

Original Research Article

Early periventricular leukomalacia in preterm neonates

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ABSTRACT

Background: Preterm neonates are at increased risk for brain injury. More than 10% will sustain neurological injuries leading to significant learning disabilities, motor developmental delay, cerebral palsy, seizures and mental retardation. Periventricular leukomalacia (PVL) is the most common form of white matter injury of prematurity. The objective of the present study was to identify the incidence of early periventricular leukomalacia (PVL) and its associated risk factors in the study group.

Methods: All preterm neonates with either Gestational age <32weeks and/or Birth weight <1500 grams who were admitted to Neonatal Intensive Care Unit within the period of 1st November 2013 to 30th April 2015 were taken for study. A total of 112 babies met the inclusion criteria but 104 were finally taken into the study. Screening of intraventricular haemorrhage and early PVL changes in VLBW babies was done by neurosonogram on day 3 and day 14 of life by a single well qualified radiologist. Follow up cranial ultrasound was done weekly for the babies who were diagnosed to have IVH and/or PVL by day 14 of life.

Results: The incidence of early periventricular leukomalacia in very low birth weight babies in present study was 7.7%. It was seen that 87.5% babies had periventricular flares and 12.5% babies had cystic changes. It was seen that birth weight<1000grams (OR 0.006; CI:0.00-0.50; p value 0.023) and neonatal sepsis (OR 80.9; CI:1.65-3947.6;p value 0.027) significantly increased the risk of developing PVL in VLBW babies. The duration of hospital stay was found to be significantly increased in babies having PVL.

Conclusions: The incidence of early periventricular leukomalacia in babies born <32weeks gestation and/or birth weight<1500grams is 7.7%. Birth weight <1000 grams and neonatal sepsis were found to increase the risk of periventricular leukomalacia in these babies.

Keywords: Incidence, Periventricular leukomalacia, Risk factors

INTRODUCTION

Preterm neonates sustain neurological injuries leading to significant learning disabilities, motor developmental delay, cerebral palsy, seizures and mental retardation.¹ Although advances in neonatal intensive care have greatly improved the survival and outcome of these 'micro' patients, brain injury remains of major concern.

Early diagnosis is important for optimal treatment, and neurological outcome.² Neuroimaging assessment of premature is becoming increasingly important as the number of premature births and survival rate of very low birth weight babies is increasing and the survivors remain at great risk for neurodevelopment impairments.³ Periventricular leukomalacia is the most common form of white matter injury of prematurity. PVL is characterized

by focal necrotic lesions in the periventricular white matter, optic radiations, acoustic radiations and less prominent, more diffuse cerebral white matter injury.⁴

Neuropathologically, PVL is characterized in the acute phase by coagulation necrosis and neuroaxonal swelling. A variable amount of hemorrhage may be present. In the subacute stage, cysts may form in the larger lesions. Ultimately, astrogliosis develops and the cysts become less apparent.⁵

Cystic periventricular leukomalacia of antenatal onset is evident by two weeks of age.⁴ After 10 to 14 days, the echogenicity of affected areas of deep white matter increases. These areas of abnormality may be focal or diffuse, symmetrical or asymmetrical.

Cystic encephalomalacia appears in the areas of increased echogenicity within 2 to 3 weeks after the initial insult.⁶ Incidence of PVL ranged from 4-15%. Part of this wide variation in incidence relates to the sonographic definition used by various authors to describe the condition. PVL is usually diagnosed in the neonatal period by CUS or less commonly by MRI.⁵

The outcome in terms of survival of VLBW babies is improving in our tertiary care centre. Besides survival, it is also important to assess the quality of care and outcome in terms of neurological injury.

Hence, we undertook this study to evaluate the incidence of a major neurological complication which is seen in these babies using neurosonogram as the diagnostic modality. The objective of the present study was to identify the incidence of Early PVL and its associated risk factors in the study group.

METHODS

This hospital based cross sectional study was done over a period of 18 months from November 2013 to April 2015. All preterm neonates with gestational age <32weeks and/or birth weight <1500grams admitted in Neonatal Intensive Care Unit were included in the study.

Initially a sample size of 100 babies was calculated however during the time period it was seen that 112 babies met the inclusion criteria. Out of them 5 babies' parents/guardians refused to give consent for participation in the study and 3 babies were discharged against medical advice on day 1 of life and lost to follow up. So, 104 babies were finally taken into the study.

Inclusion criteria

All preterm neonates with gestational age <32weeks and/or birth weight <1500grams admitted in Neonatal Intensive Care Unit within 24 hours of birth were included in the study.

Exclusion criteria

Babies with Gestational age >32weeks and/or birth weight > 1500 grams, congenital malformations and with surgical conditions were excluded from the study.

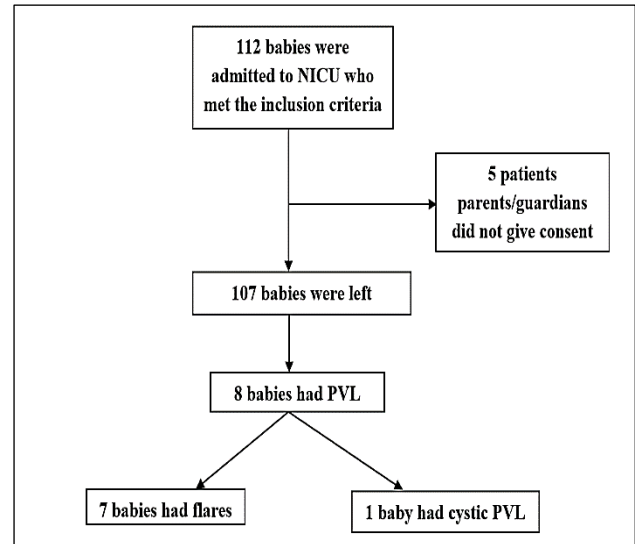


Figure 1: CONSORT diagram showing study flow

A detailed history, physical and systemic examination was carried out and recorded in a predesigned proforma at the time of enrollment. We tried to develop a cost-effective unit policy for screening of IVH and early PVL changes in VLBW babies by doing neurosonogram on day 3 and day 14 by a single well qualified radiologist using a standard (GE P6) ultrasonography machine equipped with curved linear array transducers of 8 MHz. CUS was done in both sagittal and coronal view through anterior fontanelle. De Vries grading was used for grading of PVL changes. Follow up cranial ultrasound was done weekly for the babies who were diagnosed to have PVL by day 14 of life, as a part of our unit policy. These were not included in present study as a part of the study protocol. Neurosonogram was not repeated for the babies with normal initial scans unless clinically indicated, in view of cost implications.

Statistical methods

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0.

RESULTS

Out of total 104 cases, 8 developed periventricular leukomalacia. Thus, the incidence was found to be 7.7%. Amongst these 8 cases, 7(87.5%) had Grade I periventricular leukomalacia and showed flares on cranial ultrasound whereas 1 (12.5%) baby had cystic periventricular leukomalacia as per De vries classification.

Table 1: Types of PVL changes.

PVL changes	Number of Cases	Percentage
Flares	7	87.5
Cysts	1	12.5
Total	8	100

Risk factor for PVL

It was seen that birth weight < 1000 grams (OR0.006; CI:0.00-0.50; P value 0.023) and sepsis (OR 80.9; CI:1.65-3947.6; p value 0.024) were found to be significantly associated with increased risk of PVL. Out of 8 babies who had PVL, it was seen that IVH was present in 3 babies. Amongst them, one baby had Grade I IVH, one had Grade II IVH and one had Grade III IVH. This was not found to be statistically significant (p value 0.142).

Table 2: Risk factors for PVL.

	Odds ratio	p value	95% Confidence interval
Gestational age ≤30 weeks	9.56	0.13	0.51-178.02
Birth weight ≤1000 grams	0.006	0.02	0.00-0.50
Hypertensive disorders of pregnancy	1.93	0.57	0.18-19.63
Resuscitation required	0.49	0.73	0.00-28.97
Invasive ventilation	3.67	0.50	0.08-164.47
Hypotension and use of inotropes	1.10	0.91	0.16-7.18
Sepsis	80.95	0.02	1.65-3947.69
Haemodynamically significant pda	23.58	0.06	0.87-637.68

Outcome

In the babies having PVL, 6(75%) babies out of 8 were discharged and 2 (25%) babies died during the hospital course. The mean duration of hospital stays in babies having PVL changes was seen to be 47.8 days whereas in babies not having PVL it was seen to be 35.9 days.

Table 3. Outcome of babies with PVL.

	PVL present	PVL absent	Total
Discharge	6	88	94
Mean duration of hospital stay (days)	47.80	35.90	36.90
Discharge again medical advice	0	5	5
Death	2	3	5
Total	8	96	104

DISCUSSION

The incidence of periventricular leukomalacia in VLBW babies was found to be 7.7%. Out of them 7(87.5%) babies had periventricular flares and 1(12.5%) baby had cystic changes. This was comparable to studies done by Silveira RC et al (7%-26%), Lee HJ et al (3-4%), Zupan V et al (9.2%) and Stevenson DK et al (5-15%).⁷⁻¹⁰ It was seen that lower gestational age was significantly associated with PVL. In present study 36 babies had gestational age <30 weeks, out of them 6(16.7%) babies had PVL changes (OR6.6; CI:1.15-31.42; p value 0.012). The mean gestational age in present study was found to be 30.1+1.4 weeks. This was in consensus with studies done by Barria and Flandez where they found that gestational age was inversely related to the incidence of PVL and that there was an increased risk for PVL in extreme prematurity and extremely low birth weight babies.¹¹

In another study done by Al Tawil KI et al, it was seen that lesser gestational age was associated significantly with incidence of PVL.¹² Multivariate analysis in present study showed no association (OR9.56; CI:0.5-178.02-p value 0.130).

Sepsis (both culture positive and negative) was seen in 32 babies out of 104. Of them 7(21.8%) babies developed PVL (OR 19.88;CI:2.33-169.69;p value <0.001).This was found comparable to study done by Tsuji M et al where he found that neonatal sepsis and septic shock is a major risk factor for PVL.¹³ In another study done by Silveira RC et al neonatal sepsis(OR 11.6;CI:1.42-94.9;p value 0.02) was found to increase the risk for PVL in VLBW babies.⁷ Multivariate analysis done in present study also showed that neonatal sepsis increases the risk of PVL in very low birth weight babies (OR80.9;CI:1.65-3947.6;p value 0.027).

It was seen in present study that out of 8 babies who developed PVL, 6 (75%) babies were discharged and 2 (25%) babies had mortality. Babies having PVL had a prolonged hospital stay compared to those who did not have PVL. The mean duration of hospital stays in babies having PVL was found to be 47.8 days and in those not having PVL was 35.9 days. The overall mean was 36.8 days. The study was intended to pick up early PVL changes and long term follow up of these babies was not a part of the study.

CONCLUSION

Early PVL is one of the major form of brain white matter injury that affects premature infants and it is associated with subsequent development of cerebral palsy, intellectual impairment and visual disturbances. The greatest risk for developing PVL is under 32 weeks of gestational age. The incidence of early periventricular leukomalacia is around 7.7% in our tertiary care centre. Risk of periventricular leukomalacia is increased in

babies with birth weight <1000grams and neonatal sepsis. Early recognition and timely intervention could help in parental counselling and knowing the long-term outcomes.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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