Original Article

Incidence of periventricular leukomalacia in preterm very low birth neonates – A tertiary care experience

Saika Bashir[1], Mohd Irshad[2], Waseem Iqbal[2], Mohd Ashraf[3]

From [1]Consultant Pediatrics, Department of JK Health, Subdistrict Hospital Magam, Budgam, Jammu and Kashmir, India, [2]Assistant Professor, [3]Lecturer Pediatric Nephrology, Department of Pediatrics, Government Medical College Baramulla, Baramulla, Jammu and Kashmir, India

ABSTRACT

Background: The periventricular leukomalacia (PVL) is the most common white matter injury in preterm very low birth weight (VLBW) neonates. It occurs due to ischemic injury to developing oligodendrocytes. It can be detected by cranial ultrasonography (CUS). O**bjective:** The objective of the study was to find incidence of PVL in preterm VLBW babies and its correlation with gestational age, birth weight, and arterial blood PH. **Materials and Methods:** A total of 80 preterm low birth babies admitted in our neonatal intensive care unit over 1 year were included who met the inclusion criteria. All babies were subjected to CUS starting from the 1st week of their life and repeated weekly by trained radiologist to find changes suggestive of PVL till clinically indicated or normal scan on the 14th day of life. **Results:** Among 80 preterm low birth babies in our study, 54 (67.5%) were male and 26 (32.5%) were female. Three babies had gestational age of 30 weeks or less, 25 had gestational between 30 and 32 weeks, 35 had gestational age between 32 and 34 weeks, while 17 had gestational age more than 34 weeks. A total of 62 (77.5%) were born through normal vaginal delivery and 18 (22.5%) were born by cesarean section. The incidence of PVL was 2.5%. The most common change was periventricular flare. The incidence of PVL was more in extreme preterm and those with PH <7.2. The mortality was 50% in babies with PVL. **Conclusion:** The incidence of PVL in preterm low birth weight babies is 2.5% with a mortality of 50%. Prevention and early detection are the keys to mitigate the effects of this disastrous complication of prematurity.

Key words: Low birth weight, Periventricular leukomalacia, Prematurity

White matter injury (WMI) is the most frequent type of brain lesion in preterm infants and may be present to some degree in up to 50% of very low birth weight (VLBW) infants. Due to improvement in the neonatal care, cystic WMI injury, also referred as cystic periventricular leukomalacia (PVL), has become a rare disease. On the other hand, the non-cystic, predominantly diffuse form of WMI prevails in very immature infants who survive today [1]. Early diagnosis is important for the optimal treatment and favorable neurological outcome [2]. The ultrasound remains an important bedside diagnostic tool for PVL [3]. Although magnetic resonance imaging is superior to cranial ultrasonography (CUS) for assessing more subtle WMI, the quality of neonatal CUS has improved dramatically in the past decades, in terms of resolution and image processing speed [1].

The word "leukomalacia" is derived from "leukos" meaning white and "malacia" means softening [4]. PVL is defined morphologically by two histopathologic components: (1) A "focal" necrotic component in periventricular region of the cerebral white matter and (2) a "diffuse" component characterized by reactive gliosis in the surrounding white matter [4]. PVL, a major cause of neurological disabilities in preterm infants, can be isolated or associated with intraventricular and periventricular hemorrhage [5]. The etiology of PVL is multifactorial and involves prenatal and perinatal factors. Preterm premature rupture of membranes, chorioamnionitis, birth asphyxia, recurrent apnea, patent ductus arteriosus, sepsis, seizures, duration of mechanical ventilation, and hypocarbia were found to have significant association with PVL [6]. There is an increasing evidence that pathogenesis of PVL relates to variable combination of three major factors: The distribution of arterial vascular end zones within the cerebral white matter, maturation-dependent impairment in cerebrovascular autoregulation of cerebral blood flow, intrinsic vulnerability of early differentiating oligodendroglial precursors to free radicals, and, in some instances, exposure to endotoxemia [3].

The severity of WMI ranges from minor focal areas of gliosis or necrosis to diffuse involvement. Severe focal lesions may be

Access this article online	
Received -30 October 2020 Initial Review - 05 December 2020 Accepted - 22 December 2020	Quick Response code
DOI: 10.32677/IJCH.2020.v07.i12.006	

Correspondence to: Dr. Mohd Irshad, Department of Pediatrics, Government Medical College, Baramula - 193 103, Jammu and Kashmir, India. E-mail: drirshadnabi@gmail.com

visualized *in vivo* by CUS as areas of increased echogenicity in periventricular white matter during the 1st day of life, which subsequently evolve into cystic lesions after approximately 2–3 weeks [7]. De Vries classification of PVL grading on ultrasound was used: Grade I PVL is prolonged periventricular flare present for 7 days or more. Grade II is the presence of small localized of frontoparietal cysts. Grade III is an extensive periventricular cystic lesion involving occipital and frontoparietal white matter. Grade IV PVL consists of areas of extensive subcortical cystic lesions [3].

The present study was designed to study incidence of PVL in preterm very low birth neonates, to find any correlation between gestational age, birth weight, and arterial blood gases, and PVL and find immediate outcome of preterm low birth babies with ultrasonographic evidence of PVL.

MATERIALS AND METHODS

This study was undertaken in the Department of Pediatrics of Government Medical College, Srinagar, for a period of 1 year. All preterm VLBW (birth weight ≤1500 g) babies admitted in our neonatal intensive care unit were enrolled in the study. Neonates, with CNS malformations, chromosomal anomalies, multiple congenital malformations, and those who either died before undergoing first CUS or were referred to other departments because of surgical emergencies, were excluded from the study.

Detailed history such as maternal fever, PIH, urinary tract infections, premature rupture of membranes, meconium stained liquor, and antepartum hemorrhage was taken and recorded. Apgar score, birth weight, and findings on physical examination were recorded on pre-designed pro forma. Gestational age was assessed by New Ballard score. All babies were subjected to routine investigations. A verbal informed consent was taken for serial ultrasound examinations of cranium.

Serial weekly sonographic evaluation of cranium was done on all babies starting within the 1st week of their lives by Toshiba ultrasound scanner with 3.5 MHz convex transducer and they were particularly analyzed for lesions compatible with PVL as per the standard predefined criteria. Incident lesions were either flare or cysts detected on first CUS examination. An incident lesion of flare was defined as an area of increased echogenicity present in the periventricular area on both planes seen on two separately done CUS, 7 days apart, and such that the first ultrasound should have been done in first 7 days of life. Cystic PVL was defined as single or multiple echolucent lesions visible on both planes in characteristic locations and not previously preceded by flare. These were followed up till discharge or death of baby.

Incidence of PVL was calculated and its correlation with gestational age, birth weight, Apgar score, and arterial blood gases at presentation was studied. Immediate outcomes in relation to presence or absence of PVL were studied. $p<0.05$ was considered statistically significant.

RESULTS

Out of 3131 neonates admitted during our study period, 122 (3.89%) were preterm VLBW and out of which, 42 babies were excluded from the study. Among 80 babies finally included in the study, 54 (67.5%) were male and 26 (32.5%) were female. Sixty-two (77.5%) were born through normal vaginal delivery and 18 (22.5%) were born by cesarean. The birth weight, gestational age, and Apgar score of babies are shown in Table 1.

A total of 78 (97.5%) babies had normal CUS and 2 (2.5%) had flares around the periventricular area. Both babies had gestational age between 30 and 32 weeks. Further, it was noted that 75 (93.7%) babies had PH >7.2 and 5 (6.3%) had pH <7.2 and out of those 5 babies, 2 had flares around periventricular area (Fig. 1). Out of 80 babies, 74 survived beyond 7 days up to 28 days or beyond with no evidence of PVL; out of which, four babies died because of different causes while out of two babies having PVL, one baby died. Hence, mortality rate (7–28 days) in babies with no evidence of PVL was 5.12% (4 out of 78) while mortality rate of babies with evidence of PVL was 50% (1 out of 2).

DISCUSSION

Advances in the neonatal care allow survival of extremely preterm infants, who are prone to range of long-term complications in comparison to their term counterparts [8]. The advent of ultrasonic scanning has greatly increased our understanding of the nature and evolution of lesions of neonatal brain, not least in emphasizing the very high incidence of pathology in babies weighing <1.5 kg at birth [9]. PVL is the most common ischemic injury in premature infants [3]. The clinical sequelae of these lesions have been associated with cerebral palsy, visual disturbances, and cognitive impairment; although, clinically silent lesions are being increasingly recognized [10].

In our study, the incidence of PVL in preterm VLBW neonates was 2.5%. The most common lesion was persistent flare. Our findings

Table 1: Demographic profile of the study population

Parameter	Number (percentage)
Gestational age (weeks)	
>30–32	25 (31.25)
>32–34	35 (43.75)
>34	17 (21.25)
Birth weight (g)	
1000–1100	2 (2.5)
1101–1200	2 (2.5)
1201–1300	18 (22.5)
1301–1400	9 (11.25)
1401–1500	49 (61.25)
Apgar score	
8–10	21 (26.25)
6–7	49 (61.25)
4–5	8 (10)
3 or less	29 (2.5)

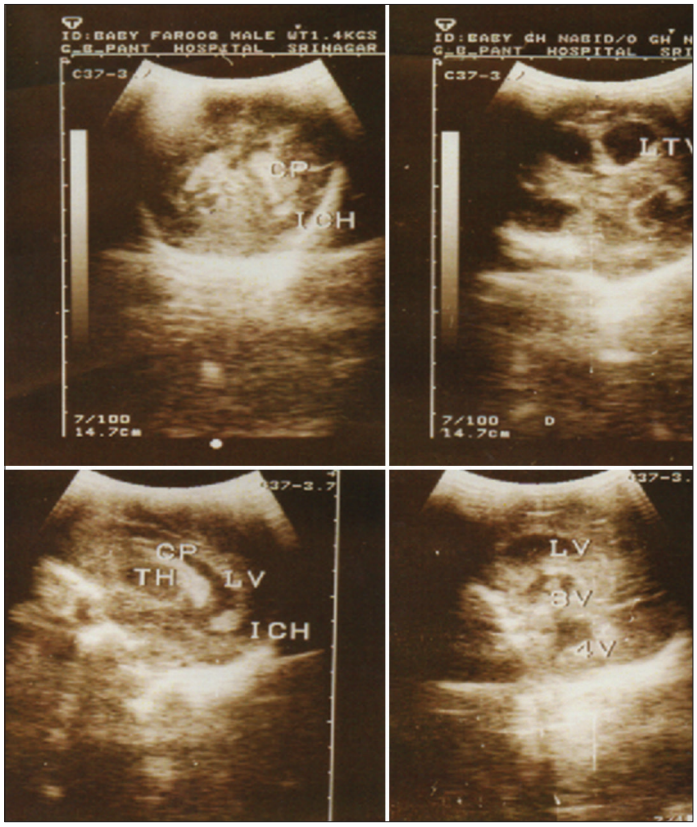

Figure 1: Ultrasonography cranium showing flares in the periventricular area

were comparable to the results of studies done by Bass *et al.* [11] (3.6%), Spinillo *et al*. [12] (5.7%) and 14% (49/349), respectively, for PVL and echo dense lesions, Kapoor *et al*. [2] (7.7%), Lee *et al*. [13] (3–4%), Rushton *et al*. [9] (7.87%), and Park *et al*. [14] (9.8%). It was found that PVL was more common in more premature babies as revealed by earlier studies (Barria *et al*.) [15]. The higher percentages reported by Trounce *et al*. [16] (26%), Maria *et al*. [3] (31.95%), and Wiswell *et al*. [17] (26.8%) could be because of higher percentages of their babies being more premature and may be because of more experienced radiologists to detect the flares.

The mean gestational age and weight of babies studied by Trounce *et al*. [16], Wiswell *et al*. [17], and Martia *et al*. [3] were 29 weeks and 1200, 27.2 weeks and 1001 g, and 31.4 weeks and 1173 g unlike our study, where 65% of babies had gestational age more than 32 weeks and 95% of babies had weight more than 1200 g. More premature or extremely low birth weight babies did not survive in our setup and thus could not be included in our study. The direct positive correlation of low PH and PVL in our study is substantiated by previous studies such as Wiswell *et al*. [17] and Spinillo *et al*. [12]. Our study revealed mortality of 50% among babies with PVL comparable to that reported by Rushton *et al*. [9] (47.05%) and Kapoor *et al*. [2] (25%).

The main limitation of our study was small sample size which was mainly because of time constraint as study had to be completed in a year period and many preterm VLBW babies either died within a week or had to be referred to other departments because of other reasons. Furthermore, our study was intended to pick up early PVL as long-term follow-up was not a part of our study.

CONCLUSION

PVL is one of the major complications of prematurity and its risk increases with decreasing gestational age besides other risk factors. It is particularly common in babies with gestational age of <32 weeks. It leads to various neurodevelopmental sequelae in the form motor, hearing and visual deficits, the management being prevention of prematurity, mitigation of risk factors, early recognition and timely intervention of neurodevelopmental sequelae, and parental counseling after knowing long-term outcomes.

REFERENCES

1. Agut A, Alarcon A, Cabanas F, Bartocci M, Biarge MM, Horsch S. Preterm white matter injury: Ultrasound diagnosis and classification. Pediatr Res 2020;87:37-49.
2. Kapoor S, Sharma R, Sapare A, Aggarwal R. Early periventricular leukomalacia in preterm neonates. Int J Contemp Pediatr 2018;5:1859-62.
3. Maria A, Gupta A, Aggarwal R, Sreenivas V, Paul VK, Deorari AK. Incidence of periventricular leucomalacia among a cohort of very low birth weight neonates(<1500g). Indian Pediatr 2006;43:210-6.
4. Ahya KP, Suryawanshi P. Neonatal periventricular leukomalacia: Current perspective. Res Rep Neonatol 2018;8:1-8.
5. Al Tawil KI, Ek Mehdy HS, Al Rifai MT, Tamim HM, Ahmed IA, Al Saif SA. Risk factors for isolated periventricular leukomalacia. Pediatr Neurol 2012;46:149-53.
6. Hatzidaki E, Giannakis E, Maraka S, Korakaki E, Manoura A, Saitakis E, *et al*. Risk factors periventricular leukomalacia. Acta Obstet Gynecol 2009;88:110-5.
7. Hill A. Neurological and neuromuscular disorders. In: Avery' Neonatology-Pathophysiology and Management of the Newborn. 6th ed. Toronto, Canada: Wolters Kluwer India Pvt. Ltd; 2011.
8. Ballot DE, Potterton J, Chirwa T, Hilburn N, Cooper PA. Develpmental outcome of very low birth weight infants in a developing country. BMC Pediatr 2012;12:11.
9. Rushton DI, Preston PR, Dubrin GM. Structure and evolution of echo dense lesions in the neonatal brain. Acombined ultrasound and necropsy study. Arch Dis Child 1985;60:798-808.
10. Mugg A, Malhotra A. Periventricular leukomalacia. In: Kreutzer JS, Deluca J, Caplan B, editors. Encyclopedia of Clinical Neuropsychology. New York: Springer; 2011.
11. Bass WT, Jones MA, Karlowich G. Ultrasonographic differential diagnosis and neurodevelopmental outcome of cerebral white matter lesions in premature infants. J Perinatol 1999;19:330-6.
12. Spinillo A, Capuzzo E, Stronati M, Ometto A, De Santolo A, Acciano S. Obestetric risk factors for periventricular leukomalacia among preterm infants. Br J Obstet Gynaecol 1998;105:865-71.
13. Lee HJ, Park SH, Na KH, Park SY, Kim EY, Kim KS, *et al*. Developmental assessment of preterm infants at two years of age with periventricular leukomalacia. J Korean Soc Neonatol 2002;9:167-75.
14. Park HA, Hwang JH. The risk factors of periventricular leukomalacia among very low birth infants. Neonatal Med 2020;27:51-6.
15. Barria RM, Flandez A. Parenchymatous Brain Injury in Premature Infants: Intraventricular Hemorrhage and Periventricular Leukomalacia Neonatal Care. London: IntechOpen; 2012.
16. Trounce JQ, Rutter N, Levene MI. Periventricular leucomalacia and intraventricular hemorrhages in the preterm neonate. Arch Dis Child 1986;61:1196-202.
17. Wiswell TE, Graziani LJ, Kornhauser MS, Stanley C, Merton DA, Mckee L, *et al*. Effects of hypocarbia on the development of cystic periventricular leukomalaciain premature infants treated with high frequency jet ventilation. Pediatrics 1996;98:918-24.

Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Bashir S, Irshad M, Iqbal W, Ashraf M. Incidence of periventricular leukomalacia in preterm very low birth neonates – A tertiary care experience. Indian J Child Health. 2020; 7(12):495-497.