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Intra-Ventricular Hemorrhage: Frequency and Outcomes at the Time of Discharge

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ABSTRACT

Background and Objective: Neonatal sepsis is associated with high mortality and has a favourable outcome when recognized and treated in a timely manner. In resource-limited settings, there is need for an affordable test with a short turnaround time for timely diagnosis of sepsis. The study was aimed to find out the role of eosinopenia and neutrophil-to-lymphocyte ratio (NLR) in screening for early-onset sepsis (EOS) and to determine the cut-off point for absolute eosinophil count (AEC) and NLR to predict early-onset neonatal sepsis.

Methods: This descriptive study was conducted on neonates with suspected EOS at Medical College Hospital, Chennai, Tamil Nadu, India. Complete blood count, C-reactive protein, blood culture, and antibacterial sensitivity were assessed, and neonates with laboratory evidence of sepsis were considered as EOS group. AEC and NLR were compared between groups. Specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Receiver operating characteristic (ROC) analysis was performed. The median value of AEC and NLR was compared with the Mann -Whitney test.

Findings: Among the 140 neonates studied, 72(51.4%) had low birth weight. The absolute neutrophil count was higher (8954 vs. 7322) and the absolute lymphocyte count (3040 vs. 5593) and platelet count were lower in sepsis (126074 vs. 239151). Eosinopenia with cut-off point of 194.5 and NLR with a cut-off point of 1.565 had higher sensitivity than specificity and a high negative predictive value (NPV).

Conclusion: It can be concluded that eosinopenia and NLR are useful tools in the diagnosis of early-onset sepsis.

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Introduction

Intraventricular hemorrhage (IVH) is a major neuropathological lesion in premature infants, which can be followed by hemorrhage in the germinal matrix of the subependymal matrix. This tissue further acts as a precursor for neurons, astrocytes and oligodendroglia [1, 2]. It is also assumed that the gestational age less than 32 weeks or the birth weight less than 1500 grams is associated with the highest risk of IVH [3- 6]. In addition, under-developed blood vessels in a vascular space combined with poor tissue support, coagulation disorders, and infections can predispose a premature baby to IVH. Therefore, the risk of developing IVH is inversely related to gestational age [5, 7, 8]. Recent advances in prenatal and neonatal care have increased the survival of high-risk preterm infants; hence, the overall incidence of IVH has decreased from about 40-50% in 1991 to 20-25% in 2005 [9, 10]. This reduction in the incidence of IVH has continued to 13% in very low birth weight (VLBW) infants with the development of neonatal care [11].

However, IVH remains one of the leading causes of death in premature infants, which affects up to 20% of infants with birth weight less than 1500 g [3]. A study on VLBW infants showed that high grades of IVH could increase the mortality of this group of infants by 30 times [12].

According to studies, the average incidence of IVH is about 5% -23% [13, 14]. This reduction in the incidence of IVH can be attributed to the use of drugs such as antenatal corticosteroids and surfactants in newborns [15, 16].

In premature infants, three syndromes can be identified through clinical manifestations. The first syndrome is known as catastrophic deterioration whose symptoms include a sudden worsening of the baby's condition leading to an increased need for oxygen or a ventilator support, a sudden drop in blood pressure, and acidosis. However, it should be noted that a decrease in hematocrit can occur even without a clear change in the clinical condition of the infant. The next syndrome, known as saltatory, is more common and its onset appears gradually in the form of changes in the baby's movements. The third and the most common condition is asymptomatic, including more than 50% of infants with IVH, and there are no obvious clinical symptoms [17].

Diagnosis can be made by observing hyperechogenic areas on brain ultrasonography (BUS). Based on the Papile classification, four degrees can be detected on ultrasound (grades I to IV) [14, 18]. The neurodevelopmental prognosis is excellent in infants with IVH grades I and II [19, 20]. Mortality in preterm infants with grades III and IV is up to about 10%, and 30 - 40 % of these infants will develop cognitive impairment and movement problems in the future [21, 22]. Complications of IVH in these infants include hydrocephalus, cerebral palsy, and seizures [23].

Determining the frequency of IVH, its most important risk factors (gestational age and birth weight) in affected infants, and its outcome is of great importance for health care providers, as any planning to improve the quality of treatment and reduce the complications of the primary lesion requires the evaluation of basic information. This retrospective study aimed to evaluate the frequency of IVH in the NICU of a tertiary referral hospital for high-risk pregnancies. With a better analytical perspective, we can plan for more appropriate services in the future.

Methods

Design and participants

This retrospective cross-sectional analytic study was carried out from Jan.2011 to Mar 2018 in Ayatollah Rohani Hospital, an academic referral hospital for high-risk pregnancies in Babol, Iran. All premature (<34 weeks of gestation) and very low birth weight (<1500 grams) infants without birth trauma and congenital anomaly in head or syndromic faces were included in the study. Cases with a diagnosis of chromosomal abnormalities and death before performing brain ultrasonography were excluded from the study.

Data collection

The patients' information such as birth weight, gestational age, and delivery route was thoroughly

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recorded by a trained medical student. Based on inward protocol, BUS was performed within 3 to 10 days after birth. Reports of all brain ultrasound records, (Conducted by EMP 76 ultrasound device model 1700 made in Japan, by 3.5 and 5 MHz convex probes and a linear probe with a frequency of 7.5 MHz), were reviewed by a radiologist, and the IVH grades were determined based on Papile criteria [14]. According to this criterion, bleeding was divided into four degrees. Grade I: Bleeding limited to the germinal matrix; Grade II: Intraventricular hemorrhage; Grade III: Bleeding with ventricular dilatation; and Grade IV: Proliferation of bleeding into the parenchyma [18]. The weight variable was subdivided into less than 1000 and 1500-1000 grams, and the gestational age variable was subdivided into less than 28, 28-32, and greater than 32 weeks.

The short-term outcome until discharge included: infant's death due to IVH, inserting shunt, seizures, decreased IVH grade, and recovery.

Statistical analysis

The data were analyzed by SPSS 16. Frequency and percentage were used to describe the qualitative data, and the mean ±standard deviation was used to describe the quantitative characteristics.

Results

Out of a total of 2563 eligible neonates in BUS, IVH was diagnosed in 138 neonates (5.38%), 99 boys (71.7%) and 39 girls (28.3%). The male to female ratio was 2.53 to 1. The mean gestational age and birth weight were 29.97±2.89 weeks and 1084.18±327.71 grams, respectively. The method of delivery for 77 patients (55.7%) was vaginal, and cesarean section for 61 patients (44.3%). Table 1 shows the frequency of IVH grades by gestational age and birth weight. The prevalence of severe IVH (grade III or IV) in 138 infants with IVH was 6.52%. The mean birth weight of infants with IVH grade I or II was 1176±114.7, and for neonates with IVH grade III or IV, it was 683.8±97.2gr. The frequency of IVH by the average gestational age and birth weight of infants in each year is shown in (Figures 1, 2). The IVH portion in each year is also depicted in Figures 1, 2.

Outcome at the time of discharge

Regarding the short-term outcome of patients until the discharge, 15 (10.8%) cases demonstrated seizures and used anticonvulsant drugs (including one case of grade III and fourteen cases of grade II). In 4 cases (2.9%), ventriculoperitoneal shunting was performed (including two cases of grade III and two cases of grade IV). There were 3 cases (2.2%) of death, including one grade III and two grade IV of IVH.

Discussion

According to the findings, the frequency of IVH over the eight-year period in preterm low birth weight infants was 5.38%. In a study by Aqha Ghazvini et al., the frequency was reported to be 28% [24]. In another study, conducted by Fouladinejad et al., on 71 infants with less than 34 weeks of gestational age and the birth weight of less than 1500 gr, the prevalence of IVH was reported to be 64% [25]. This prevalence was also 19% in a study conducted by Marzban et al. in Iran [26].

Table 1. Frequency of IVH grades by gestational age and birth weight

Variable	IVH grade	I N=106 (76.81%)	II N=23 (16.67%)	III N=7(5.07%)	IV N=2 (1.45%)
Gestational age (week)	<28 (n=25)	17 (68%)	5 (20%)	3 (12%)	-
	28-32 (n=75)	58 (79.4%)	13 (17.8 %)	2 (2.7%)	2 (%2.7)
	>32 (n=38)	31 (81%)	5 (13.5%)	2 (5.4%)	-
Birth weight (gram)	<1000 (n =55)	41 (47.5%)	10 (18.2%)	3 (5.5%)	1 (1.8%)
	1000- 1500 (n=83)	65 (78.3%)	13 (15.6%)	4 (4.8%)	1 (1.3%)

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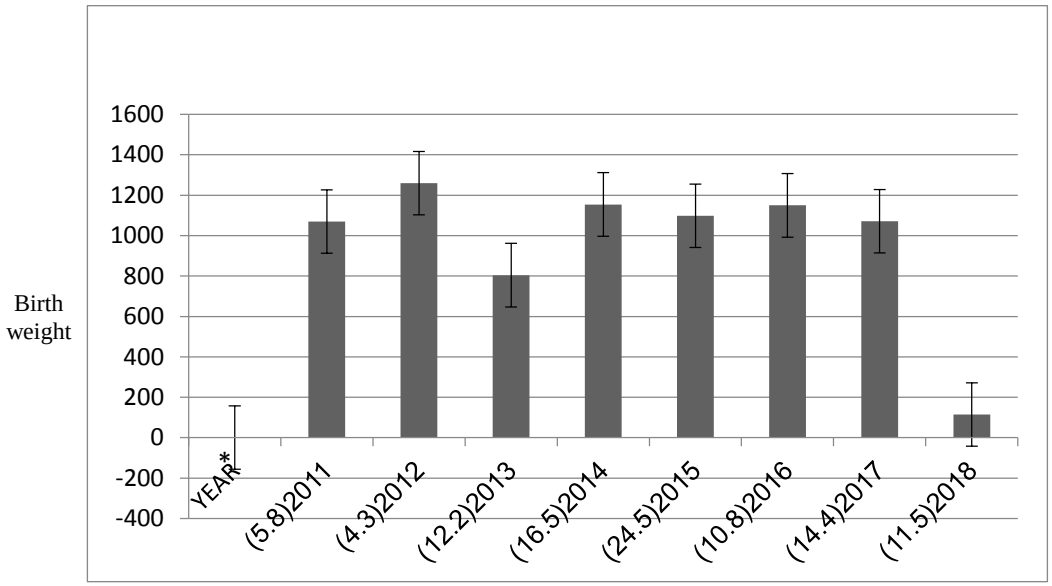
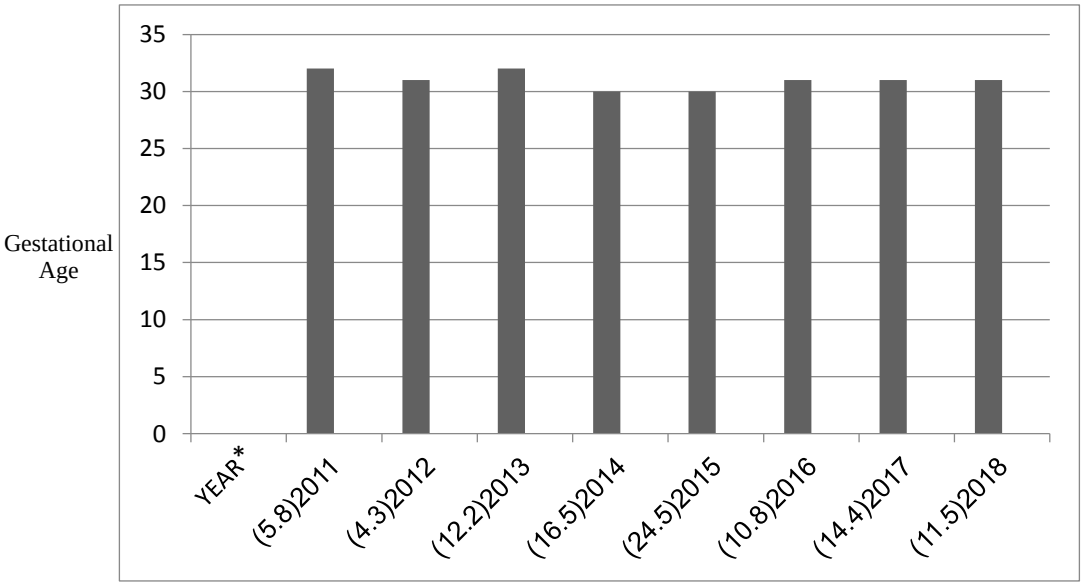


* Frequency in each year (%)

Figure 1. Mean birth weight of neonates with IVH parting by years



* Frequency in each year (%)

Figure 2. Mean gestational age of neonates with IVH parting by years

The reason for these higher frequencies compared to that of the present study could be ascribed to the fact that the referred infants were from other centers and that there were more expected cases by transporting premature infants. In the present study, the frequency of severe IVH (grades III and IV) in 138 neonates with IVH was 6.52%. In another study conducted by Badiei et al., this value was 5.9%, which is similar to that of the present study [27].

In the present study, the average weight of infants with IVH was measured between 2011 and 2018, and the frequency of IVH in each year was also assessed. The lowest frequency of IVH was in 2012 when the average weight of newborns was higher than that of other years (figure 1). On the other hand, if we consider the average gestational age in these years, it becomes apparent that among the gestational age of 32 weeks, we have an increase in frequency due to lower average weight

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(804.21 vs. 1069.87 g) in 2013 (figure 1). The same trend of changes is seen in the gestational age of 30 weeks, and in 2015, compared to 2014 (figure 2), we had an increase in frequency due to the decrease in the average birth weight (1098.64 vs. 1154/13). At 31 weeks of gestation, the highest frequency belonged to 2017, when infants had the lowest average weight (1071.22 g) compared to other infants with the same gestational age (figure 2). Therefore, it seems that the weight of premature infants had been one of the most important factors influencing the frequency of IVH. The importance of birth weight, in addition to increasing the frequency of IVH, also had an effect on its severity. In this study, the mean weight in severe IVH (grade III or IV) was 683.8 ± 97.2 grams, and in mild to moderate IVH (grade I or II), it was 1176 1± 114.7grams.

In the present study, 71.7% of cases were male and 28.3% were female (M/F: 2.53/1). In a study conducted by Gleissner et al., out of 136 infants with IVH, 61% were male and 39% were female, which is similar to our study [28]. Also, as demonstrated by a review study, the IVH in boys was more than that of girls [28].

Moreover, there was a control group in Gleissner's study, but due to the fact that determining the risk factors were not one of the objectives of the present study, we did not have a control group. The present study only reflects the prevalence of IVH in two genders, and perhaps if the control group had been considered in our study, male gender would have been regarded as a risk factor.

It is thought that prognosis in IVH could be attributed to the severity of bleeding, involvement and damage of the white matter, the presence of seizure, and shunt surgery [28, 29].

In this study, out of 15 cases (10.8%) who required anticonvulsant treatment, 14 were grade II and one case was grade III. This could be due to the higher survival of infants in the case of lower compared to higher IVH grades.

Post hemorrhagic hydrocephalus, which is a prognostic factor [28], was observed in 4 patients, all of whom were grades III and IV, who needed a ventriculoperitoneal shunt.

As expected, IVH death occurred in grades III and IV, which was 2.9% of the total cases. A study on 239 preterm VLBW infants demonstrated that the mortality rate at weights below 1000 g increased significantly by 29.2% [12].

Limitations of the study

The retrospective design, the use of patients' records, and lack of access to IVH status of infants who died during the first week before performing BUS were among the limitations of this study. Data on VLBW infants who were severely premature and died during the first few days without a brain ultrasound were not included in the analysis. Ultimately, as severe IVH is deemed to be more frequent, it was not included in the study. These factors may explain the low frequency of IVH in our study.

Conclusion

This study showed that the frequency of IVH was lower in our study, compared to that of developed countries; however, severe IVH (grades III and IV), which is of particular importance in terms of morbidity and mortality, had a relatively low prevalence in this study. Due to neurological complications, especially in severe cases of IVH, premature delivery and VLBW should be prevented with appropriate measures.

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Ethical approval

This study was conducted based on the medical student's thesis with university ethics committee code number IR.MUBABOL.HRI.REC.1397.164.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Takashima S, Mito T, Ando Y. Pathogenesis of periventricular white matter hemorrhages in preterm infants. Brain develop 1986; 8(1): 25-30.
2. Gould SJ, Howard S, Hope PL, Reynolds EO. Periventricular intraparenchymal cerebral haemorrhage in preterm infants: the role of venous infarction. J Pathol 1987; 151(3): 197-202.
3. Radic JA, Vincer M, McNeely PD. Temporal trends of intraventricular hemorrhage of prematurity in Nova Scotia from 1993 to 2012. J Neurosurg Pediatr 2015; 15(6): 573-9.
4. Mukhopadhyay K, Louis D, Mahajan G, Mahajan R. Longitudinal growth and post-discharge mortality and morbidity among extremely low birth weight neonates. Indian Pediatr 2014; 51(9): 723-6.
5. Vergani P, Patane L, Doria P, et al. Risk factors for neonatal intraventricular haemorrhage in spontaneous prematurity at 32 weeks gestation or less. Placenta 2000; 21(4): 402-7.
6. Linder N, Haskin O, Levit O, et al. Risk factors for intraventricular hemorrhage in very low birth weight premature infants: a retrospective case-control study. Pediatrs 2003; 111(5): 590-5.
7. Mercer JS, Vohr BR, McGrath MM, et al. Delayed cord clamping in very preterm infants reduces the incidence of intraventricular hemorrhage and late-onset sepsis: a randomized, controlled trial. Pediatrs 2006; 117(4): 1235-42.
8. Stoll BJ, Hansen NI, Bell EF, et al. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. Pediatrs 2010; 126(3): 443-56.
9. Hack M, Fanaroff AA. Outcomes of children of extremely low birthweight and gestational age in the 1990's. Early Hum Dev 1999; 53(3): 193-218.
10. Marba S, Caldas JP, Vinagre LE, Pessoto MA. Incidência de hemorragia peri-intraventricular em recém-nascidos de muito baixo peso: análise de 15 anos. J Pediatr 2011; 87: 505-11.
11. He L, Zhou W, Zhao X, et al. Development and validation of a novel scoring system to predict severe intraventricular hemorrhage in very low birth weight infants. Brain Develop 2019; 41(8): 671-7.
12. Gupta S, Adhisivam B, Bhat BV, et al. Short Term Outcome and Predictors of Mortality Among Very Low Birth Weight Infants - A Descriptive Study. Indian J Pediatrs 2021; 88(4): 351-7.
13. Obeid R, Chang T, Bluth E, et al. The use of clinical examination and cranial ultrasound in the diagnosis and management of post-hemorrhagic ventricular dilation in extremely premature infants. J Perinatol 2018; 38(4): 374-80.
14. Tabrizi PR, Obeid R, Mansoor A, et al., editors. Cranial ultrasound-based prediction of post hemorrhagic hydrocephalus outcome in premature neonates with intraventricular hemorrhage. In2017 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2017 Jul 11 (pp. 169-172). IEEE.
15. Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2017; 3: 44-54.
16. Handley SC, Passarella M, Lee HC, Lorch SA. Incidence trends and risk factor variation in severe intraventricular hemorrhage across a population based Cohort. J Pediatr 2018; 200: 24-9.
17. Volpe JJ. Neurology of the newborn. 5th ed. Philadelphia: Saunders/Elsevier. 2008; p: 899.
18. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr 1978; 92(4): 529-34.
19. Robinson S. Neonatal posthemorrhagic hydrocephalus from prematurity: pathophysiology and current treatment concepts: A review. J Neurosurg Pediatrs 2012; 9(3): 242-58.
20. Radic JA, Vincer M, McNeely PD. Outcomes of intraventricular hemorrhage and posthemorrhagic hydrocephalus in a population-based cohort of very preterm infants born to residents of Nova Scotia from 1993 to 2010. J Neurosurg Pediatr 2015; 15(6): 580-8.
21. Vohr BR, Wright LL, Dusick AM, et al. Neurodevelopmental and functional outcomes of extremely low birth weight infants in the National Institute of Child Health and Human Development

[DOI: 10.22088/CJP.BUMS.8.1.6]

Neonatal Research Network, 1993-1994. Pediatrs 2000; 105(6): 1216-26.
22. Resch B, Gedermann A, Maurer U, et al. Neurodevelopmental outcome of hydrocephalus following intra-/periventricular hemorrhage in preterm infants: short- and long-term results. Childs Nerv Syst 1996; 12(1): 27-33.
23. Schulzke SM, Deshpande GC, Patole SK. Neurodevelopmental outcomes of very low-birth-weight infants with necrotizing enterocolitis: a systematic review of observational studies. Arch Pediatr Adolesc Med 2007; 161(6): 583-90.
24. Gleiβner M, Jorch G, Avenarius S. Risk factors for intraventricular hemorrhage in a birth cohort of 3721 premature infants. J Perinatal Med 2000; 28(2): 104-10.
25. Fouladinejad M, Nematollahi N, Alaee E. Incidence and Severity of Intra-Ventricular Hemorrhage (IVH) in Preterm Infants, Northeast of Iran. J Nepal Paediatr Soc 2016; 36(1): 38-41.
26. Linder N, Haskin O, Levit O, et al. Risk factors for intraventricular hemorrhage in very low birth weight premature infants: a retrospective case-control study. Pediatrs 2003; 111(5 Pt 1): e590-5.
27. Badiei Z. Prevalence and Risk Factors of Intraventricular Hemorrhage in Premature Newborns less than 35 Weeks in Neonatal Intensive Care Units of Isfahan. J Isfahan Med Sch 2007; 24(83): 15-23.
28. Özek E, Kersin SG. Intraventricular hemorrhage in preterm babies. Turk Pediatri Ars 2020; 55(3): 215-21.
29. Miranda P. Intraventricular hemorrhage and posthemorrhagic hydrocephalus in the preterm infant. Minerva Pediatrica 2010; 62(1): 79-89.

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