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ORIGINAL ARTICLE

Intraventricalar Hemorrhage in Preterm Infants Identification of Risk Factors and Related Outcome

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Abstract

Background: **Intraventricular hemorrhage (IVH) is the most common intracranial hemorrhage in preterm newborns. The high incidence and problems made it important. Many etiologies and risk factors have been found. Newborns can get IVH.**

Methods: **This study included 100 neonates, 59% of cases were males and 41% cases were females. Gestational age ranged from 27 to 36 weak, with a mean of 31.9 ± 1.67 weak. The weight ranged from 750 g. to 2.93 kg, with a mean of 1.7 ± 0.44 kg. Trans cranial US was done on day 1, 3, and day 7 after delivery.**

Results: **The study found that IVH rates were significantly higher in males than in females, and that IVH rates were significantly higher in those who delivered normally than those delivered with cesarean section. Her IVH rate in neonates delivered out-of-hospital was significantly higher than in neonates delivered in-hospital. Regarding ventilator support, there was a large significant difference between the groups. Frequency of the IVH grades by cranial ultrasound (CUS). Grade I occurred in 12 (44.4%) neonates, grade II in 4 (14.8%) neonates, and grade III in 8 (29.6%) neonates. Grade IV occurred in 3 (11.1%) neonates.**

Conclusion: **IVH developed in (27%) of cases from 1st to 7th day postnatal, with mean gestational age was 30.03 weeks, from which 20 (74.1%) were males and 7 (25.9%) females. Prematurity, low birth weight, and excessive respiratory support are major risk factors for IVH.**

Keywords: Intraventricular hemorrhage, Perinatal, Preterm, Risk factors

1. Background

Intraventricular hemorrhage (IVH), is the most common cranial acute complication of neonates.[1] This event is strongly related to the continued presence of germinal matrix (GM). Germinal matrix hemorrhage (GMH) is the dominant kind of cerebral bleeding observed in neonates, primarily affecting neonates. The significance of the lesion is related not only to its elevated occurrence but also to the associated complications.[2]

In recent years, the incidence of IVH has decreased prematurely to varying degrees in most neonatal centers. He has two reasons. First, incidence closely correlates with preterm birth degree, and second, the survival rate of the smallest preterm infants is rising.[3]

GMH/IVH occurs primarily in preterm infants. Currently, the incidence is 15−20% in neonates born before 32 weeks of gestational age (GA), but is rare in term neonates.[4]

Maternal factors like infection/inflammation and bleeding, prenatal steroid deficiency, external

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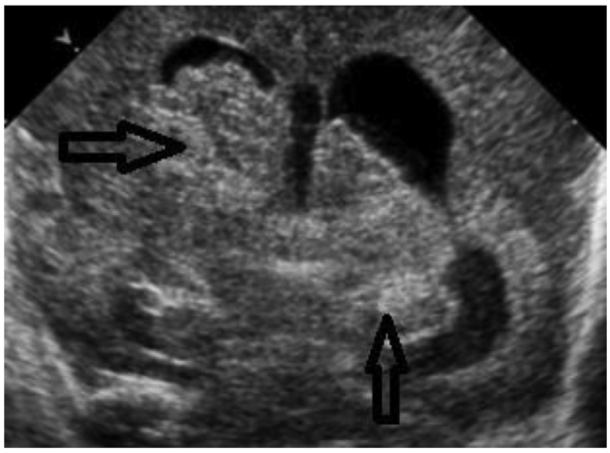

Fig. 1. Coronal and Sagittal ultrasound scan of neonatal brain shows hyperechoic blood density at the caudothalamic groove (open black arrows) denoting germinal matrix grade I intracranial hemorrhage.

factors like delivery method and transfer to another hospital, and increasingly recognized genetic factors can cause IVH. Factors are identified. Influencing neonatal IVH causes.[5]

The subependymal GM develops IVH with cerebral neural progenitor cells between 10 and 20 weeks GA. Many thin-walled matrix vessels bleed. IVH development involves intravascular, vascular, and extravascular components. Low birth weight, preterm, respiratory distress syndrome (RDS), pneumothorax, ventilator use, and hypoxia are the most risks. Identifying and screening at-risk infants for IVH is essential[6] (Fig. 1).

Trans cranial ultrasonography is best for ventricular hemorrhage screening and diagnosis. MSCT and MRI are appropriate but costly and require transportation to imaging centers.[7]

Periventricular infarction, posthemorrhagic hydrocephalus, cerebellar injury, and leukomalacia all occur after IVH and increase infant morbidity, death, and neurodevelopmental damage[2] (Figs. 2 and 3).

Prematurity, low birth weight, poor Apgar score, RDS that requires mechanical breathing, high oxygen consumption in the first 24 h, pneumothorax, hypotension, and acidosis are IVH risk factors. The main PV-IVH risk factor is preterm.[8,9]

Pulmonary disease, cyanotic coronary heart disease, urinary tract infection, sickle cell anemia, and low oxygen levels affect the fetus. Blood flow to the uterus can be affected by hypertension and diabetes,[10] At least 25% of infants have no ventricular hemorrhage risk factors.[11]

History, clinical signs, birth-weight measures, and IVH risks suggest cerebral hemorrhage. IVH has no characteristic symptoms,[12] making IVH diagnosis challenging based on clinical criteria.[13] Intracranial hemorrhages are most common in the first 3 days. IVH after day 5 is rare.[14]

Cranial ultrasound is recommended for IVH screening in premature infants less than 34 weeks gestation through the anterior fontanel.[15] Infants less than 1.000 g are at high risk and should have a cranial ultrasound within the first 3–5 days of age, as about 75% of lesions will be detectable.[16]

Transcranial ultrasonography is usually performed on postnatal days 1, 3, 7, 14, 30, and 60 (or at discharge) for infants under 32 weeks old (or birth weight <1500 g). However, in severely unwell newborns with very low birth weight, do the first cranial ultrasound (CUS) within 24 h of delivery to detect quickly growing ventricular dilatation and recommend early CUS follow-up. GM-IVH infants

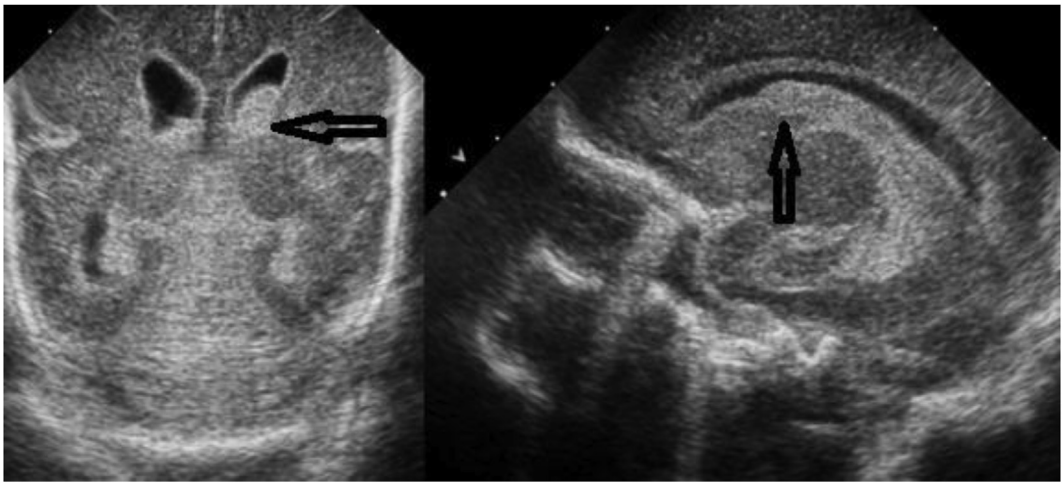

Fig. 2. Coronal ultrasound scan of neonatal brain shows bilateral intra ventricular hyper echoic blood hemorrhagic changes (open black arrows) with moderate dilated both lateral ventricle prominent at the left side.

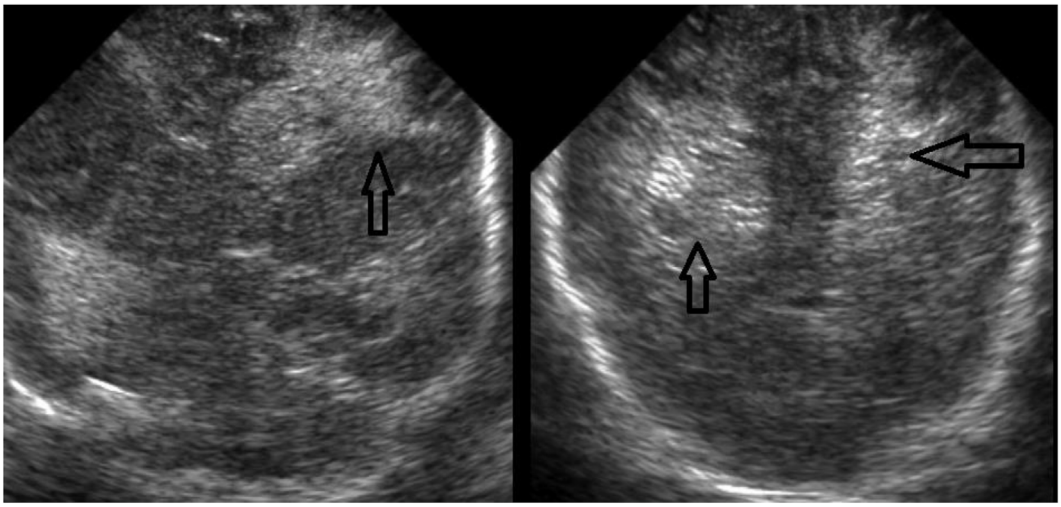

Fig. 3. Coronal scans of neonatal brain ultrasound shows periventricular extension of the hemorrhagic changes seen as hyperechoic pattern of the brain parenchyma prominent at the frontal lobe (open black arrows).

need more frequent CUS to check hydrocephalus and periventricular ischemia.[11] Cranial ultrasonography is standard for GM-IVH detection in preterm babies.[17]

Computed tomography (CT) scans were done if CUS showed a midline shift.[18] CT is readily available and has excellent image resolution. CT has high brain parenchyma anatomical resolution. It is also operator-independent, cheap, and fast compared to MRI.[19]

CT is still useful for newborns hospitalized after a delivery trauma and suspected extra-axial hemorrhage. In such cases, CUS may miss these hemorrhage unless they are large and associated midline shift. CT may be more accessible than MRI.[20]

MRI is the best radiological tool for examining newborns and children's brains. MRI is sensitive to intracranial hemorrhage (ICH) and better than CT for birth trauma development.[21]

This work is aimed to determine the incidence and risk factors for IVH in preterm infants admitted to the neonatal intensive care unit (NICU).

2. Methods

This follow-up cohort study was conducted with 100 preterm infants admitted to the NICU from March 2021 to May 2022.

This study included 100 preterm newborns, 59 (59%) cases were males and 41 (41%) cases were females. GA ranged from 27 to 36 weeks, with a mean of 31.9 ± 1.67 weeks. Birth weight ranged from 750 g, to 2.93 kg with a mean of 1.7 ± 0.44 kg.

The studied cases were divided into two groups by CUS findings:

Group I: Neonates with no evidence of ventricular hemorrhage by cranial ultrasound from birth to the end of postnatal day 7, in about 73 of 100 (73%) cases.

Group II: Neonates with IVH by cranial ultrasound from birth to the end of postnatal 7th day, it about 27 cases out of 100 cases (27%).

2.1. All neonates had been subjected to the following

(1) Complete medical-history taking:
Prenatal medical history: mother's age, GA, medical issues (hypertension, infections, diabetes, anemia, heart disease), drug use, abdominal trauma, preterm membrane rupture, etc.
(2) Postnatal medical history: Apgar scores, resuscitation data, patient manipulations, delivery trauma.
(3) Clinical examination

General examination:

(a) Ballard score for GA assessment.
(b) Weight, length and head circumference measurements.
(c) Vital signs: (Temperature, Respiratory rate, Heart rate, Blood pressure, oxygen saturation).
(4) Neurological exam: awareness level, irritability, head circumference, ant. fontanel, tone, involuntary movements.
(5) Ultrasonography examination:

In all cases, transcranial ultrasound was performed through the anterior fontanelle in both the

coronal and sagittal planes. Ultrasonography of the brain was performed on days 1, 3, and 7 postnatal. In addition, CUS was performed for cases with symptoms or signs of IVH during these days.

(6) Lab. tests:
Complete blood count.
Coagulation profile.
Total serum bilirubin.
Arterial blood gases and Serum electrolytes (Na and K).

2.2. Ethical approval

An approved was obtained from the Ethical Research Board before the study proceeding, all parents assigned informed consent after explanation of the procedure.

2.3. Statistical analysis

Statistical analysis of the present study was conducted, using the mean, standard deviation and Linear Correlation Coefficient [r] by SPSS V.20. The accepted level of significance in this work was stated at 0.05 ($P < 0.05$ was considered significant and highly significant result was considered if $P < 0.001$).

3. Results

Neonates males had significantly higher IVH rates than females, and normal delivery had significantly higher IVH rates than cesarean section delivery. The IVH rate in outside delivered neonates was significantly higher than in neonates delivered in-hospital (Table 1).

There was insignificant statistical effect between both groups as regard the maternal risk factors (Table 2).

A significant inverse link exists between IVH and low birth weight, particularly in newborns under 1500 g (Table 3, Fig. 4).

The risk factors for various respiratory support in developing IVH. There are large significant differences between groups with respect to ventilatory support, saturation variation, and surfactant administration (Table 4, Fig. 5).

There was significant difference between groups in PCO_2 and high significant difference in HCO_3 (Table 5, Fig. 6).

CUS grade frequency of IVH was 12 (44.4%) grade I, 4 (14.8%) grade II, eight (29.6%) grade III, and three (11.1%) grade IV. Occurred (Table 6, Fig. 6).

Mean value of time of occurrence of IVH 2.75 ± 1.25 days (range from 1 to 7 days) (Table 7, Fig. 7).

4. Discussion

IVH is the second leading cause of neonatal death after congenital abnormalities and the most prevalent postnatal finding in 20% of infants who die. Only preterm newborns account for 50–70%.[22]

A total of 100 patients were included in this study, 73 (73%) of whom had no IVH and a mean GA of 32.5 weeks. Twenty-seven (27%) neonates developed IVH between postnatal days 1 and 7, with a mean GA of 30.03 weeks, including 20 (74.1%) males and seven (25.9%) females.

IVH cases exhibited considerably decreased GA. There were 20 (74.1%) occurrences of GA less than or equal to 32 weeks. 7 (25.9%) 32 weeks. This supported Khodapanahandeh *et al*. Lower GA increased the probability of high-grade IVH. Roze *et al*. (2008)

Table 1. Demographic data of the studied cases.

Characters	Total no (%)	Group I no (%)	Group II no (%)	χ^2	*P*	Significance
Sex				6.48	0.01	S
Male	59 (59)	39 (66.1)	20 (33.9)			
Female	41 (41)	34 (83)	7 (17)			
MOD						
VD	32 (32)	18 (56.2)	14 (43.8)	9.65	0.002	HS[b]
CS	68 (68)	55 (80.8)	13 (19.2)			
Place of delivery						
In hospital	68 (68)	52 (76.4)	16 (23.6)	5.34	0.02	S[a]
Out hospital	32 (32)	21 (65.6)	11 (34.4)			
Multiple birth	17 (100)	12 (70.6)	5 (29.4)	2.24	0.02	S[a]

Neonates males had significantly higher IVH,i hemorrhage rates than females, and normal delivery had significantly higher IVH rates than CS, Cesarean section delivery. The IVH rate in outside delivered neonates was significantly higher than in neonates delivered in-hospital.

[a] Significant.
[b] Highly significant.

Table 2. Maternal risk factors in relation to intraventricular hemorrhage.

Maternal risk factor	Group I ($N = 73$) [n (%)]	Group II ($N = 27$) [n (%)]	χ^2	P
Maternal disease				
Diabetes mellitus	4 (5.5)	2 (7.4)	0.05	0.8190
Hypertension	2 (2.7)	2 (7.4)	0.52	0.4704
Anemia	5 (6.8)	1 (3.7)	0.01	0.9045
Cardiovascular disease	2 (2.7)	0	0.39	0.5335
Epilepsy	2 (2.7)	2 (7.4)	0.52	0.4704
Myasthenia graves	1 (2.7)	0	0.39	0.5335
Preeclampsia	5 (6.8)	4 (14.8)	0.42	0.5158
Antepartum hge	1 (2.7)	3 (11.1)	2.42	0.1198
Instrumental delivery	7 (9.6)	3 (11.1)	0.11	0.7394
PROM	19 (26)	7 (26)	0.01	0.9262

This table shows that there was insignificant statistical effect between both groups as regard the maternal risk factors.

Table 3. Relation between birth weight and intraventricular hemorrhage in studied neonates.

Weight	Total cases No	Group I ($N = 73$) [n (%)]	Group II ($N = 27$) [n (%)]	χ^2 test	P	Significance
<999 g	4	0	4 (14.8)	5.34	0.0207	S
1000–1499 g	41	25 (34.2)	16 (59.2)	17.07	0.0001	HS
≥1500 g	55	48 (65.8)	7 (26)	2.10	0.1474	NS

A highly significant inverse relationship was found between IVH, intraventricular hemorrhage and decreased birth weight, especially in neonates less than 1500 g.

revealed that IVH infant mortality was related with decreased GA. Low GA is linked to PV-IVH by Lee *et al*., 2010. Preterm birth is the main PV-IVH risk factor. Miranda (2010) discovered that IVH increased with decreasing GA.

In our study, 27 of 100 NICU-admitted newborns developed IVH. 20 of 30 neonates less than or equal to 32 weeks developed IVH (66.7%), while 7 of 70 neonates greater than 32 weeks developed IVH (10%). We agree the 1994 Andrerson *et al*. study,

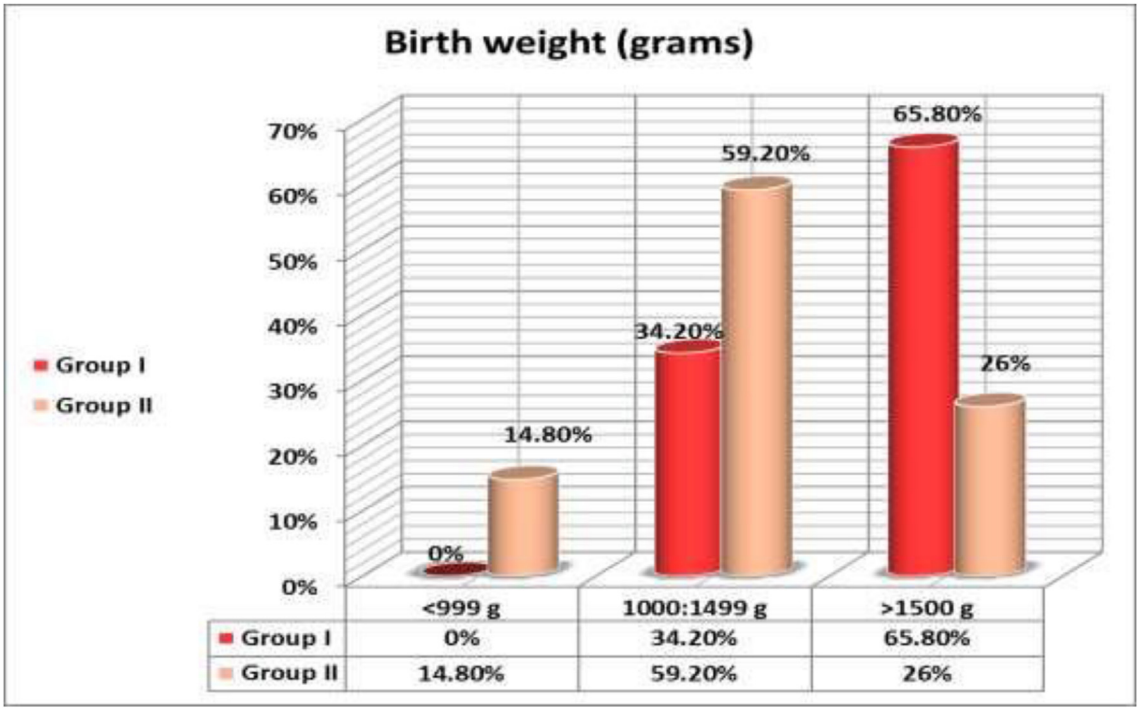

Fig. 4. Relation between birth weight and intraventricular hemorrhage.

Table 4. Relation between respiratory support and intraventricular hemorrhage in studied groups.

Respiratory support	Group I (No = 73)	Group II (No = 27)	χ^2	*P*	Significance
Nasopharyngeal CPAP	19 (26)	11 (40.7)	1.67	0.1963	NS
Ventilator	27 (37)	25 (92.6)	17.95	0.0001	HS
Saturation Fluctuation	2 (2.7)	7 (25.9)	7.52	0.0060	HS
Surfactant	2 (2.7)	10 (37)	13.47	0.0002	HS

CPAP, continues positive airway pressure.
This table shows the risk factors for various respiratory support in developing IVH, intraventricular hemorrhage. There are large significant differences between groups with respect to ventilator support, saturation variation, and surfactant administration.

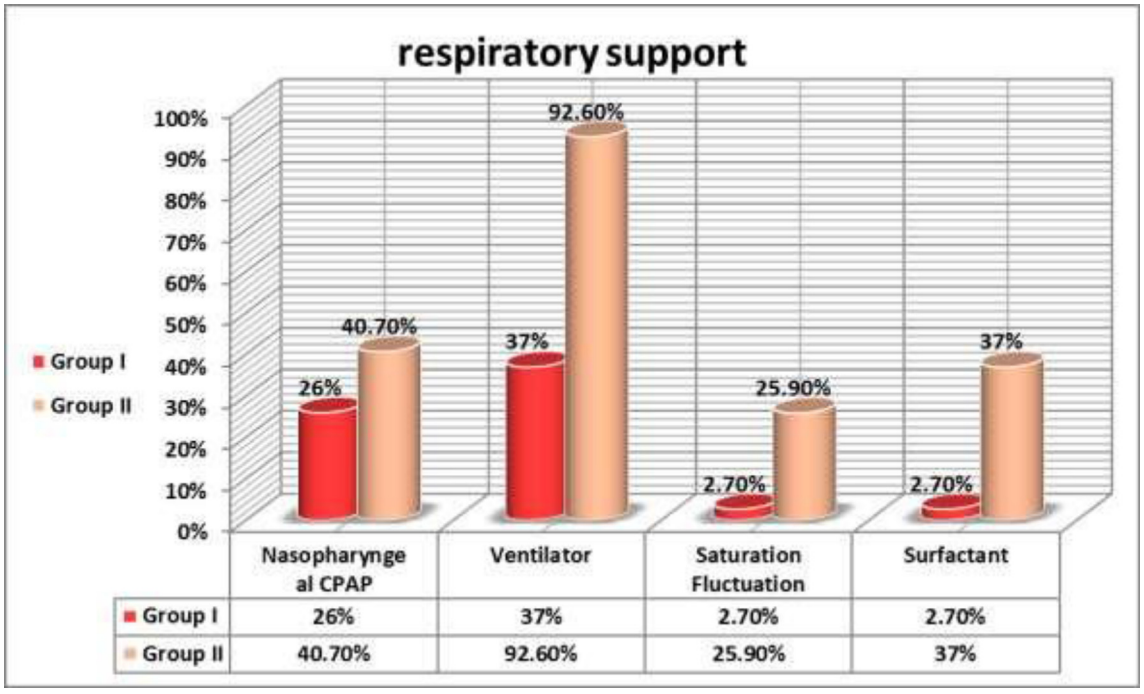

Fig. 5. Relation between respiratory support and intraventricular hemorrhage in studied groups.

revealed that 21% of preterm births had IVH. In 1994, Dolfin *et al.*[21] showed that IVH was 45% for newborns under 29 weeks and 19% for those over 29 weeks. IVH is most common in preterm newborns, with 15–20% of GA infants born before 32 weeks [Volpe *et al.* 2001]. Hamrick *et al.*, 2004 found that GM-IVH in preterm newborns has decreased from 50% in the late 1970s to 15%–25% nowadays. Mc Crea and Ment found IVH in 20–25% of premature VLBW children in 2008.

The birth weight of IVH cases was substantially lower than that of non-IVH cases. Seven infants weighing 1500 g or more developed IVH (12.7%), while all four very low birth weight infants

Table 5. Blood gases at admission and after active intraventricular hemorrhage in (group II).

ABG results	Group II at admission (*N* = 27) [n (%)] Mean ± SD	Group II after active IVH (*N* = 27) [n (%)] Mean ± SD	Paired T test	*P*	Significance
PH	7.11 ± 0.10	7.07 ± 0.10	1.4	0.1	NS
PCO2	39.3 ± 2.8	37.9 ± 1.2	2.3	**0.02**	S
PaO2	67.6 ± 7.2	67.4 ± 4.1	0.1	0.8	NS
HCO3	17.8 ± 1.9	15.5 ± 1.6	4.6	**<0.001**	HS
Na	128.5 ± 3.2	129.7 ± 1.7	−1.6	0.1	NS
K	3.6 ± 0.16	3.8 ± 0.6	−1.008	0.3	NS

This table shows that there was significant difference between groups in PCO2 and high significant difference in HCO3.

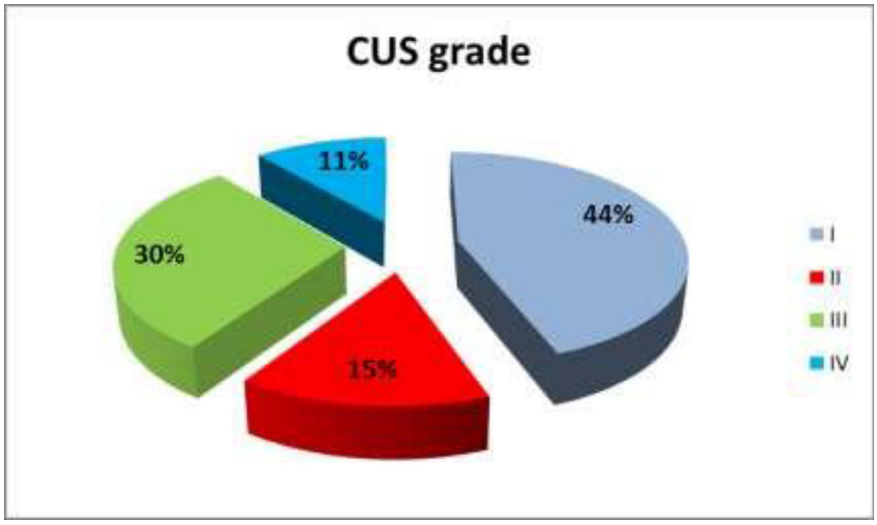

Fig. 6. CUS grades for cases with intraventricular hemorrhage. CUS, cranial ultrasound.

Table 6. Cranial ultrasound grades for neonates with intraventricular hemorrhage.

CUS grade	Number of infants (%)
Ihco	12 (44.4)
II	4 (14.8)
III	8 (29.6)
IV	3 (11.1)
Total	27 (100)

CUS grade frequency of IVH, intraventricular hemorrhage was 12 (44.4%) grade I, 4 (14.8%) grade II, 8 (29.6%) grade III, and 3 (11.1%) grade IV. Occurred. CUS, cranial ultrasound.

developed IVH (100%). This supports Dykes *et al*. Since 2000, birth weight under 1200 g has been associated with PIVH. Patra *et al*. (2006) found similar outcomes in preterm newborns. Lower birth weight increases IVH risk, according to Khodapanahandeh *et al*., 2008. PIVH babies had lower birth weights than non-IVH babies, according to Barnette *et al*., 2010. This matches Barnette *et al*. In 2010, infants under the 10th percentile were at risk of IVH and bad outcomes. According to Mohammed *et al*. (2010), IVH rates in males increased significantly in the less than 1000 g and 1000–1499 g birth weight groups. Low birth weight was linked to PVIVH by Lee *et al*., 2010. Miranda found in 2010 that low-birth-weight babies have greater high-grade hemorrhage.

Table 7. Time detection of intraventricular hemorrhage by CUS.

	Number of cases (%)
1st day	6 (22.2)
3rd day	16 (59.3)
7th day	5 (18.5)

Mean value of time of occurrence of IVH, intraventricular hemorrhage 2.75 ± 1.25 days (range from 1 to 7 days). CUS, cranial ultrasound.

Examining the gender relationship with IVH, males had a significantly higher prevalence of IVH than females, with 59 (59)% of all newborns examined being male, of which 20 (33.9%) had IVH. 41 (41%) were female, of whom seven (17%) had IVH. This finding is consistent with the opinion of Dykes *et al*. They found that male gender was more strongly associated with IVF than females.

IVH developed in 43.8% of vaginal deliveries and 19.2% of cesarean section deliveries. This supports Wen *et al*. observed that assisted vaginal birth increased ICH risk in 2001. Loony *et al*., 2007 found IVH in 26% of vaginally delivered babies. Vaginal delivery can traumatize the infant brain and cause subarachnoid, subdural, and GMH. Vassilyadi M *et al*., 2009 observed that surgical vaginal birth with vacuum increased subcapsular hemorrhage and ICH. Baud observed in 2008 that ICH was the most common neonatal adverse event of forceps or vacuum delivery. Villarejo *et al*., 2009[20] found that forceps or vacuum delivery promotes perinatal cranioencephalopathy.

The current study found that 29.6% of IVH cases had neurological symptoms and 70.4% were asymptomatic and resolved with regular CUS, done at 1, 2, and 7 days after birth in all cases. These results are consistent with Loony *et al*., 2007, who found a high prevalence of IVH in asymptomatic neonates. IVH causes even more subtle damage to the developing brain.

We showed 92.5% of IVH patients needed ventilator assistance. IVH substantially reduced O2 saturation. Pneumothorax was the most common IVH ventilation effect (44.4%). Mechanical ventilation, peak pressure greater than 25 cm H_2O, inspiratory-to-expiratory ratio, and positive end-

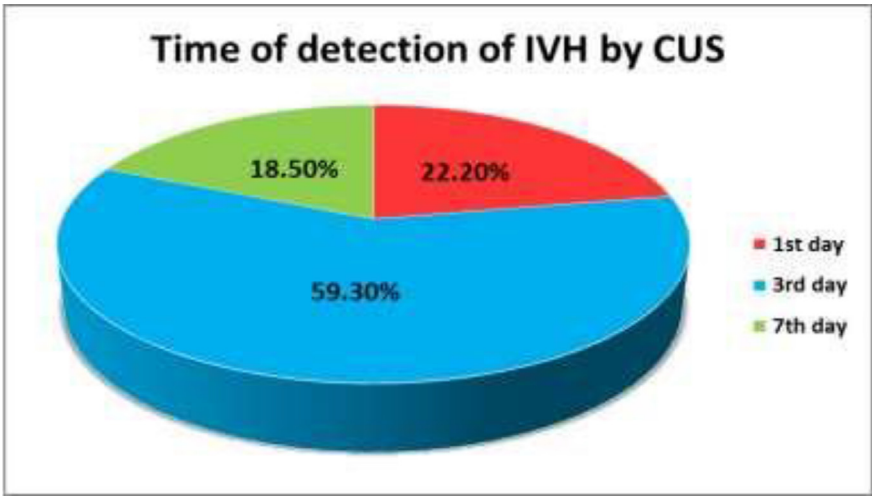

Fig. 7. Time of detection of intraventricular hemorrhage by CUS. CUS, cranial ultrasound.

expiratory pressure greater than 5 cm H_2O were linked with IVH in Dykes *et al*., 2000. These findings complement Roze *et al*., 2008, who demonstrated that respiratory failure and ventilator support were risk factors for neonatal ICH. Ventilator use increased the probability of high-grade IVH, according to Khodapanahandeh *et al*., 2008. Pneumothorax was the most prevalent ventilation effect. These happened 76.9% in IVH neonates and 23.1% in his control group.

We found the following IVH stage frequencies: 44.4% were grade I, 14.8% grade II, 29.6% grade III, 11.1% grade IV. This matches Kadri *et al*., 2006, who found 44.68% IVH in preterm newborns. The bulk were grade I and II. Unlike Kliegman *et al*., 2008, who indicated grade I accounted for 35% of IVH patients and grade II 40%. Lee *et al*. (2010) reported 79.7% grade I IVH, 6.9% grade II, 4.8% grade III, and 8.6% grade IV. According to Sajjadian *et al*., 2010, 40% of GM-IVH patients had grade I, 11% grade II, 25.7% grade III, and 2.8% grade IV.

In this study, all neonatal mortality in IVH was found to be 30 and 63%, with higher mortality in high-grade IVH. Synnes *et al*.,[23] 2006 found a mortality rate of 27–50% from severe (high-grade) PIVH. There was an inverse relationship between the severity of bleeding and survival, with significantly lower mortality from low-grade bleeding (5%). Yilmaz *et al*.,[24] 2009 reported an overall IVH mortality rate of 33%. Vassilyadi *et al*., 2009 reported an all-cause mortality rate of nearly one in five patients with primary IVH grade IV. Barnette *et al*., 2010 found that IVH with parenchymal disease was associated with a risk of adverse neurologic sequelae with a mortality rate of 24.5%. Lee *et al*., 2010 found an infant mortality rate of 35.6% for PV-IVH and 52% for IVH grade IV infants.

4.1. Conclusion

(1) IVH is a major cause of infant death after congenital anomalies (the study did not include all birth anomalies).
(2) 27% of cases of IVH occurred on postnatal days 1–7, with a mean gestational age of 30.03 weeks, with 20 (74.1%) males and 7 (25.9%) females.
(3) IVH risk factors include premature birth, low birth weight, and intensive respiratory support.
(4) High-grade IVH cases have the worst prognosis.

Authorship (Authors' contribution)

Tarek Mansour, Mostafa Abd El-Azim, Mohamed El-baroudy contributed in data collection, image revision and final editing, Mahmoud Elfayoumy, Mohamed Talaat and Mohamed farouk: share in data collection and editing, Mostafa Abdel-Azim and Mohamed farouk: Revision.

All authors have read and approved the research, and agree for the submission.

The authors declare that they have no conflict of interests.

Conflicts of interest

Conflict of interest disclosure statement: the authors declare that they have no conflict of interests.

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