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Original Research Article

Intraventricular haemorrhage in very preterm neonates

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ABSTRACT

Background: The objective of the current study was to evaluate the incidence of intraventricular haemorrhage and its associated risk factors in preterm neonates.
Methods: This cohort study done at Neonatal Intensive Care Unit of a tertiary care hospital in south India enrolled 104 preterm neonates with either gestational age <32weeks and/or birth weight <1500 grams at birth. These babies were serially screened for intraventricular haemorrhage by doing a neurosonogram on day3 and day 14 of life.
Results: Incidence of IVH was found to be 18.2%. Amongst these cases 52.6% babies had Grade I, 36.8% babies had Grade II and 10.6% babies had Grade III intraventricular hemorrhage with ventriculomegaly, as per Papile grading system. It was seen that hypotension needing use of inotropes and neonatal sepsis were significantly associated with IVH.
Conclusions: The incidence of IVH in babies born with gestational age <32weeks and/or birth weight <1500 grams was 18.2% in our study. Neonatal sepsis and hypotension requiring use of inotropes were found to be the significant risk factors in this population.

Keywords: Intraventricular haemorrhage, Incidence, Risk factors

INTRODUCTION

Approximately 12.8% of newborns are born premature.[1] Preterm neonates are at risk for brain injury. Of these children more than 10% will sustain neurological injuries leading to significant learning disabilities, motor developmental delay, cerebral palsy, seizures and mental retardation.[2]

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 of intraventricular haemorrhage is important for optimal treatment, and neurological outcome.[3] 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 survivors are at great risk for neurodevelopment impairments.[4]

IVH is a common injury in preterm brain, originating in the subependymal germinal matrix. The incidence and severity of IVH increase with decreasing gestation. The incidence of IVH in very low birth weight infants (<1500g) has declined from 40–50% in the early 1980s to 20% in the late 1980s.[5] In neonates weighing 500–750g, IVH occurs in about 45%.[6] It is seen that most IVH are evident by 3rd day of life but they can develop any time during the first 2 weeks of life.[7] Although IVH continues to be a major problem of premature infants in modern neonatal intensive care units worldwide, there are very few studies from India reporting the present incidence of

this dreadful condition which is seen so often in our day to day practice.

It is also important to assess the quality of care and know the outcome of these babies in terms of neurological injury. Hence, we undertook this study to evaluate intraventricular haemorrhage in terms of its incidence and associated risk factors.

METHODS

This cross-sectional study was conducted at Neonatal Intensive Care Unit, Department of Paediatrics, Narayana Hrudayalaya Hospital, Bangalore, on all preterm neonates with either gestational age <32weeks and/or Birth weight <1500 grams within the period 1st November 2013 to 30th April 2015. Neonates with major congenital malformations and surgical conditions were excluded from the study.

A detailed history, physical and systemic examination was carried out and recorded in a predesigned proforma at the time of enrolment. In case of outborn neonates detailed antenatal, natal and postnatal history was taken. For inborn babies, type of delivery and any complications in the mother were recorded.

Resuscitative measures were done according to standard NRP guidelines 2010. In all neonates, Apgar score at 1 minute and 5 minutes was assessed. Gestational age assessment, in completed weeks, was done on the basis of the mother's last menstrual period as confirmed or modified where necessary by routine early antenatal ultrasound examination. All babies admitted to the NICU who met the inclusion criteria were examined daily in detail for the various systemic findings, laboratory and radiological findings and all the data was entered into the proforma by a study physician.

Babies were monitored for various complications like respiratory distress syndrome, necrotizing enterocolitis, early onset sepsis, haemodynamically significant patent ductus arteriosus and were treated with oxygen, intravenous fluids, antibiotics, inotropic support, ventilator support and surfactant as and when required.[8,9] Investigations like haemoglobin, packed cell volume and platelets were done as and when required. Septic work up with total leukocyte count, absolute neutrophil count, serum C reactive protein and blood culture were done when indicated.

Radiological assessment was undertaken with serial chest X rays and abdominal X rays as directed by the condition. 2D echocardiography was done according to baby condition. Transient metabolic disturbances with blood glucose, serum calcium, electrolytes and arterial blood gases (ABG) were done and interpreted when required.

We tried to develop a cost-effective unit policy for screening of IVH in these 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. Papile grading system (1978) for IVH was followed with Grade I showing isolated germinal matrix haemorrhage, Grade II showing IVH without ventricular dilatation, Grade III showing IVH with ventricular dilatation and Grade IV showing IVH with parenchymal haemorrhage.

Follow up cranial ultrasound was done weekly for the babies who were diagnosed to have IVH 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.

Taking the incidence of IVH in babies born <32weeks to be (p)=15% as seen in previous studies with 95% confidence limits and precision error of estimation (d) = 0.07, the sample size was estimated to be 100 using the formula ($Z^2 \times p \times q)/d^2$), where z = 1.96 (95% Confidence Interval), p = expected proportion, d=margin of error and q = 1-p.)

Statistical analysis

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0. Continuous variables were presented as mean±SD or median if the data was unevenly distributed. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student's t test. Nominal categorical data between the groups was compared using Chi-square test or Fisher's exact test as appropriate. Binary logistic regression analysis was performed to determine significant independent variables associated with an increased risk of IVH. Adjusted odds ratio (OR) and their 95% confidence intervals (CI) were calculated. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

An informed written consent was obtained from parents or guardians in the language they understood. Parents were allowed to opt out from the study at any time.

RESULTS

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 1of life and lost to follow up. So, 104 babies were finally taken into the study.

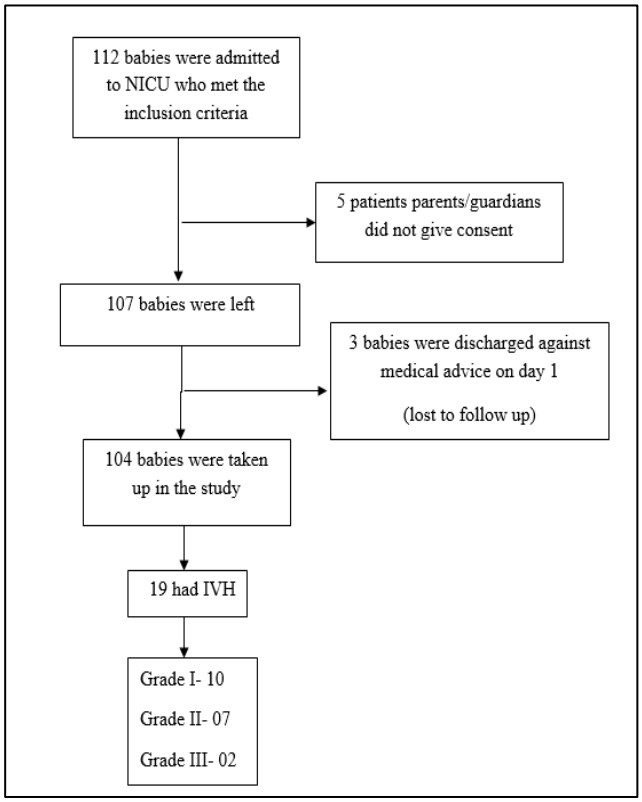

Figure 1: Flow chart depicting the inclusion of study subjects and outcome.

Incidence of Intraventricular Haemorrhage

Out of 104 babies who were included in the study, 19 babies developed intraventricular haemorrhage i.e the incidence was found to be 18.2%.

Amongst these cases 10 (52.6%) babies had Grade I, 7 (36.8%) babies had Grade II and 2 (10.6%) babies had Grade III intraventricular hemorrhage with ventriculomegaly, as per Papile grading system.

These two babies with Grade III IVH initially had Grade II IVH on Day 3 of life which later progressed to Grade III IVH with ventriculomegaly in scan done on Day 14 as per study protocol.

Risk Factors

Various factors were assessed for their association with IVH. It was seen that gestational age <30 weeks 16/19(84.2%) (p value <0.001), birth weight<1000grams 12/19(63.1%) (p value <0.001), premature rupture of membranes 13/19(68.4%) (p value 0.003), hypertensive disorders of pregnancy 17/19(89.4%) (p value <0.001) were significantly associated with IVH on univariate analysis.

Resuscitation required at birth in the form of either positive pressure ventilation and/or chest compressions was associated with increased risk of IVH (p value <0.001).

Babies having 5 min Apgar score <7/10 were found to have increased risk of IVH (p value <0.001). The mean 5-minute Apgar score in babies having IVH was found to be 5.94±0.84.

Other factors which were found to be significantly increasing the risk of IVH were hypercarbia with PaCO2 >50mmHg on arterial blood gas (p value <0.001) and invasive ventilation (p value <0.001).

Hypotension with use of inotropes 18/19(94.7%) (p value <0.001), neonatal sepsis (both culture positive and negative) 16/19(84.2%) (p value <0.001), respiratory distress syndrome (p value <0.001) and haemodynamically significant PDA 13/19(68.4%) (p value 0.001) were found to increase the risk of IVH significantly.

Acidosis with pH<7.3 was significantly associated with IVH (p value <0.001). Hyperglycemia (p value 0.001), hyperkalemia (p value <0.001), and thrombocytopenia (p value 0.001) also independently increased the risk of IVH in VLBW babies.

Multivariate Analysis

Table 2 represents the multivariate analysis for the various risks factors. It was seen that neonatal sepsis (OR13.0; CI:1.40-120.96; p value 0.024) and hypotension (OR34.7; CI:2.14-562.25; p value 0.013) were found to be significantly associated with increased risk of IVH.

Outcome

The mean length of hospital stays in babies having IVH was 58.42+36.70 days and overall length of stay was found to be 36.87+25.03 days whereas mean length of stay in babies not having IVH was found to be 32.05+18.70 days.

In the babies having IVH, 13 (68.4%) babies out of 19 were discharged. 3 (15.8%) babies were discharged against medical advice and 3 (15.8%) babies died during the hospital course. Out of them 2 babies had Grade II IVH and 1 baby had Grade I IVH. The cause of death in these babies was attributed to neonatal sepsis.

Table 1: Risk factors seen in the IVH and non IVH groups.

Risk factor	IVH present (n=19) (%)	IVH absent(n=85) (%)	p value
Gestational age ≤30 weeks	16 (84.2)	20 (23.5)	<0.001
Birth weight ≤ 1000 grams	12 (63.1)	9 (10.5)	<0.001
Premature rupture of membranes	13 (68.4)	27 (31.7)	0.003
Hypertensive disorders of pregnancy	17 (89.4)	32 (37.6)	<0.001
Vaginal delivery	4 (21.0)	36 (42.3)	0.084
Resuscitation required at birth			
Positive pressure ventilation	18 (94.7)	38 (44.7)	0.001
Chest compressions	8 (42.1)	4 (4.7)	0.001
5 Min apgar score <7	16 (84.2)	10 (11.7)	<0.001
Hypercarbia	16(84.2)	6 (7.0)	0.001
Invasive Ventilation	18 (94.7)	25 (29.4)	<0.001
Hypotension	18 (94.7)	30 (35.3)	<0.001
Neonatal Sepsis	16 (84.2)	16 (18.8)	<0.001
Haemodynamically significant PDA	13 (68.4)	9 (10.5)	0.001
Respiratory distress Syndrome	19 (100)	28 (32.9)	<0.001
Acidosis (Metabolic and Respiratory)	19 (100)	40 (47.0)	<0.001
Hyperglycemia	13 (68.4)	1 (1.1)	0.001
Thrombocytopenia	16 (84.2)	13 (15.2)	0.001

Table 2: Multivariate analysis of various risk factors assessed.

	Odds ratio	P value	95% confidence interval
Gestational age ≤30 weeks	5.49	0.164	0.50-60.21
Birth weight ≤1000 grams	0.40	0.517	0.02-6.51
Hypertensive disorders of pregnancy	6.36	0.150	0.51-79.02
Resuscitation required at birth	1.98	0.693	0.06-57.37
Invasive ventilation	7.10	0.224	0.30-168.08
Hypotension	34.71	0.013	2.14-562.25
Neonatal sepsis	13.02	0.024	1.40-120.96
Haemodynamically significant PDA	9.64	0.060	0.90-102.31

DISCUSSION

In present study the incidence of intraventricular haemorrhage in VLBW babies was found to be 18.2%. Out of them 52.6% babies had Grade I intraventricular haemorrhage, 36.8% babies had Grade II intraventricular haemorrhage and 10.6% had Grade III IVH. This was comparable to other studies done earlier by Barria and Flandez and Sergio TM et al.[10,11] Multivariate analysis in present study showed that hypotension was significantly associated with IVH (OR 27.8; CI:1.64-470.8; p value 0.021). This was in consensus with a study done by Ballabh P in which hypotension was found to be a significant risk factor for IVH.[12] In another study done by Linder N et al it was seen that use of inotropes was associated with increased risk of IVH (p value 0.06).[13] Hypotension was also found to be significantly associated with IVH in a study done by Sarkar S et al.[14]

Sepsis (both culture positive and negative) was seen in 32 babies out of 104. Of them 16(50%) babies developed IVH (OR 23.0; CI:5.97-88.52; p value <0.001). This was found comparable to study done by Ballabh P where he found that neonatal sepsis is a major risk factor for IVH.[12] In another study done by Linder N et al sepsis was found in 7 babies out of 36 in IVH group with a p value 0.04.[13]

Sarkar S et al and Lee J Y et al also showed in their studies that neonatal sepsis is a major risk factor for IVH.[14,15] It was also shown by Adegoke SA et al that neonatal sepsis brings an increased risk for IVH in VLBW babies.[16] Hence neonatal sepsis and hypotension in these preterm babies pose the infant at great risk of intraventricular haemorrhage which increases the morbidity and mortality in this population significantly.

CONCLUSION

The incidence of IVH in babies born with gestational age <32weeks and/or birth weight <1500 grams was 18.2% in present study. Neonatal sepsis and hypotension requring use of inotropes were found to be the significantly risk factors in this population.

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

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