%)
	Squeezing chest or taking medication	6(28.6%)	5(5.6%)	11(10.0%)

## Discussion

One of the most common outcomes among premature neonates is IVH, which is caused by a number of prenatal and postpartum factors, including the fact that the quality of therapeutic measures for the recovery and rehabilitation of a newborn in the first days of life can contribute to the possibility of brain damage. IVH can be diagnosed by cranial ultrasound [10,11]. The aim of this study was to determine the relative frequency of IVH in neonates with birth weights of less than 1500 g and some of the factors affecting IVH, including recovery and stabilization of premature neonates. In this study, the relative frequency of IVH in neonates less than 1500 g was 19%. Of these, 11(52%), 5(23.8%) and 5(23.8%) suffered from Grade I, II and III IVH, respectively. The result of this study was similar to the findings of the study conducted by Badiiee in Isfahan (2007). They showed that IVH prevalence was 25% in neonates weighing less than 1500 g [12]. In another study by Khodapanahandeh et al (2007) at the NICU Akbarabadi Center in Tehran, the IVH prevalence was 64.4% in 57 neonates, of which 40, 11, 25.7, 8.8% were Grade I,II,III and IV, respectively [3]. However, due to limitations faced by patients in our study, we did not perform brain CT scans on the first days, so Grade IV IVH was not considered [3]. Also in Turkey, Koksall et al. (2002) conducted another study on 120 neonates less than 1500 g and results showed that the prevalence of IVH was 15% in these neonates, of which 50, 17, 11 and 22% were Grade I, II, III and IV, respectively. Also, 78% of cases were identified on the first days of birth [5], which is in line with the present study in terms of frequency and severity of hemorrhage. A previous study in London between 1979 and 1981 showed that 50% of neonates born at or below 30-week gestational age suffered from IVH, while 23% of neonates born at gestational age between 31 and 34 weeks had the same problem. This suggests that the more a child is premature, the more likely it is to develop IVH, which is maybe attributed to the fragility of the cerebral vessels in these neonates. In the present study, 30% of neonates who weighed less than 1000 g had IVH, 50% of which were severe and Grade III IVH. This finding is

consistent with the results of the study of Koksall who reported the IVH prevalence rate of 56% in neonates weighting less than 1000 g [5]. In the present study, female and male neonates accounted for 49 and 61 neonates of the population, respectively. Girls accounted for 33% of IVH cases and the rest were boys. Although the hemorrhage rate was higher in boys, it was not statistically significant, and there was no significant difference between male and female genders in a study conducted in Kashan [14]. In the present study, 38.1 and 61.8% of IVH cases were born using normal and cesarean section delivery, respectively. The results obtained were similar to the findings obtained in the study conducted in Kashan [14] which is similar to our study, and there was no significant difference between the incidence of intracerebral hemorrhage and the delivery method, which could be due to low number of IVH cases. Moreover, in our study, Apgar score of less than 7 at 5 min after birth was higher in the IVH group compared with the non-IVH group 42.8% compared with 22.4% in the non-IVH group; but it was not statistically significant and this could refer to the role of Apgar score at 5 min after birth in increasing the prevalence of IVH. Also, in their study, which was consistent with the results of our study, Koksall et al. showed that the mean of 5 min Apgar score in the IVH and non-IVH groups was  $2\pm 5$  and  $7\pm 3$ , respectively suggesting that the lower Apgar score is associated with increased risk of IVH [5]. The present study showed that there was a significant relationship between recovery steps in the delivery room and IVH, but not statistically significant. Of the 110 neonates, recovery was not performed for 81.8% and 18.2% had not been recovered. This recovery included initial recovery (recovery with ambu bag and advanced recovery (by compression of the chest or use of medication). The recovery rate in the IVH group was higher than that of non-IVH group (100% vs. 77.5%). Of the neonates who were recovered, 7 (33.3%) underwent recovery with positive pressure with ambu bag and 6 (28.5%) underwent advanced recovery with chest massage. In other words, 61.9% of neonates in the first few minutes of life underwent serious pulmonary heart disease. In a study by Deulofeuta et al. (2007) in

Atlanta [15], 13% of patients underwent recovery using chest compression or drug use, which is in line with our study. Also, in this study, 37 and 12% of recovered and non-recovered subjects suffered from severe hemorrhage; however, our study showed that Grade 1 IVH occurred in even the most advanced hemorrhage (52%). Another study by Finer et al. (1999) in Oxford on 2212 neonates weighing between 500 and 1500 g, revealed that the prevalence of hemorrhage with any grade in those undergoing advanced recovery was greater than those who underwent no recovery [16]. Our study showed that 19% of the neonates had cerebral hemorrhage. The birth recovery rate was higher in the IVH group in comparison with the non-IVH group; therefore, according to the present study, the neonatal recovery process has been identified as a risk factor for the occurrence of IVH and emphasizes the need for a more standardized recovery in the delivery room and experienced recovery team with up-to-date knowledge and skills. Therefore, the infant's health status, prevention of disability and future disabilities can be improved by optimizing the above process.

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**Conflict of interest:** It should be noted that there is no conflict of interest in this article.

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#### References

1. Martins L, Borges MJ, Gomes SM, et al. Intraventricular hemorrhage risk factors in very low birth weight newborns. *Einstein*. 2009; 7(3 Pt 1): 279-83.
2. Sajjadi N, Fakhrai H, Jahadi R. Incidence of intraventricular hemorrhage and post hemorrhagic

hydrocephalus in preterm infants. *Acta Med Iran*. 2010; 48(4): 260-62.

3. Khodapanahandeh F, Khosravi N, Larijani T. Risk factors for intraventricular hemorrhage in very low birth weight infants. *Iran J Ped*. 2007; 17(2), 101-107.

4. Adams-Chapman I, Stoll BJ. The fetus and the neonatal infant: Nervous system disorders. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, eds. *Nelson Textbook of Pediatrics*. 18<sup>th</sup>ed. Philadelphia: WB Saunders; 2016: 715-717.

5. Köksal N, Baytan B, Bayram Y, Nacarküçük E. Risk factors for intraventricular hemorrhage in very low birth weight infants. *Indian J Pediatr*. 2002; 69(7): 561-64.

6. Lee JY, Kim HS, Jung E, et al. Risk Factors for Periventricular-Intraventricular Hemorrhage in premature infants. *J Korean Med Sci*. 2010; 25(3): 418-24.

7. Linder N, Haskin O, Levit O. Risk Factors for Intraventricular Hemorrhage in Very Low Birth Weight premature infants. *Pediatrics*. 2003; 111(5): 590-95.

8. Kadri H, Mawla AA, Kazah J. The incidence, timing, and predisposing factors of germinal matrix and intraventricular hemorrhage (GMH/IVH) in preterm neonates. *Childs Nerv Syst*. 2006; 22(9): 1086-1090.

9. Patra K, Wilson-Costello D, Gerry Taylor H, Mercuri N, Hack M. Grades I-II intraventricular hemorrhage in extremely low birth weight infants: Effects on neurodevelopment. *J Peds*. 2006; 149(2): 169-73.

10. Martin RJ, Fanaroff AA, Walsh MC. Fanaroff and Martin's Neonatal-Perinatal Medicine: Diseases of the Fetus and Infant. 10<sup>th</sup> ed. United States: Elsevier Health Sciences; 2015: 887-88.

11. Kattwinkel, J. Neonatal Resuscitation Program (NRP Textbook). Jannatdoost A, Habibollahi A, Heidarzadeh M, Shahhoseini P, Sadeghnia AR, Mirnia k. (Persian translator), 6<sup>th</sup>ed, Tehran: Idehpardazan; 2011: 268. [In Persian]

12. Badie Z, Prevalence and Risk Factors of Intraventricular Hemorrhage in Premature Newborns less than 35 Weeks in Neonatal Intensive Care Units of Isfahan. *J Isfahan univ Medi sci*. 2007; 24(83): 15-23. [In Persian]

13. Levene M, Fawer CL, Lamont RF. Risk factors in the development of intraventricular haemorrhage in the preterm neonate. *Arch Dis Child*. 1982; 57: 410-17.

14. Mosayebi Z, Movahedian AH, Khezri M. Incidence and risk factors of intrventricula haemorrhage in preterm neonatal in Kashan hospitals in 1996-2000. *Feyz*. 2002; 23(81): 63-68. [In Persian].

15. Deulofeuta A, SolaabB, Leeab M. Delivery room cardiopulmonary resuscitation of the very preterm infant is associated with adverse short and long term outcomes. *An Pediatr (Barc)*. 2007; 66(1): 31-37.

16. Finer NN, Horbar JD, Carpenter JH. Cardiopulmonary Resuscitation in the Very Low Birth Weight Infant: the Vermont Oxford Network experience. *Pediatrics*. 1999; 104 (3 Pt1): 428-34.