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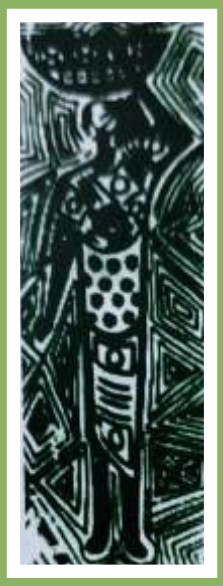

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A Retrospective Study of the Prevalence and Pattern of Intraventricular Haemorrhage Among Preterm Neonates in Makurdi, Nigeria

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Abstract

Background: Globally, an estimated 2.5 million newborns died in the first month of life in 2018, with preterm birth complications as the leading cause of death. Preterm neonates who survive are at greater risk of a range of short-term and long-term morbidities. Intraventricular haemorrhage (ICH) is an important cause of brain damage in premature newborns.

Objective: To determine the prevalence, risk factors, pattern and outcomes of intraventricular haemorrhage amongst the preterm neonates in a tertiary facility.

Methods: A six-year (Jan 2018-Dec 2023) retrospective study was carried out at the Special Care Baby Unit (SCBU) of the Benue State University Teaching Hospital, Makurdi. The hospital records of all preterm neonates admitted into the unit during the period under review were retrieved and assessed using the study proforma.

Results: A total of 121 preterm neonates were admitted with a male-to-female ratio of 1.1:1. The majority, (93; 76.9%) of the neonates had the first brain scan within the first seven days of life, while 10.7% had the scan between 8 and 14 days. Intraventricular haemorrhage was observed in 39 (32.2%), while 82 (67.8%) had normal brain scans. The severity pattern revealed Grade I, Grade II, and Grade III haemorrhages in 16.5%, 10.7%, and 5%, respectively. There were seven deaths accounting for 17.9% mortality.

Conclusion: Intraventricular haemorrhage in preterm neonates is a silent cause of mortality among preterm neonates. Proactive measures are needed to prevent the condition and manage affected babies.

Keywords: Germinal matrix, Preterm, Neonates, Intracranial, Intraventricular, Haemorrhage

Introduction

The World Health Organization (WHO) defines preterm birth as any birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the woman's last menstrual period (LMP). [1,2] Globally, 15 million babies are born preterm every year, with 81% of them delivered in Asia and sub-Saharan Africa, with Nigeria as the country with the third highest rate of preterm delivery globally.[3,4] Prematurity is the leading cause of death in children under the age of five years globally, and in almost all countries, preterm birth rates are increasing. [2,4]

Globally, an estimated 2.5 million newborns died in the first month of life in 2018 – approximately 7,000 every day, with preterm birth complications as the leading cause of death.[5–7]

Preterm neonates who survive are at a greater risk of a range of short-term and long-term morbidities.[4] Common complications of preterm birth are: high rates of respiratory distress syndrome, infections, feeding difficulties, necrotizing enterocolitis, seizures, intraventricular haemorrhage, periventricular leukomalacia, hypoxic-ischemic encephalopathy, bronchopulmonary dysplasia, in the acute phase. Cerebral palsy, visual and hearing problems complicate prematurity on long-term basis. [4,8,9]

Intracranial haemorrhage (ICH) is an important cause of brain damage in premature newborns, and it is also a serious cause of morbidity and mortality in the neonate.[10–12] The incidence of intracranial haemorrhage varies from about 2% to greater than 30% in newborns, depending on the gestational age at birth and the type of ICH.[13] Intraventricular haemorrhage in preterm neonates usually develops spontaneously; less frequently, it may be caused by trauma or asphyxia, and rarely, it occurs from a primary haemorrhagic disturbance or a congenital cerebrovascular anomaly.[14–17] Intracranial haemorrhage often involves the ventricles (intraventricular haemorrhage- (IVH) of premature infants delivered spontaneously without apparent trauma[14] IVH in premature neonates occurs in the gelatinous sub-ependymal germinal matrix; this periventricular area is the site of origin for embryonal neurons and foetal glial cells, which migrate outwardly to the cortex[16–19] Immature blood vessels in this highly vascularized region of the developing brain, combined with poor tissue vascular support, predispose premature neonates to haemorrhage.[14–15] The germinal matrix involutes as the foetus approaches full-term gestation and the tissues' vascular integrity improves; therefore, IVH is much less common in the term neonate.[14,19] Approximately 30% of premature infants <1500g have IVH, and the risk is inversely related to the gestational age and birth weight, with the smallest, most immature neonates being at the most significant risk.[14] Studies in Nigeria have reported a prevalence of 16.2% and 31.7%, respectively.[20, 21]

Although preterm survival rates have increased in high-income countries, preterm newborns still die because of a lack of adequate newborn care in many low-income and middle-income countries, including Nigeria, where complications of preterm delivery remain the leading cause of neonatal mortality.[4,22] Since ICH causes mortality and long-term neurodevelopmental sequelae, it is important to determine the prevalence and risk factors of ICH in order to highlight its importance, advocate for necessary measures required to improve anticipatory care, reduce its occurrence in order to prevent the neurological consequences, hence lessen the resultant burden of neurological disease.[12,23] In this study, we aimed to determine the prevalence, risk factors, pattern, and outcomes of intraventricular haemorrhage amongst hospitalized preterm newborns.

Methods

This was a six-year (Jan 2018- Dec 2023) retrospective study carried out at the Special Care Baby Unit (SCBU) of the Department of Paediatrics, Benue State University Teaching Hospital, Makurdi. The special care baby unit is manned by a consultant paediatrician and paediatric residents along with trained nurses. The SCBU is further divided into the out-born unit and an inborn unit. It has 17 cots and 10 incubators, with three resuscitaires, six oxygen concentrators, four replaceable oxygen cylinders,13 phototherapy units, a CPAP machine, multi-parameter monitors, apnea monitors, and other essential equipment for newborn care.

As a unit protocol, every preterm neonate admitted into the unit undergoes a transfontanelle ultrasound scan within the first 72 hours of life with a repeat scan seven days later whenever any abnormality is seen on the ultrasound scan.

Records of all preterm neonates admitted into the unit during the period under review were retrieved and assessed using the study proforma, which contains information including gestational age at birth, sex, birth weight, mode of delivery, age when transfontanelle ultrasound scan was done, findings on ultrasound and the outcome of hospitalization.

Inclusion criteria
All neonates delivered at gestations below 37 completed weeks of gestation and admitted into the unit during the period under review.
Exclusion criteria
All neonates admitted during the period under review with incomplete information or undocumented gestational age.

The neonatal details and the maternal information and the details of the transfontanelle ultrasonography findings were recorded. Gestational age was determined from the last menstrual period and also using the new Ballard score.[24,25] Newborns with birth weight <10th percentile were classified as small-for-gestational age (SGA), those between 10th and 90th percentile as appropriate-for-gestational age (AGA) and those with >90th percentile as large-for-gestational age (LGA). [26]
The Papille classification was used for staging intraventricular haemorrhage:
Grade I: Haemorrhage limited to the germinal matrix.
Grade II: Intraventricular haemorrhage but with normal ventricle width.
Grade III: Intraventricular haemorrhage with ventricular dilatation.
Grade IV: Intraventricular haemorrhage and spread of bleeding into the adjacent brain parenchyma.
Grades I and II haemorrhages were classified as mild, and Grades III and IV haemorrhages, as severe. [27]

Data was analysed using the IBM SPSS Statistic software version 23. Chi-Squared test and Fisher's Exact test were used for data analysis as appropriate. The level of statistical significance was set at $P < 0.05$.

Ethical consideration
Ethical clearance for the study was obtained from the Hospital's Health Research Ethics Committee (BSUTH/CMAC/HREC/101/V. II/196).

Results

A total of 121 preterm neonates comprising 63 males and 58 females were hospitalized with a male-to-female ratio of 1.1:1. The majority of the neonates (112; 92.6%), were admitted within the first seven days of life, while a smaller fraction was admitted between 8 and 21 days (8; 6.6%). Regarding birth weight, 70 (57.9%) were low birth weight (LBW), 38 (31.4%) were very low birth weight (VLBW), and 12 (9.9%) were extremely low birth weight (ELBW). While only a few were born below 28 weeks gestation (4; 3.3%), the majority were born between 28 and 32 weeks gestation (65; 53.7%), as shown in Table I.

Most mothers were aged between 21-30 years (54; 44.6%), followed by the 31-40 years group (49; 40.5%). Meanwhile, a small proportion were aged 20 years or younger, comprising 10.7%. Most mothers had booked for antenatal care (89; 73.6%), though a significant proportion were un-booked (32; 26.4%). The majority of mothers had no history of assisted conception (118; 97.5%) or tocolysis (117; 96.7%); however, a small percentage of mothers had received antenatal steroids (9; 7.4%), as shown in Table II.

Most transfontanelle scans (93; 76.9%) were conducted within the first seven days of life, while a small proportion of scans (`13; 10.7%) were performed between 8 and 14 days. The scan results showed that one-third (39; 32.2%) of

preterm neonates had intraventricular haemorrhage (IVH), while the majority (82; 67.8%) had normal findings. Amongst neonates with IVH, the severity varied, with Grade I, Grade II, and Grade III haemorrhages accounting for 16.5%, 10.7%, and 5%, respectively. Among neonates who had a repeat scan (n = 39), 41% (n = 16) had a persistent IVH, while 59.0% (n = 23) had normal findings. The age distribution at repeat USS indicates that the majority (22; 56.4%) occurred between 11 and 20 days, as shown in Table III.

Table I: Neonatal characteristics

Variable	Frequency (n = 121)	Percentage
Sex		
Female	58	47.9
Male	63	52.1
Age(days)		
1-7	112	92.6
8-14	3	2.5
15-21	5	4.1
>21	1	0.8
Weight at birth		
ELBW (≤1000g)	12	9.9
VLBW (1001-1500g)	38	31.4
LBW (1500-<2500g)	70	57.9
Normal Weight (≥2500g)	1	0.8
Weight on admission		
<1.00 kg	2	1.7
1.00-1.50 kg	66	54.5
1.51-2.50 kg	52	43
> 2.50 kg	1	0.8
Birthweight for GA		
AGA	49	40.5
SGA	72	59.5
OFC		
21-25 cm	5	4.1
26-30 cm	97	80.5
> 30 cm	19	15.7
Mode of delivery		
C/S	41	33.9
SVD	80	66.1
Gestational Age		
<28	4	3.3
28-32	65	53.7
32-34	32	26.4
34-36	20	16.5

ELBW - Extremely low birth weight, VLBW - Very low birth weight, LBW - Low birth weight, OFC - Occipitofrontal circumference, C/S - Caesarean section, GA – Gestational age, SVD – Spontaneous Vaginal Delivery.

Table II. Maternal Risk factors

Variable	**Categories**	**Frequency (n = 121)**	**Percentage**
Age in years	≤20 years	13	10.7
	21-30 years	54	44.6
	31-40 years	49	40.5
	> 40 years	5	4.1
Parity			
	1	37	30.6
	2	27	22.3
	3	16	13.2
	4	2	1.7
	≥5	39	32.2
Types of gestation			
	Singleton	65	53.7
	Triplet	8	6.6
	Twin	46	38.0
	Others	2	1.7
ANC	Booked	89	73.6
	Unbooked	32	26.4
Assisted conception	No	118	97.5
	Yes	3	2.5
Tocolysis	No	117	96.7
	Yes	4	3.3
PROM	No	82	67.8
	Yes	39	32.2
Antenatal steroids	No	112	92.6
	Yes	9	7.4
Assisted delivery	No	115	95.0
	Yes	6	5.0

ANC - Ante-natal Care, PROM - Prolonged Rupture of Membranes

Neonates aged 1-7 days (n = 29) had a higher incidence of IVH (29; 28.93%) compared to older neonates (5; 4.1%) aged 15-21 days. This disparity was statistically significant ($\chi^2 = 6.732$, $p = 0.035$). Based on birth weight, IVH was found in 7 (5.79%) ELBW neonates, 11 (9.09%) VLBW, and 21 (17.36%) LBW groups. These patterns lacked statistical significance ($\chi^2 = 4.566$, $p = 0.206$). Neonates delivered via Caesarean section (CS) showed a lower incidence of IVH (10; 8.26%) compared to those delivered per vagina (29; 23.97%). This difference was not statistically significant ($\chi^2 = 1.746$, $p = 0.186$) as shown in Table IV.

Neonates born to mothers aged 21-30 years and 31-40 years showed relatively higher IVH frequencies (14; 35.9% and 17; 43.6%, respectively) compared to those born to mothers younger than 20 years or older than 40 years showing a significant association between maternal age and IVH prevalence ($\chi^2 = 3.115$, $p = 0.374$). Notably, the number of neonates delivered as singletons that had IVH was less (24;

19.83%) than the singletons those without IVH (41; 33.88%). Among neonates whose mothers booked for antenatal care, 27 had IVH compared to 62 whose mothers booked for ANC but had no IVH. Among neonates whose mothers did not receive antenatal steroids, 35 had IVH while 77 not have IVH as shown in Table V.

Table III. Ultrasound characteristics and findings in preterm neonates

Variable	Categories	Frequency (n = 121)	Percent (%)
Age at USS (days)	1-7	93	76.9
	8-14	13	10.7
	15-21	7	5.8
	>21	8	6.6
USS findings	IVH	39	32.2
	Normal	82	67.8
If IVH as above	Grade 1	20	16.5
	Grade 2	13	10.7
	Grade 3	6	5.0
	NA	82	67.8
Repeat USS	No	82	67.8
	Yes	39	32.2
If yes above findings	IVH	16	41.0
	Normal	23	59.0
Age at repeat scan	<10 days	8	20.5
	11-20 days	22	56.4
	21-30 days	7	18.0
	>30 days	2	5.1

The majority of the neonates with IVH (15; 38.5%) stayed on admission for 21-30 days, and most were successfully managed and discharged home (29; 74.4%). One infant was discharged against medical advice (2.6%), two were referred (5.1%) while seven died giving a mortality rate of 17.9 % as shown in Table VI.

Discussion

The findings in this study showed that among preterm neonates with IVH, neonates born with LBW had a higher prevalence of IVH followed by VLBW neonates, and the least were ELBW neonates, and this finding is in contrast with the documented reports of more IVH amongst VLBW. [28] Babies born via a Caesarean section had a lower risk of IVH, and this finding is consistent with previous reports by Macleod *et al*. in Uganda.[29] This could be due to the less stress associated with Caesarean delivery compared to vaginal delivery. Few of the mothers received antenatal steroids before preterm delivery, and this points to a suboptimal uptake of antenatal corticosteroid therapy for women with inevitable preterm births. Even antenatal corticosteroids are an effective intervention in reducing intraventricular haemorrhage.[12,29] Antenatal steroid therapy has been shown to reduce the incidence of any grade of intraventricular haemorrhage and a reduction in the incidence of severe intraventricular haemorrhage in preterm neonates.[30,31] Though the occurrence of IVH was higher amongst babies whose mothers did not receive antenatal steroids, there was no significant association in contrast to the report of Dawid *et al*.[32]

The majority of the transfontanelle scans were performed within the first seven days of life (76.9%), in keeping with the report of Adekunle *et al*. in Lagos [21] and Macleod *et al*.,[29] who reported 90.2% of all IVH by the seventh day of life. This implies that most haemorrhages will be identified if ultrasound scans are done early, and most cases will be missed if late scans are done in the second week of life. The prevalence of IVH was 32.2% similar to the findings by Adekunle *et al*,[21] in Lagos (31.7%), Macleod *et al*,[29] in Uganda (34.2%), but higher than the report by Tadasa *et al*.,[33] in Ethiopia (27.0%), Gross *et al*.,[34] in Germany, and Rajesh *et al.* in India (19.5%).[35]

Table IV: Relationship between neonatal factors and prevalence of intraventricular haemorrhage

Variable		IVH present n = 39	IVH absent n = 82	Chi-Square	p-value
Age(days)	1-7	29 (74.4)	77 (93.9)	6.732	0.035
	8-14	4 (10.3)	1 (1.2)		
	15-21	5 (12.8)	3 (3.7)		
	>21	1(2.6)	1(1.2)		
Gender	Female	20 (51.3)	38 (46.3)	0.258	0.611
	Male	19 (48.7)	44 (53.7)		
Birth weight	ELBW	7 (17.9)	5 (6.1)	4.566	0.206
	VLBW	11 (28.2)	27 (32.9)		
	LBW	21 (53.8)	49 (59.8)		
	NBW	0 (0.00)	1 (1.2)		
Weight at admission	<1.00	1 (2.6)	1 (1.2)	2.973	0.396
	1.00-1.50	25 (64.1)	41 (50.0)		
	1.51-2.50	13 (33.3)	39 (47.6)		
	> 2.50	0 (0.00)	1 (1.2)		
OFC (cm)	21-25	3 (7.7)	2 (2.4)	4.259	0.119
	26-30	33 (84.6)	64 (78.1)		
	>30	3 (7.7)	16 (19.5)		
Birth weight for GA	AGA	11 (28.2)	38 (46.3)	3.608	0.058
	SGA	28 (71.8)	44 (53.7)		
Mode of delivery	C/S	10 (25.6)	31 (37.8)	1.746	0.186
	SVD	29 (74.4)	51 (62.2)		
Gestational Age	<28	2 (5.1)	2 (2.4)	3.21	0.073
	28-32	22 (56.4)	43 (52.4)		
	32-34	9 (23.1)	23 (28.1)		
	34-36	6 (15.4)	14 (17.1)		

Figures in parentheses are percentages of the respective columns

The prevalence of IVH was highest amongst the preterm neonates of 28-32 weeks gestational age (56.4%), in agreement with the report of Tadasa *et al*.,[33] from Ethiopia and MacLeod *et al*. from Uganda.[29] The occurrence of intraventricular haemorrhage has been documented to be

inversely proportional to the gestational age due to the immaturity of the germinal matrix, and this finding in the present study is consistent with the previous findings.[12,28,29,35,36]

Amongst babies with an intraventricular haemorrhage, most had grade I IVH (16.5%), followed by grade II (10.7%) and grade III (5.0%), and these were lower than 35.4%, 41.7% and 16.4% respectively as reported by Rajesh *et al*. in India.[35]

Table V. Relationship between maternal factors and the prevalence of intracranial haemorrhage

Variable		IVH present n = 39	IVH absent n = 82	Chi-Square	p-value
Age (years)	<20	5 (12.8)	8 (6.61)	3.115	.374
	21-30	14 (35.9)	40 (33.06)		
	31-40	17 (43.6)	32 (26.45)		
	>40	3 (7.7)	2 (1.65%)		
Parity	Para 1	9 (23.1)	28 (34.2)	12.093	.017
	Para 2	10 (25.6)	17 (20.7)		
	Para 3	1 (2.6)	15 (18.3)		
	Para 4	0 (0.0)	2 (2.4)		
	> Para 5	19 (48.7)	20 (24.4)		
Type of gestation	Singleton	24 (61.5)	41 (50.0)	4.419	.220
	Triplet	4 (10.3)	4 (4.9)		
	Twin	10 (25.6)	36 (43.9)		
	Others	1(2.6)	1(1.2)		
ANC	Booked	27 (69.2)	62 (75.6)		
	Unbooked	12 (30.8)	20 (24.4)	.553	.457
Assisted conception	No	39 (100.0)	79 (96.3)		
	Yes	0 (0.00)	3 (3.7)	1.463	.226
Tocolysis	No	38 (97.4)	79 (96.3)		
	Yes	1 (2.6)	3 (3.7)	.099	.753
PROM	No	25 (64.1)	57 (69.5)		
	Yes	14 (35.9)	25 (30.5)	.354	.552
Antenatal steroids	No	35 (89.7)	77 (93.9)		
	Yes	4 (10.3)	5 (6.1)	.664	.415
Assisted delivery	No	36 (92.3)	79 (96.3)		
	Yes	3 (7.7)	3 (3.7)	.913	.339

Figures in parentheses are percentages of the respective columns

The dominance of neonates with grades I and II haemorrhage in the present study is consistent with the report of Wang *et al*,[37] from China, and Treluyer *et al*.,[38] from the French cohort, but in contrast with the report of Piccolo *et al*. in Italy which reported higher rates for grade III intraventricular haemorrhages.[23] The grade of haemorrhage depicts severity, and having more babies with mild haemorrhages gives room for good outcomes. Repeat scans were done a week later, and by then, most of the haemorrhages had resolved (59%); this shows that later scans would have missed the haemorrhages earlier seen, and it

emphasizes the need for early scans in preterm neonates.

Most of the neonates with IVH were managed successfully and were discharged (74.4%), which showed good outcomes in most babies. However, IVH was also seen to be associated with prolonged hospitalization, and in some cases, with mortality.

Conclusion

The prevalence of IVH was high amongst preterm neonates in Makurdi. Although, most of the cases resolved by the second scan, it may be associated with mortalities. Hence, continued surveillance is important to identify cases of IVH and proactively plan effective management.

Table VI. Relationship between clinical outcomes and the prevalence of intracranial haemorrhage

Variable	IVH (n = 39)	Normal (n = 82)	Total (n = 121)	Chi-Square (p-value)
Duration of hospital stay				
< 10 days	7 (17.9)	20 (24.4)	27	5.643 (.342)
11-20 days	9 (23.1)	19 (23.2)	28	
21-30 days	15 (38.5)	20 (24.4)	35	
31-40 days	4 (10.3)	12 (14.6)	16	
41-50 days	2 (5.1)	10 (12.2)	12	
51-60 days	2 (5.1)	1 (1.2)	3	
Outcome				
DAMA	1 (2.6)	3 (3.7)	4	7.147 (.067)
Died	7 (17.9)	3 (3.7)	10	
Discharged	29 (74.4)	71 (86.6)	100	
Referred	2 (5.1)	5 (6.0)	7	

Figures in parentheses are percentages of the total in each column

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