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RESEARCH ARTICLE

RISK FACTORS AFFECTING SEVERITY OF INTRAVENTRICULAR HEMORRHAGE IN PRETERM INFANTS OF AN NICU OF A TERTIARY CARE CENTRE

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Abstract

Background: As severe germinal matrix intraventricular haemorrhage (GM-IVH) causes neurological sequelae in 50–75% of preterm survivors, it is still a major global public health problem. [1].By studying the association and severity with risk factors for IVH in preterms we can make preventive measures for the same.

Objective: The purpose of this study is to identify the risk factors associated with the development IVH in the preterm infants of an NICU of a tertiary care centre and the relationship of the severity of disease and these risk factors.

Methods: It is a retrospective study. A total of 160 premature neonates of gestational age ≤34 weeks were examined by cranial ultrasound (CUS) for detection of GM-IVH among the babies admitted in neonatal intensive care unit of a tertiary teaching hospital at Pune, Maharashtra. The babies were divided into two groups: GM-IVH and non-IVH. The association and severity of neonatal and maternal risk factors were analysed.

Results: In our study, out of 160 neonates, 75 neonates (46.8%) developed intraventricular haemorrhage, of which 8% developed severe IVH (grade 3 and 4). Use of inotropes ($p = 0.008$), surfactant ($p < 0.0001$), blood transfusions(p=0.005),HsPDA(p=0.006) were highly significant for developing intraventricular haemorrhage.

Conclusions: Clinicians and healthcare policy makers should consider these factors during decision-making; coverage of (complete) antenatal steroid therapy, early diagnosis and treatment of PDA with paracetamol/ibuprofen, delayed cord clamping in labour room to prevent hypotension hence, use of inotropes and boluses can prevent GM-IVH in preterms.

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Introduction:-

Since severe intraventricular haemorrhage (IVH) is associated with neurological sequelae in 50–75% of preterm survivors, it continues to be a major global public health problem [1].

The development of IVH was detected in 23.7% of sonograms of infants with extremely low gestational age (GA) and very low birth weight (VLBW) in 2016, with severe IVH being present in 31.6% of these cases, according to the Neonatal Research Network of the National Institute of Child Health and Human Development (NICHD) [2]. Recent data from the Korean Neonatal Network showed that theoverall incidence of IVH in preterm and VLBW

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infants was 42.5%, while severe IVH was10.3% [3], and few studies in the Middle East have reported that severe IVH occurs in 8.1%and as high as 11% among high-risk infants [4],[5]. Various studies looked into the risk factors for IVH in premature newborns. It was discovered that prenatal steroid medication is linked to a reduction in the incidence of severe IVH [6]. Several techniques, including the preventive use of indomethacin for HsPDA (hemodynamically significant patent ductus arteriosus), restricting attempts at intubation for very preterm infants, and sparingly using inotropes, have been utilised to lower the rate of severe IVH [7].

Therefore, the purpose of this study is to identify trends and maternal and neonatal risk factors for intraventricular haemorrhage (IVH) incidence and severity among infants born between 24 and 34 weeks.

Aim:-

To identifyrisk factors affecting severity of intraventricular hemorrhage in preterms of an NICU of a tertiary care center.

Objectives:-

1. To determine the incidence, trends, maternal and neonatal risk factors of intraventricular haemorrhage (IVH) among preterm infants of an NICU of a tertiary care centre
2. To assess the severity of intraventricular haemorrhage due to each risk factor.

Materials And Methods:-

1. Study design- This was a hospital based retrospective study.
2. Study site-Study was conducted in the NICU attached to a tertiary care hospital during the month of March 2022.
3. Sample size-A time bound sample of 160 preterm neonates formed the study.
4. Inclusion and Exclusion criteria- Preterm infants less than 24 weeks were excluded from the study.
5. Data Source- health record of these 160 neonates were used. Data regarding the risk factors associated with intraventricular haemorrhage (IVH) was collected and then entered in Microsoft Excel spreadsheets 2016. Statistical analysis was done on IBM SPSS STATISTICS VERSION 20.Categorical variables were taken in the form of frequencies and percentages. Distribution was represented by pie charts or bar graphs. Continuous variables were expressed in the descriptive statistics tables as means, standard deviation and range. The categorical variables in the groups IVH and non IVH were cross tabulated using chi square T test. Further IVH was classified as mild(grade 1 and 2) and severe(grade 3 and 4).P value < 0.05 was considered significant and p value < 0.01 was considered highly significant.

Papile's classification of IVH(intraventricular haemorrhage)/ GMH(germinal matrix haemorrhage) [8]:

Severity of GMH/IVH	Description of findings
I	Isolated GMH
II	IVH without ventricular dilatation
III	IVH with ventricular dilatation
IV	IVH with parenchymal haemorrhage

Results:-

Table 1:- Distribution based on grades of GMH/IVH:

Grade of IVH	Number	%
Grade 1	31	41.3
Grade 2	38	50.7
Grade 3	4	5.3
Grade 4	2	2.7

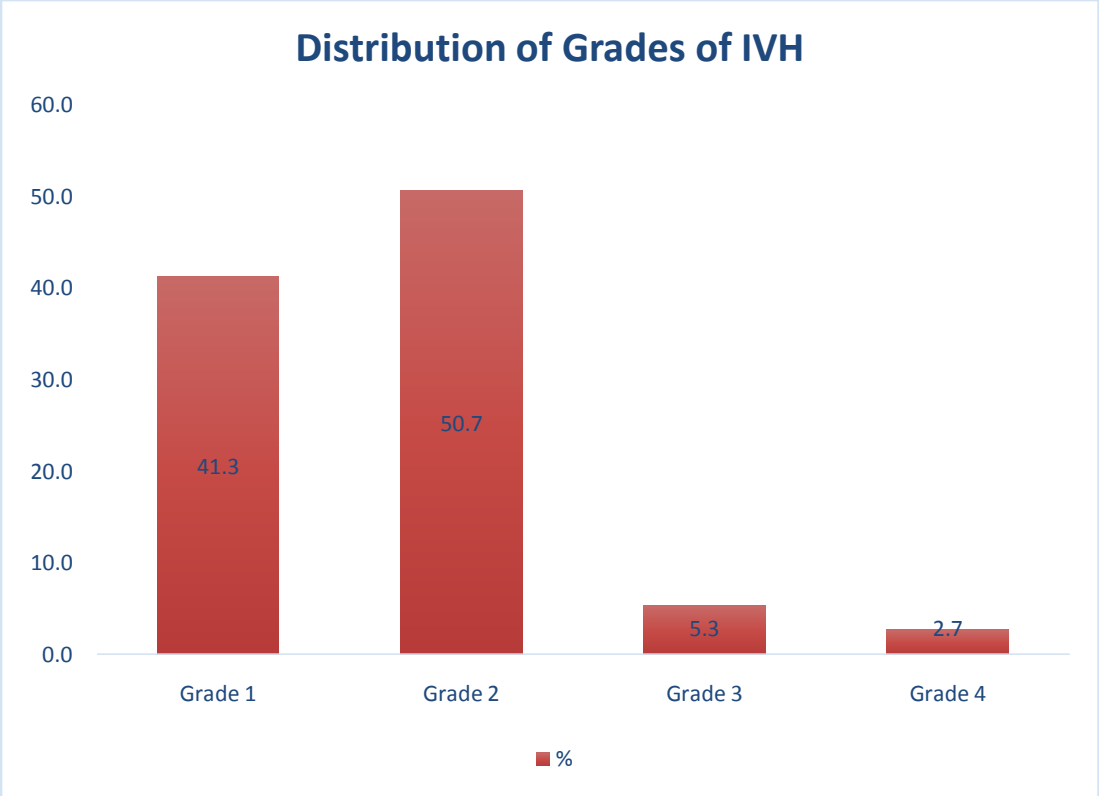

Table 2:- Distribution of foetal risk factors between absence and presence of intraventricular haemorrhage(IVH).

FOETAL RISK FACTORS			IVH absent (N=85)	IVH present (N=75)	Total	P value
Gender	Female	Count	49	34	83	0.154
		%	57.6%	45.3%	51.9%	
	Male	Count	36	41	77	
		%	42.4%	54.7%	48.1%	
Gestation	Greater than 32 weeks	Count	39	21	60	0.023
		%	45.9%	28.0%	37.5%	
	Below 32 weeks	Count	46	54	100	
		%	54.1%	72.0%	62.5%	
APGAR at 5 Minutes	> 7	Count	68	55	123	0.351
		%	80.0%	73.3%	76.9%	
	<7	Count	17	20	37	
		%	20.0%	26.7%	23.1%	
Blood transfusion	Not received	Count	68	44	112	0.005
		%	80.0%	58.7%	70.0%	
	Received	Count	17	31	48	
		%	20.0%	41.3%	30%	
Sepsis	Absent	Count	55	36	91	0.038
		%	64.7%	48.0%	56.9%	
	Present	Count	30	39	69	
		%	35.3%	52.0%	43.1%	
Inotropes	Not given	Count	64	41	105	0.008
		%	75.3%	54.7%	65.6%	
	Given	Count	21	34	55	
		%	24.7%	45.3%	34.4%	
Mechanical ventilation	Not given	Count	74	54	128	0.028

		%	87.1%	72.0%	80.0%	
	Given	Count	11	21	32	
		%	12.9%	28.0%	20.0%	
Bubble continuous positive airway pressure(CPAP)	Not given	Count	26	8	34	0.003
		%	30.6%	10.7%	21.3%	
	Given	Count	59	67	126	
		%	69.4%	89.3%	78.8%	
Respiratory distress syndrome (RDS)	Absent	Count	26	8	34	0.002
		%	30.6%	10.7%	21.3%	
	Present	Count	59	67	126	
		%	69.4%	89.3%	78.8%	
Hemodynamically significant patent ductus arteriosus(hsPDA)	Present	Count	71	48	119	0.006
		%	83.5%	64.0%	74.4%	
	Absent	Count	14	27	41	
		%	16.5%	36.0%	25.6%	
Fetoplacental insufficiency	Absent	Count	77	66	143	0.617
		%	90.6%	88.0%	89.4%	
	Present	Count	8	9	17	
		%	9.4%	12.0%	10.6%	
Uteroplacental insufficiency	Present	Count	55	55	110	0.315
		%	64.7%	73.3%	68.8%	
	Absent	Count	30	20	50	
		%	35.3%	26.7%	31.3%	
Surfactant	Not given	Count	67	37	104	<0.0001
		%	78.8%	49.3%	65.0%	
	Given	Count	18	38	56	
		%	21.2%	50.7%	35.0%	

Table 3:- Distribution of maternal risk factors between absence and presence of intraventricular haemorrhage(IVH).

MATERNAL RISK FACTORS			**IVH absent (N=85)**	**IVH present (N=75)**	**Total**	**P value**
Gravidity	Multigravida	Count	65	46	111	0.041
		%	76.5%	61.3%	69.4%	
	Primigravida	Count	20	29	49	
		%	23.5%	38.7%	30.6%	
Maternal corticosteroids	Not received	Count	8	5	13	0.575
		%	9.4%	6.7%	8.1%	
	Received	Count	77	70	147	
		%	90.6%	93.3%	91.9%	
Magnesium sulphate	Not received	Count	61	58	119	0.471
		%	71.8%	77.3%	74.4%	
	Received	Count	24	17	41	
		%	28.2%	22.7%	25.6%	
Pregnancy induced hypertension (PIH)	No	Count	65	60	125	0.703
		%	76.5%	80.0%	78.1%	
	Yes	Count	20	15	35	
		%	23.5%	20.0%	21.9%	
Preeclampsia	No	Count	67	61	128	0.843
		%	78.8%	81.3%	80.0%	
	Yes	Count	18	14	32	
		%	21.2%	18.7%	20.0%	
Eclampsia	No	Count	82_a	72_a	154	0.99
		%	96.5%	96.0%	96.3%	
	Yes	Count	3_a	3_a	6	

		%	3.5%	4.0%	3.8%	

Table 4:- Distribution of foetalrisk factors between mild and severe IVH:

FETAL RISK FACTORS			Mild IVH (N=69)	Severe IVH (N=6)	Total	P value
Gender	Female	Count	30	4	34	0.401
		%	43.5%	66.7%	45.3%	
	Male	Count	39	2	41	
		%	56.5%	33.3%	54.7%	
Gestation	Greater than 32 weeks	Count	19	2	21	1.00
		%	27.5%	33.3%	28.0%	
	Below 32 weeks	Count	50	4	54	
		%	72.5%	66.7%	72.0%	
APGAR at 5 Minutes	> 7	Count	53	2	55	0.04
		%	76.8%	33.3%	73.3%	
	<7	Count	16	4	20	
		%	23.2%	66.7%	26.7%	
Blood transfusion	Not received	Count	43	1	44	0.041
		%	62.3%	16.7%	58.7%	
	Received	Count	26	5	31	
		%	37.7%	83.3%	41.3%	
Sepsis	Absent	Count	34	2	36	0.676
		%	49.3%	33.3%	48.0%	
	Present	Count	35	4	39	
		%	50.7%	66.7%	52.0%	
Inotropes	Not given	Count	41	0	41	0.007
		%	59.4%	0.0%	54.7%	
	Given	Count	28	6	34	
		%	40.6%	100.0%	45.3%	
Mechanical ventilation	Not given	Count	52	2	54	0.048
		%	75.4%	33.3%	72.0%	
	Given	Count	17	4	21	
		%	24.6%	66.7%	28.0%	
Bubble continuous positive airway pressure (CPAP)	Not given	Count	8	0	8	1.00
		%	11.6%	0.0%	10.7%	
	Given	Count	61	6	67	
		%	88.4%	100.0%	89.3%	
Respiratory distress syndrome (RDS)	Absent	Count	8	0	8	1.00
		%	11.6%	0.0%	10.7%	
	Present	Count	61	6	67	
		%	88.4%	100.0%	89.3%	
Hemodynamically significant patent ductus arteriosus(hsPDA)	Present	Count	44	4	48	1.00
		%	63.8%	66.7%	64.0%	
	Absent	Count	25	2	27	
		%	36.2%	33.3%	36.0%	
Fetoplacental insufficiency	Absent	Count	62	4	66	0.149
		%	89.9%	66.7%	88.0%	
	Present	Count	7	2	9	
		%	10.1%	33.3%	12.0%	
Uteroplacental insufficiency	Absent	Count	51	4	55	0.654
		%	73.9%	66.7%	73.3%	
	Present	Count	18	2	20	
		%	26.1%	33.3%	26.7%	
Surfactant	Not Given	Count	34	3	37	1.00

		%	49.3%	50.0%	49.3%	
	Given	Count	35	3	38	
		%	50.7%	50.0%	50.7%	

Table 5:- Distribution of maternal risk factors between mild and severe IVH:

MATERNAL RISK FACTORS			Mild IVH (N=69)	Severe IVH (N=6)	Total	P value
Gravidity	Multigravida	Count	43	3	46	0.041
		%	62.3%	50.0%	61.3%	
	Primigravida	Count	26	3	29	
		%	37.7%	50.0%	38.7%	
Maternal corticosteroids	Not Received	Count	3	2	5	0.048
		%	4.3%	33.3%	6.7%	
	Received	Count	66	4	70	
		%	95.7%	66.7%	93.3%	
Magnesium sulphate	Not received	Count	53	5	58	1.00
		%	76.8%	83.3%	77.3%	
	Received	Count	16	1	17	
		%	23.2%	16.7%	22.7%	
Pregnancy induced hypertension (PIH)	No	Count	54	6	60	0.339
		%	78.3%	100.0%	80.0%	
	Yes	Count	15	0	15	
		%	21.7%	0.0%	20.0%	
Preeclampsia	No	Count	56	5	61	1.00
		%	81.2%	83.3%	81.3%	
	Yes	Count	13	1	14	
		%	18.8%	16.7%	18.7%	
Eclampsia	No	Count	66	6	72	1.00
		%	95.7%	100.0%	96.0%	
	Yes	Count	3	0	3	
		%	4.3%	0.0%	4.0%	

Our study included 160 preterm neonates of which 51.9% were female and 48.1% male children.Out of 160 neonates, 75 developed IVH, of which 33.3% developed right, 22.7% developed left and 44% developed bilateral IVH.Analysing severity, out of total 75 preterms, 41.3% and 50.7% developed grade 1 and 2 IVH (mild form) respectively ,5.3% and 2.7% grade 3 and 4 IVH (severe form)respectively.Gestational age was a significant factor to develop IVH (p=0.023) with 28% of greater than 32 weeks developing IVH and 72% below 32 weeks gestation develop IVH. Blood transfusion was highly significant risk factor (p=0.005) to develop IVH with 41.3% developing IVH who got blood transfusion. Use of inotropes(p=0.008), surfactants(p<0.0001), bubbleCPAP for oxygen support(p= 0.003), respiratory distress syndrome(p=0.002), HsPDA(p=0.006) were highly significant risk factors to develop IVH.

Sepsis (p=0.038) and mechanical ventilation(p=0.028) were also significant for developing IVH in preterms.

Assessing the severity,foetal risk factors like Apgar's at 5 minutes was significant for developing severe IVH(p=0.04), with 66.7% developing severe IVH when Apgar's were <7 at 5 minutes. Getting blood transfusion(p=0.041) mechanical ventilation(p=0.048) were significantly contributing to severe IVH. Use of inotropes was highly significant for severe IVH with p= 0.007.

In maternal risk factors, gravidity (p=0.041) came as a significant risk factor for developing IVH.

We found in those who received corticosteroids, 95.7% developed mild IVH, hence, corticosteroids can decrease severity of IVH.

Discussion:-

Preterm infants frequently experience GM-IVH, which can have serious consequences like cerebral palsy and mental impairment. Finding the risk factors for the development of GM-IVH and being ready for them are therefore crucial. There are many known risk factors for the occurrence of GM-IVH. Gender, absence of prenatal steroids, low APGAR scores at birth, mechanical ventilation, hemodynamically significant PDA, RDS, and blood product transfusions are among them[9].

However, in our study, there was no significant difference in gender, birth weight, preeclampsia, uteroplacental insufficiency, fetoplacental insufficiency.The factors such as gestational age and presence of PDA, blood transfusion,administration of surfactant and inotropes, respiratory distress syndrome, mechanical ventilation, oxygen support via bubble CPAP, sepsis, were statistically meaningful risk factors for development of GM-IVH. Given that birth weight is a less accurate indicator of foetal maturity than gestational age, this conclusion is simply understandable. It is undeniable that younger gestational age is associated with a higher risk for severe GM-IVH, which develops in the germinal matrix, an intensely vascularized glioblast tissue, as previous papers and our results have indicated. It can be explained in terms of its pathophysiology and anatomy. The subependymal area has a tight network of capillaries that is primarily supplied by the Huebner's artery and is present in children who were born before 32 weeks of gestation. The vessels will be distinguished after the germinal matrix involutes during 32 weeks of pregnancy. A unique combination of pathophysiological variables in preterm newborns renders them virtually defenceless to cerebrovascular damage.As decreasing gestational age, the autoregulation pressure range is narrower and lower. Certain situation like presence of PDAcould result in hypoperfusion-reperfusion state.[10]The absence or disruption of the autoregulation system in premature babies is a significant pathophysiological characteristic. This implies that changes in the systemic blood pressure have a direct impact on the cerebral blood flow. Alveolar rupture, RDS, inotropes, and mechanical ventilation of the newborn are triggers that can result in an ICH. Positive pressure breathing during endotracheal intubation raises central venous pressure, which may cause intermittently inadequate cerebral perfusion. Preeclampsia and other high-risk pregnancy conditions, however, were not linked to the emergence of GM-IVH in the current investigation. In preterm newborns, antenatal steroids dramatically decreased the percentage of severe IVH but not moderate IVH. These findings highlight the value of prenatal treatment, especially prenatal steroids, in preventing severe IVH.[11]

There are several limitations in our study. First, the population of our study was small in number. Second is a retrospective study from a single institution, although this also might be an advantage due to consistency of practice and expertise. Last, this study did not evaluate the neurodevelopmental outcome of patients.

Conclusion:-

Clinicians and healthcare policy makers should consider these factors during decisionmaking: coverage of (complete) antenatal steroid therapy, early diagnosis and treatment of hsPDA with paracetamol/ibuprofen, delayed cord clamping in labour room to prevent hypotension hence, reducing use of inotropes and boluses to prevent GM-IVH in preterm infants. Improving delivery practices can reduce severe IVH. Careful handling of these babies in NICU and better infection control can help us prevent sepsis.

In our country antenatal care still remains a challenge due to many reasons.Unmotivated couples towards family planning and maternal care, unsupportive family members, illiteracy are some challenges that we still face. By bridging the gap between community and health we can overcome them. We need health programmes focusing on preterm health, ASHA workers can help us bridge this gap by educating mothers and family members and mobilising them to health care centres for regular health check-up, mobile sonography services for ANC scans in distant villages can help in scanning high risk preterm babies.

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