Cross-sectional Study

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Magnitude and associated factors of intraventricular hemorrhage in preterm neonates admitted to low resource settings: a cross-sectional study

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Background: Intraventricular hemorrhage (IVH) is one of the medical issues that preterm infants are susceptible to as a result of their difficulty adjusting to life outside the womb. It is bleeding into the ventricular system from the germinal matrix, a highly cellular and vascular tissue that is only seen in preterm newborns and ruptures easily. The study aims to assess the magnitude and associated factors of IVH in preterm neonates.

Methods: A hospital-based cross-sectional study was conducted at Tibebe Ghion Specialized Hospital (TGSH) from 14 March 2022 to 15 August 2022. The neonatal referral form, the mother's medical file, an in-person interview with the mother, and bedside cranial sonography were used to collect clinical data. After data were entered into Epi Info and exported to Scientific Program for Social Science (SPSS), analysis was carried out using binary and multivariable logistic regression.

Results: The overall magnitude of IVH in preterm newborns among preterm neonates admitted to TGSH was 53 (27.04%) (95% CI: 20.9–32.2%). In the multivariable logistic regression analysis, a birth weight of between 1500 and 2000 g (OR: 0.38, 95% CI: 0.18–0.79) were negative, and those neonates with gestational age between 28 and 32 weeks (OR: 2.14, 95% CI: 1.04–4.41) were positively associated with the occurrence of IVH.

Conclusion: The study discovered that the magnitude of IVH is slightly higher than that of prior studies done in different parts of the world, and those neonates delivered at early gestational ages and those with very low birth weight have a higher incidence of IVH. Both guardians and health providers should give more attention to those neonates born at an early gestational age and with small birth weight.

Keywords: associated factors, Ethiopia, intraventricular hemorrhage, preterm neonates

Background

Intraventricular hemorrhage (IVH) refers to the presence of blood inside the cerebral ventricular system as a result of germinal matrix hemorrhage[1]. IVH cases are detectable by the first 24 h after birth[2]. Preterm neonates have a high risk of bleeding due to the presence of this germinal matrix[1,3]. IVH is very common in very low and extremely low birth weight babies[3].

HIGHLIGHTS

- Intraventricular hemorrhage (IVH) refers to the presence of blood inside the cerebral ventricular system.
- The incidence of IVH in neonates who are very low birth weight and extreme low birth weight is estimated to be 50% worldwide.
- The reports showed that about 90% of IVH cases occur in the first 5 days of life.

IVH is a common complication in neonates and is related to neurodevelopmental outcomes. Infants with severe IVH are at higher risk of adverse neurological outcomes and death[4–6].

Ethiopia had a death rate of 29% for preterm newborns hospitalized in neonatal intensive care units (NICUs)[7]. Advances in medical care have led to more premature babies surviving the neonatal period[5]. Despite advances in the care of newborns, IVH remains a common complication in preterm infants, especially in those less than 32 weeks gestation. The overall incidence of IVH is about 36% in preterm infants, and the incidence of IVH increases as gestational age and birth weight decrease[4,5,8].

There are a number of investigative techniques, including computed tomography (CT), Magnetic Resonance Imaging, and ultrasonography, that can be used to diagnose neonatal cranial hemorrhages. Head ultrasound (HUS) is a less expensive and noninvasive way to check for IVH in newborns[9]. The germinal matrix hemorrhages occur as echogenic areas along the

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caudothalamic groove on a sonographic scan[1]. The treatment modalities available for IVH are supportive and concentrate on controlling the consequences. The typical course of treatment focuses on controlling intracranial pressure and treating coagulopathy to stop bleeding from progressing and leading to the onset of hydrocephalus. The management of IVH consequences involves combining surgical therapy with fibrinolysis[1,10].

Identification of risk factors and IVH magnitude may lead to improvements in newborn ICU care standards[11]. Therefore, the institution will use the study's findings as a starting point for more research in an effort to enhance IVH diagnosis and care. Additionally, the research will assist physicians in understanding the severity and contributing factors of IVH. Consequently, those risk groups will receive increased attention in their medical care, and any linked factors can be used to inform prevention strategies and emphasize the value of routine screening for high-risk neonates.

There are few statistics available on the prevalence and risk factors of IVH in low-income countries[12]. There is no study that used sonographic scan as a diagnosis tool before, and this is the first of its kind done in the country. Therefore, our study was aimed to assess the magnitude and predictors of IVH among preterm neonates by using a sonographic scan.

Patients and methods

Study area, design, and period

An institutional-based cross-sectional study design was employed at Tibebe Ghion Specialized Hospital (TGSH) from 14 March 2022 to 15 August 2022. The hospital provides various clinical services to more than 6 million people in its catchment region.

Study participants and eligibility criteria

All preterm neonates (gestational age, 28–37 weeks) admitted to the hospital during the study period and whose parents gave consent to be enrolled in the study were included, whereas preterm neonates with known genetic diseases or congenital anomalies were excluded.

Study variables and outcome endpoints

The magnitude of IVH was the primary outcome. The HUS was used as a diagnostic tool for IVH. The work has been reported in line with the Strengthening of the Reporting of Cohort Studies in Surgery (STROCSS) criteria[13].

Sample size and sampling technique

The single population proportion formula was used to calculate the required sample size by considering the following assumptions: proportion of IVH $p = 0.5$, or 50.0%, 95% CI, and 5% margin of error (absolute level of precision),

$$n = \frac{(Z_{\alpha/2})^2 \quad p \quad (1 - p)}{d^2},$$

$Z = 1.96$,
$P = 50.0\%$ (0.5),
$d = 0.05$,

$$n = \frac{(1.\ 96)^2 \quad (0.\ 5) \quad (0.\ 5)}{(0.\ 05)^2} = 385,$$

where
n = sample size,
P = proportion of IVH (P) = 50.0%,
$Z = Z$ is the standardized normal distribution value at the 95% CI: 1.96,
d = the margin of sample error tolerated = 5%.

The expected number of populations in the study period (N), based on the average number of neonates coming to the NICU for the previous 6 months, was 400. The corrected sample size (nf) was calculated by using the correction formula as follows: nf =

$$\frac{(n \times N)}{(n + N)},$$

nf =

$$\frac{(385 \times 400)}{(385 + 400)}.$$

nf = 196. After adding a 5% contingency, it becomes 206. Systematic random sampling was used with $K = 2$ (400/206), and the first neonate was selected by lottery method, and the others were taken every second interval.

Data collection process and management

To compile demographic and clinical data on the mother and the infant, a standardized questionnaire was employed. The data was gathered by the principal investigator and a trained nurse working in the NICU from maternal and newborn charts, referral paperwork, and interviews. IVH diagnosis was conducted using a Siemens ultrasound scanner outfitted with both a curved probe (5 MHz) and a linear probe (8 MHz). The sonographic examination was conducted using the anterior fontanels as an acoustic window in sagittal, axial, and coronal perspectives. The scan was performed at the patient's bedside in the NICU ward for newborns between the fourth and seventh postnatal days.

The HUS was examined by senior radiologists. During a HUS, sound waves are used to create images of the brain. A computer records the images while sound waves from an ultrasound machine are transmitted through the probe into the head. The medical gel was applied to the scanning zone once the newborns had been placed supine on the scan table or neonatal bed and the fontanels had been identified. We can obtain high-quality images of the brain by moistening the area with gel that removes air between the probe, skin, and skull. The scan may take 10–15 min, and we can adjust the probe's location and angle until we achieve the desired image quality.

Prior to conducting regular data gathering, the data collecting tool underwent pretesting at the adjacent Felege Hiwot Referral Hospital to ensure consistency. The study was registered with the unique reference number of researchregistry 8647.

Data processing and analysis

EPI-data version 3.1 was used to enter the data into a computer. Prior to analysis, the data were verified daily and cleaned by the

lead investigator. The Scientific Program for Social Sciences (SPSS) 24.0 was then used to export the data for analysis. The variable was examined using crude odds ratio (COR) and adjusted odds ratio (AOR) with a 95% CI using multivariable logistic regression. In order to account for confounders, a multivariable logistic regression analysis was performed on all variables having a *P* value of 0.25 on the bivariable analysis that was connected to IVH. If a *P* value of 0.05 was obtained, the predictors of IVH were declared.

Operational definitions

IVH: Are those having IVH showing echogenic regions close to the caudothalamic groove extending along the floor of the frontal horn of the lateral ventricle on the cranial sonographic study?

Results

Sociodemographic and clinical characteristics of neonates

The response rate was 95% and the study contains 196 preterm neonates admitted to TGSH throughout the study period, of which 105 (53.6%) are male and 91 (46.4%) are female. The majority of the preterm birth women live in metropolitan areas (46.4%), while rural areas make up 34.2%. Among neonates enrolled in the study, 61.7% of them are singletons and 37.2% of them are twins.

Most of the neonates in the study have birth weights between 1500 and 2000 g (61.7%). A total of 38.3% of babies born before 32 weeks of gestation. There were a variety of neonatal problems, and of these, 82.7% of the babies admitted to this hospital have neonatal infections (sepsis or meningitis), 56.6% of them experience respiratory distress, and 9.2% of newborns suffer hypoglycemia (Table 1).

Table 1

Descriptive data on sociodemographic and clinical traits of preterm newborns

Variables	Frequency (%)
Place of residency	
Rural	67 (34.2%)
Semiurban	38 (19.4%)
Urban	91 (46.4%)
Sex	
Female	91 (46.4)
Male	105 (53.6)
Place of delivery	
Health center	25 (34.2)
Hospital	171 (87.2)
GA (weeks)	
28–32	75 (38.3)
32–37	121 (61.7)
Birth weight (g)	
1000–1500	75 (38.3)
1500–2000	121 (61.7)
Pregnancy	
Singleton	121 (61.7)
Twins	73 (37.2)
Triplets	2 (1)
Mode of delivery	
SVD	120 (61.2)
Cesarian delivery	76 (38.8)
Newborn major diagnosis	
Neonatal infections	162 (82.7)
Respiratory distress syndrome	111 (56.6)
Hypoglycemia	18 (9.2)
Hypothermia	140 (71.4)

GA, gestational age; SVD, spontaneous vaginal delivery.

Obstetric characteristics of mothers

Numerous obstetric problems occurred during the births of these premature infants. Of these mothers who gave preterm births, 20.9% of them were given steroid injections to accelerate fetal lung maturity. 23.5% of mothers have one of the hypertension disorders of pregnancy, and they contributed to 6.1% of total IVH. Preeclampsia affects the majority of women with hypertension (13.3% of total hypertension, 23.5%) (Table 2).

Sonographic study of IVH

The overall magnitude of IVH in preterm newborns (28–37 weeks) admitted to this hospital was found to be 27.04% (95% CI: 20.9–32.2%), and the magnitude is 42.6% for very preterm (28–32 weeks) and 41.3% for very low birth weight (VLBW) (1000–1500 g) (Fig. 1). Regarding the grading system of IVH, grade I is the most observed 24 (12.24%) which was followed by grade II 19 (9.7%) and grade III 9 (4.6%). Finally, the severe form of IVH grade IV accounts 1 (0.5%) only.

Factors associated with IVH among preterm neonates

Bivariable logistic regression was utilized to examine the relationship between independent factors and the binary dependent variable. Independent variables with *P* values less than 0.25 were then entered into multivariable logistic regression. Hosmer and Lemeshow test was run and it indicates that the model has a good fit.

Table 2

The distribution of common obstetric problems of preterm neonates admitted to the hospital

Variables	Category	Frequency (%)
Antenatal steroids	Not Given	155 (79.1)
	Given	41 (20.9)
Hypertensive disorder of pregnancy	Hypertension	
	Preeclampsia	26 (13.3)
	Eclampsia	15 (7.7)
	Superimposed preeclamsia	6 (3.1)
	Total	46 (23.5)
	No hypertension	150 (76.5)
Alcohol use	No	179 (91.3)
	Yes	17 (8.7)
APH	No	184 (93.9)
	Yes	12 (6.1)
PROM	No	173 (88.3)
	Yes	23 (11.7)
Spontaneous labor	Yes	174 (88.8)
	No	22 (11.2)
Labor induction	Yes	12 (6.1)
	No	184 (93.9)

APH, antepartum hemorrhage; PROM, premature rupture of the membrane.

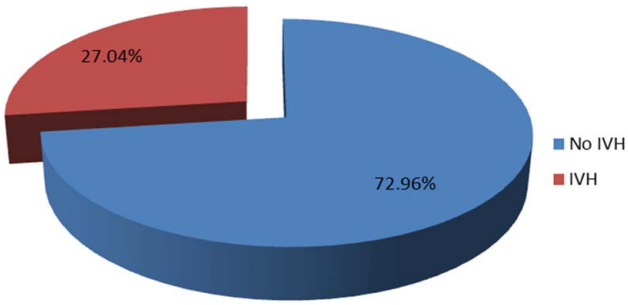

Figure 1. The magnitude of intraventricular hemorrhage among preterm neonates.

Multivariable logistic regression analysis has identified factors that were associated with IVH ($P < 0.05$). These were the gestational age and birth weight of the preterm neonates. The odds of IVH were low among preterm neonates with birth weight between 1500 and 2000 g than neonates having birth weight between 1000 and 1499 g (AOR: 0.38, 95% CI: 0.18–0.79). The odds of IVH were high among women who had a gestational age between 28 and 32 weeks than those women of gestational age between 33 and 36 weeks. Findings indicate that newborns that were very preterm (28–32 weeks) have developed IVH two times more than moderate to late preterm (33–36 weeks). (AOR: 2.14, 95% CI: 1.04–4.41). As compared to newborns with VLBW (1000–1499 g), low birth weight (LBW) neonates (1500–2000 g) have a 62% lower risk of developing IVH (AOR: 0.38, 95% CI: 0.18–0.79) (Table 3).

Discussion

This study is one of the few studies of IVH in preterm neonates in Sub-Saharan Africa and the first in Ethiopia to use cranial sonography to determine the status of IVH. In this institutional-based study in which 196 preterm neonates were included, the magnitude of IVH was 27.04% for gestational age less than 36 weeks and it more than 40% for those neonates gestational ages more than 32 weeks and birth weight less than 1500 g. Regarding the severity of IVH occurrence, 81% of total IVH was mild (I and II) and severe (III and IV) account for 19%.

The magnitude of IVH was comparable with the study conducted in the United States and Germany[14,15] and lower than the finding of Uganda and Zambia[16,17]. The main distinction is that both of their sample populations included higher risk categories with gestational age less than 32 weeks, whereas our study included all preterm newborns.

The previous reports of Tikur Anbessa Specialized Hospital found a higher magnitude of IVH as compared to our findings[18]. The reason for the discrepancy could be because the neonates in this study were already deceased, suggesting they may have had serious problems that increased their likelihood of developing IVH and that the diagnosis method employed was an autopsy, which is more sensitive to IVH than the sonographic study.

Sonography, although the most commonly used imaging technique in neonates, is less sensitive and less specific for the detection of intracranial ischemia and hemorrhage compared with CT or Magnetic Resonance Imaging. CT and Magnetic Resonance Imaging have a significantly better interobserver agreement for cortical hypoxic–ischemic injury and germinal matrix hemorrhage (grades I and II) compared with sonography.

The infants who were born weighing more than 1500 g experienced less IVH than their counterparts (AOR = 0.38, CI (0.18–0.79). Similarly, the babies born after 32 weeks of gestation experienced less IVH (AOR = 2.14, CI (1.04–4.41)[16,17,19–21].

The study conducted in various locations revealed that vaginal delivery was linked to a higher risk of IVH than elective cesarean section (C/S) delivery; however, in our cases, there was no

Table 3

Bivariable and multivariable logistic regression results of factors associated with *$P \leq$

Variables	Category	IVH status, *N* (%)		Bivariable logistic regression	Multivariable logistic regression	
		No	Yes	COR (95% CI)	AOR (95% CI)	*P*
Birth weight (g)	1000–1499	43 (21.9)	32 (16.3)	1	1	
	1500–2000	100 (51.0)	21 (10.7)	0.28 (0.14–0.54)	0.38 (0.18–0.79)*	0.038
Mode of delivery	SVD	84 (42.9)	36 (18.4)	0.67 (0.34–1.30)	0.92 (0.44–1.92)	0.40
	C/S	59 (30.1)	17 (8.7)	1	1	
Sex	Female	70 (35.7)	21 (10.7)	0.68 (0.36–1.29)	0.64 (0.31–1.31)	0.25
	Male	73 (37.2)	32 (16.3)	1	1	
Steroids given	Given	34 (17.3)	7 (3.6)	1.68 (0.72–3.93)	1.84 (0.69–4.89)	0.18
	Not given	109 (55.6)	46 (23.5)	1	1	
Gestational age (in weeks)	28–32	44 (22.4)	31 (15.8)	3.17 (1.62–6.08)	2.14 (1.04–4.41)*	0.000
	33–37	99 (50.5)	22 (11.2)	1	1	
Respiratory distress	No distress	69 (35.2)	16 (8.2)	0.46 (0.23–0.9)	0.98 (0.41–2.35)	0.91
	Distress	74 (37.8)	37 (18.9)	1	1	
PROM	No PROM	122 (62.2)	51 (26.0)	4.39 (0.99–19.41)	4.20 (0.90–19.54)	0.13
	PROM	21 (10.7)	2 (1.0)	1	1	
APH	No APH	132 (67.3)	52 (26.5)	4.3 (0.54–34.41)	6.30 (0.74–53.56)	0.06
	APH	11 (5.6)	1 (0.5)	1	1	
Hypoglycemia	No	126 (64.3)	52 (26.5)	7.01 (0.91–54.09)	4.49 (0.55–36.42)	0.12
	Yes	17 (8.7)	1 (0.5)	1	1	

*$P = 0.05$.

AOR, adjusted odds ratio; APH, antepartum hemorrhage; COR, crude odds ratio, C/S, cesarean section; IVH, intraventricular hemorrhage; PROM, premature rupture of the membrane; SVD, spontaneous vaginal delivery.

significant link between the mode of delivery and IVH risk because the majority (93%) of C/S deliveries were done in emergency situations and our study did not separate emergency from elective C/S deliveries[15,17,22].

Furthermore, a small percentage of our sample may have used steroids, which could explain why no connection was seen in our investigations, despite some studies showing a decreased incidence of IVH in mothers who received steroids during pregnancy (20.9 vs. 57% of steroid usage)[23].

The study's limitations include the fact that the date of the last menstrual cycle was seldom recalled, gestational age was calculated using Ballard scoring, which has inter-user variability and accuracy of ±2 weeks, additionally; a cross-sectional study design was used here, making it impossible to infer causal links.

Conclusion

The prevalence of IVH was found to be high in preterm neonates. The magnitude was greater in newborns that were born very early and in infants who had very low birth weight, showing having a smaller birth weight and earlier gestational age increased the risk of IVH. Mild IVH accounts for more than three-fourths of all IVH cases. Therefore, the reduction of preterm births and low birth weight should be outlined by prenatal care providers as a significant objective of prenatal care that may call for various changes in clinical practice. Besides this, pregnant mothers should be strict in attending antenatal care follow-up appointments to identify potential risk factors for the development of IVH.

Ethical approval and consent to participate

The ethical clearance was obtained from the institutional review board of Bahirdar University with reference number BU/CHS/RERC147/2022, granting ethical approval. The family was informed of the study's purpose prior to the commencement of data collection. The written informed consent was obtained from the parents. The examination's findings were kept private and accountable, and only the investigator and the medical professionals who were caring for the newborn used them. The study protocol was carried out in conformity with the Helsinki Declaration.

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Patient consent

Not applicable. No individual person's personal details, images, or videos are being used in this study.

Author contribution

S.T. and H.T.: contributed to the methodology and statistical analysis; M.M. and S.G.: participated in preparing the first draft of the manuscript; G.R.D. and F.B.: contributed to the methodology and editing of the manuscript. All authors checked and confirmed the final version of the manuscript.

Conflicts of interest disclosure

The authors declared that they have no conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: Research Registry, https://www.researchregistry.com.
2. Unique identifying number or registration ID: researchregistry 8647.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not https://www.researchregistry.com/registernow#home/registrationdetails/5d70f2520791fb0011b79e9f/.

Data availability statement

The materials used while conducting this study are obtained from the corresponding author on reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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