2022-09-29

Magnitude and Associated Factors of Intraventricular Hemorrhage in Preterm Neonates Admitted to Tibebe Ghion Specialized Hospital

Shimalis, Tadasa

BAHIRDAR UNVERSITY

COLLAGE OF MEDICINE AND HEALTH SCIENCE

DEPARTMENT OF CLINICAL RADIOLOGY

MAGNITUDE AND ASSOCIA TED FACTORS OF INTRAVENTRICULAR HEMORRHAGE IN PRETERM NEONATES ADMITTED TO TIBEBE GHION SPECIALIZED HOSPITAL

BY DR. SHIMALIS TADASA

SEPTEMBER, 2022

A RESEARCH PAPER TO BE SUBMITTED TO COLLAGE OF MEDICINE AND HEALTH SCIENCE, DEPARTMENT OF CLINICAL RADIOLOGY, BAHIR DAR UNVERSITY IN PARTIAL FULFILLMENT OF A SPECIALTY IN CLINICAL RADIOLOGY

PRINCIPAL INVESTIGATOR;-

Dr. SHIMELIS TADESSE (RADIOLOGY RESIDENT)

ðÉ: + 2 5 1 9 1 1 9 4 3 1 1 0 shimemd@yahoo.com

ADVISORS;-

1, Dr. HABTAMU TILAHUN (MD, ASSISTANT PROFFESOR OF RADIOLOGY) ðÉ: + 2 5 1 9 1 2 2 7 2 7 8 3 Htilahun25@gmail.com

2, Mr. MEKONNEN MELKIE (MSc, in Reproductive health)

ðÉ: + 2 5 1 9 3 0 5 2 5 0 1 0 mekimeki18@gmail.com

SEPTEMBER, 2022

BAHIR DAR,

Declaration

This is to certify that the thesis entitled "Magnitude and associated factors of intraventricular hemorrhage in preterm neonates admitted to Tibebe Ghion specialized hospital" submitted in partial fulfillment of the requirements for certificate of specialty in clinical radiology of Department of clinical radiology, Bahir Dar University, is a record of original work carried out by me and has never been submitted to this or any other institution to get any other degree or certificates. The assistance and help I received during the course of this investigation have been duly acknowledged.

Name of the candidate	Date	Place

BAHIR DAR UNVERSITY

COLLAGE OF MEDICINE AND HEALTH SCIENCE

DEPARTMENT OF CLINICAL RADIOLOGY

Acknowledgment

I'm really appreciative that Bahir Dar University and Tibebe Ghion Specialized Hospital gave me the opportunity to learn more about the magnitude and attributing factors of intraventricular hemorrhage in premature newborns. My advisors, Dr. Habtamu Tilahun (MD, Assistant Professor of Radiology) and Mekonnen Kiros (Bsc, MSc in Reproductive Health), deserve a special word of appreciation for their unwavering support and guidance throughout the process of writing this paper.

In addition to my supervisors, I want to recognize and thank my friends Dr. Netsanet Workneh (MD, Pediatrician, PhD) and Ms. Selamawit Getachew (Mph), who guided me to compose my report, and the NICU nurses who took part in data gathering.

ABSTRACT

Background- Intraventricular hemorrhage is one of the medical issues that preterm infants are susceptible to as a result of their difficulty adjusting to life outside the womb. The term "intra

ventricular hemorrhage" refers to bleeding into the ventricular system from the germinal matrix, a highly cellular and vascular tissue that is only seen in preterm newborns and is quite easily disrupted, causing bleeding into the ventricles and the parenchyma in the presence of perinatal stressors.

Objectives- To assess magnitude and associated factors of intraventricular hemorrhage in preterm neonates admitted to Tibebe Ghion specialized hospital.

Methods- 196 preterm newborns hospitalized to Tibebe Ghion specialty hospital were the subject of a cross-sectional investigation. The neonatal referral form, the mother's medical file, and an in-person interview with the mother and bedside cranial sonography used to collect clinical data. After data was entered into Epi Info and exported to SPSS, analysis was carried out using Bi- and multivariable logistic regression.

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

Conclusion and recommendation;-The study discovered that the magnitude of IVH is slightly higher than that of prior studies done in different part of the world and those neonates delivered at early gestational ages and those with very low birth weight have a higher incidence of IVH Therefore, both guardians and health providers should give more attention for those neonates born at early gestational and with small birth weight.

Key word: Intra ventricular hemorrhage, preterm neonates, Associated factors, Tibebe Ghion specialized hospital.

Contents

Acknowledgment iv
ABSTRACT v
Abbreviation and acronym ix
1, Introduction 1
1.1, Background 1
1.2. Statement of the problem 4
1.3, Justification and Significance of the study 5
2, LITERATURE REVIEW 6
2.1. Magnitudes 6
2.2, Associated Factors 8
Conceptual frame work 10
3. Objectives 11
3.1. General objectives 11
3.2 Specific objectives 11
4. METHODS 12
5, RESULTS 19
7, CONCLUSIONS AND RECOMMENDATIONS 28
Questionnaire 29
References 32

List of Tables

Table 1 Showing grading of intraventricular hemorrhage according to modified papile classification. 8
Table 2 Descriptive data on sociodemographic and clinical traits of preterm newborns admitted to Tibebe Ghion specialized hospital, Bahardar, Ethiopia, in 2022 with IVH status 20
Table 3 showing distribution of common obstetric disorder of preterm neonates admitted to Tibebe Ghion specialized hospital, bahardar, Ethiopia 2022 22
Table 4 Grading of severity of IVH in preterm neonates admitted neonates admitted to Tibebe Ghion specialized hospital, bahardar, Ethiopia, 2022 23
Table 5 Bivariable and Multivariable logistic regression results of factors associated with Intraventricular hemorrhage in preterm neonates admitted to Tibebe Ghion specialized hospital, bahardar, Ethiopia, 2022 25

List of figures

Figure 1 conceptual frame work that shows the relationship between IVH and other independent variable. 10
Figure 2 Showing magnitude of intraventricular hemorrhage among preterm neonates admitted to Tibebe Ghion specialized hospital, bahardar, Ethiopia, 2022 23

Abbreviation and acronym

CSF- cerebro spinalfluid

C/S-cesarean section

CT-Computed tomography

EC-Ethiopian calendar

ELBW- extremelow birth weight

GC-Gregorian calendar

HICS-high income countries

IVH - intraventricular hemorrhage

LICS- low income countries

LBW - low birth weight

MRI-magnetic resonance imaging

NICU-neonatal intensive carunit

PIVH-periventricular intraventricular hemorrhage

U/S- ultrasound

VLBW - very low birth weight

WHO- world health organization

1, Introduction

1.1, Background

The term "intraventricular hemorrhage" refers to the presence of blood inside the cerebral ventricular system as a result of germinal matrix hemorrhage, which tears through the ependymal lining and into the lateral ventricles. The germinal matrix evolved early in the process of brain development and served as the site of glial and neuronal differentiation. Given the burden on it, its dense cellular and vascular nature prevents it from adequately controlling cerebral blood flow. As a result, both prenatal stress and stress during birth cause arteries to easily rupture [6]. The periventricular region first encounters bleeding, and if it persists, the increased blood volume dissects into the surrounding lateral ventricles, causing intraventricular hemorrhage (IVH). This form of bleeding is only possible when the germinal matrix is present. The germinal matrix does not exist in term babies and begins to form by 28 weeks and regress around 35weeks. Therefore, the only group at risk for this type of bleeding is preterm newborns [6]. about 90% of all IVHs in the newborn period occur in infants of <35 weeks, gestation and based on birth weight. IVH is very common in the very low and extremely low birth weight babies [7].

Around the world, more than 15 million newborns are born prematurely every year, with low-income nations accounting for more than half of these births. Additionally, more premature newborns are surviving in high income nations as a result of improved neonatal care, contributing to a rise in preterm births worldwide [1]. However, preterm birth-related complications are the main causes of infant death in low- and middle-income countries (LMIC) [2]. Ethiopia had a death rate of 29% for preterm newborns hospitalized to neonatal intensive care units (NICUs); respiratory distress syndrome, infection, and perinatal asphyxia were the three main causes of preterm deaths, and mortality rates were higher in lower gestational ages [3].

A preterm birth is defined by the World Health Organization as any birth that takes place before 37 complete weeks of gestation or 259 days after the mother's last menstrual cycle. Additionally, newborns are classified according to their birth weight as having a low birth weight (LBW; 1500 to 2500 g), a very low birth weight (VLBW; 1000 to 1499 g), or an extremely low birth weight (ELBW< 1000 g) [14].

Intraventricular hemorrhage, the most common neonatal intracranial disease, is one of the most frequent problems created by the immaturity brought on by premature birth [5].

Preterm birth is frequently associated with complications, both metabolic and structural. The IVH problem in preterm infants delivered before 35 weeks of gestation is still quite serious. The incidence of IVH in neonates who are VLBW and ELBW is estimated to be 50% worldwide. The risk increases with lower gestational age and in babies that are smaller than normal. The frequency varies according to birth weight and gestational age. The majority of infants with severe IVH die and those who do survive the acute problems are likely to develop long-term neurologic squeals [14].

IVH is related to alterations in cerebral blood flow to the immature germinal matrix microvasculature. The germinal matrix is richly supplied with micro vessels, but lacking basement membrane deposition, tight junctions, and glial end foot investiture. When the infants experience hypotension, hypoxemia, hypercapnia, or acidosis, cerebral blood flow rises as a response to the insult. Then, ventricular distension compromises blood flow, which further causes venous stasis within the periventricular white matter and parenchymal venous infarction happens this makes the hemorrhage occurs within the germinal matrix to bleed and as it grows may extend into the ventricular system [17].

Premature membrane rupture, protracted labor, male sex, metabolic acidosis, postnatal resuscitation, early-onset neonatal sepsis, and respiratory distress syndrome are all recognized risk factors for IVH in premature infants [12]

90% of IVH cases occur in the first five days of life, with the majority occurring in the first 24 hours. The severity of these cases increases throughout the course of the following days. Thus, according to the IVH grading, head ultrasound (HUS) is typically conducted in clinical practice between days 5 and 7 when it is at its most severe[8]. In the first 24 hours, some high-risk preterm newborns can need head ultrasound[9].

There are a number of investigative techniques, including computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography, that can be used to diagnose neonatal cranial hemorrhages. U/S is a less expensive and non-invasive way to check for IVH in newborns. It is highly sensitive, practical, dynamic, radiation-free, and used in the diagnosis of IVH and sub ependymal hemorrhage[10]. On a sonographic scan, germinal matrix hemorrhages occur as echogenic areas along the caudothalamic groove that run along the frontal horn of the lateral ventricle.[6].

The severity of PIVH is described using modified Papile classification (see Table 1)[11].

Table1 Showing grading of intraventricular hemorrhage according to modified papile classification.

Grade	Description
I	being confined to sub ependymal region/germinal matrix
II	Occupying <50% of the lateral ventricle volume and no ventricular dilatation.
III	Hemorrhage in to lateral ventricle, resulting in dilatation of the ventricle.
IV	Ventricular hemorrhage with parenchymal extension/presence infarction.

1.2. Statement of the problem

Worldwide under-five mortality has dramatically decreased recently, including in Ethiopia. Neonatal mortality in Ethiopia, however, has remained constant and is even thought to be rising over the previous several years; it was 29 per 1000 live births in 2016 and 30 per 1000 live births in 2019 [13]. Newborn morbidity and death would be decreased with early detection and treatment of neonatal problems. IVH is one of complication associated with preterm and significantly contribute to death and lasts lifelong impact on survivors. neonates that born prematurely and who are fewer than 35 weeks gestational age are more likely to develop IVH. Children who survive the immediate complications are likely to experience conditions like cerebral palsy, post-hemorrhagic hydrocephalus, cognitive/intellectual impairment, and epilepsy later in childhood. These conditions could significantly hinder the growth and development of the affected children [14].

Once IVH develops, there are few treatment options, most of which are supportive and concentrate on controlling the consequences. The majority of therapies now utilized to treat intraventricular hemorrhages are ones that are focused on treating 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 [6, 15].

Preventing early birth is the best way to lower IVH-related morbidity and death rates. Therefore, it is necessary to identify high risk neonates in order to settle on prevention methods. There are few statistics available on the prevalence, risk factors, and consequences of IVH in low-income countries [16].

1.3, Significance of the study

Intraventricular hemorrhage is one of significant sign of poor neurodevelopmental outcomes in newborns. Preterm neonates who develop IVH are more likely to die, and survivors are more likely to be permanently disabled. It is difficult to produce local statistics in Ethiopia since the setting and care provided to preterm newborns varies from high income nations, and the majority of the literatures that are currently available are reported from high income countries.

There are a few studies on the prevalence of IVH in preterm newborns in east Africa, and there is only one study in Ethiopia which employed autopsy of deceased neonates to diagnose IVH done 20 years ago. there is no study that used cranial sonographic scan as a diagnosis tool before and this is the first of its kind done in Ethiopia.

Identification of risk factors and IVH magnitude may lead to improvements in newborn intensive care unit care standards. 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 and those neonates who are at risk. 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.

2, LITERATURE REVIEW

2.1. Magnitudes

Several publications have documented various incidence rates of IVH in premature newborns, ranging from 5% to 90% [18].

In the US, 20 to 25% of all VLBW infants experience IVH, and 10 to 15% of this group's experience severe IVH. More than 75 percent of these infants grow up with cerebral palsy or mental disability. [17].

The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) examined 9575 children born at network hospitals between January 1, 2003, and December 31, 2007, who had extremely low GA (22-28 weeks) and very low birth weights (401-1500 g). They found that 32% of newborns with birth weights of 1500 gm or less had IVH, compared to 23% of neonates weighing up to 2200 gm [20].

In cohort study done in Germany on 2203 singleton, VLBW (<1500gm) and GA <36 weeks between 2009-2015 prevalence of IVH is higher in vaginal delivery(26%) and emergency C/S (31.1%) as compared to planned C/S(17.2%) [41]

The prevalence of IVH was found to be 20% in a retrospective cross-sectional study on 178 newborns with a gestational age of less than 32 weeks that was conducted in Fatemieh Hospital in Iran. IVH is becoming more common, and there is a clear correlation between factors including low birth weight, a low 5-minute Apgar score, small gestational age, and the need for mechanical breathing [40]

In 2012, a cross-sectional study was conducted on 298 preterm neonates (GA < 32 weeks, birth weight <1500 g) at the University Teaching Hospital of Lusaka, Zambia. IVH is diagnosed by cranial ultrasonography, which detects it in 34.2% of newborns. Risk factors significantly associated with IVH were birth weight and gestational age [22].

In a cross-sectional study conducted in 2014 at the Aminu Kano Teaching Hospital in Nigeria on 99 preterm neonates (37 completed weeks), IVH was found in 16.2% of the newborns and lower gestational age, and the need for respiratory support was identified as the risk factor. [39]

A prospective cohort study on 120 neonates with birth weight less than 2000gm is conducted in Uganda in 2019. They discovered that 34.2% of newborns had IVH, and the risk was increased by vaginal birth, early gestation, and the requirement for resuscitation after admission.[37]

One study was conducted in Ethiopia in 2001 in the newborn unit of Tikur Anbessa Hospital among preterm neonates (gestational age <36 weeks and birth weight <2000 g and who died while in the ward). Autopsies were performed on 56 infants and the prevalence of IVH was 32%.[38]

2.2, Associated Factors

Numerous literatures have discussed the causal factors of IVH in preterm deliveries, their potential effects on the health of the neonates, how to manage the condition, and the challenges associated with IVH.

Infants born prematurely before 35 weeks of gestation are at risk for intrauterine growth restriction (IVH), which is connected to the presence of germinal matrix at this gestational age that involutes by 34 to 36 weeks. Majority of IVHs are discovered after the third day, but they can appear at any point in the first two weeks of life. Routine screening can be postponed until the second week without endangering patient care. In clinical practice, routine screening is recommended for preterm infants delivered before 32 weeks of gestation since they have a higher risk of IVH.[26, 27, 28]. .

Antenatal steroids have been proven to lessen the risk of IVH in preterm neonates, and IVH incidence in premature newborns born across Saudi Arabia was lower than other reports worldwide, ranging from 13% to 27%.[23].

The results of a retrospective chart study of preterm infants born at King Abdulaziz Medical City-Riyadh, Saudi Arabia, between 2016 and 2018 demonstrated that C/S delivery is related with a general decrease in IVH and severe IVH prevalence compared to vaginal birth [24].

According to a prospective cohort study done on 160 asphyxiated babies treated with hypothermia between August 2008 and June 2013, IVH prevalence is higher in these groups of neonates than in is in asymptomatic newborns [25].

According to a 2017 meta-analysis (46,244 infants, 13,432 Chorioamnionitis cases). Infants born very preterm were more likely to develop IVH when they had clinical and pathological Chorioamniotis [44]

Management and prognosis factors are impacted by the IVH severity grading. In terms of severity grading, the distribution of IVH varies between literatures as well. The most prevalent type of IVH, grade 1 and 2, is present in 54.9% of cases, while grade 3 and 4 account for 16.% to 27.5% of cases. A study from Zambia indicated that the grade 4 IVH in preterm newborns in the first three days of life has 85.7% case fatality rate [22. 24].

Post hemorrhagic hydrocephalus and periventricular leukomalacia are the two main consequences of IVH. Hydrocephalus manifests with increased head circumference, enlarged ventricles and signs of increased intracranial pressure. Both types of hydrocephalus (communicating and obstructive) can occurs and the neonates may not show the signs during neonatal period, follow up is required then after [34].

The severity of IVH and the presence of concomitant conditions affect the prognosis. As many as 50% of children with severe IVH experience post hemorrhagic hydrocephalus, and 5-10% experience neonatal seizures. Long-term, 75% of these infants exhibit major neurodevelopmental problems. Those who have mild IVH are not exempt to developmental disability [17,18,30,31]

Management and prognosis factors are impacted by the IVH severity grading. In terms of severity grading, the distribution of IVH varies between literatures as well. The most prevalent type of IVH, grade 1 and 2, is present in 54.9% of cases, while grade 3 and 4 account for 16.% to 27.5% of cases. A study from Zambia indicated that grade 4 IVH in preterm newborns in the first three days of life has 85.7% case fatality rate. [22. 24.25]

As IVH has a complex etiology, both prevention and management of the problem after it occurs might lessen the complications it causes in the future. Preventive approach aims to address the risk factors and decrease preterm births. Preventing IVH from progressing and identifying and treating problems are the main goals of IVH management. These include breathing assistance and blood pressure regulation. both indomethacin given to close patent ductus arteriosus and prenatal glucocorticoids given to expedite lung development have been demonstrated to improve the stability of the germinal matrix vasculature in test animals [33, 35, 36].

Interventions targeting prevention of fluctuation in the cerebral blood flow, platelet and coagulation disorders have been researched. Early diagnosis and treatment of conditions such as severe respiratory distress syndrome, pneumothorax, hypoxia, hypercapnia, seizures, patent ductus arteriosus and infections can reduce the risk of IVH, as these are the risk factors identified to cause fluctuation in the cerebral blood flow [35,36].

Conceptuaframe work

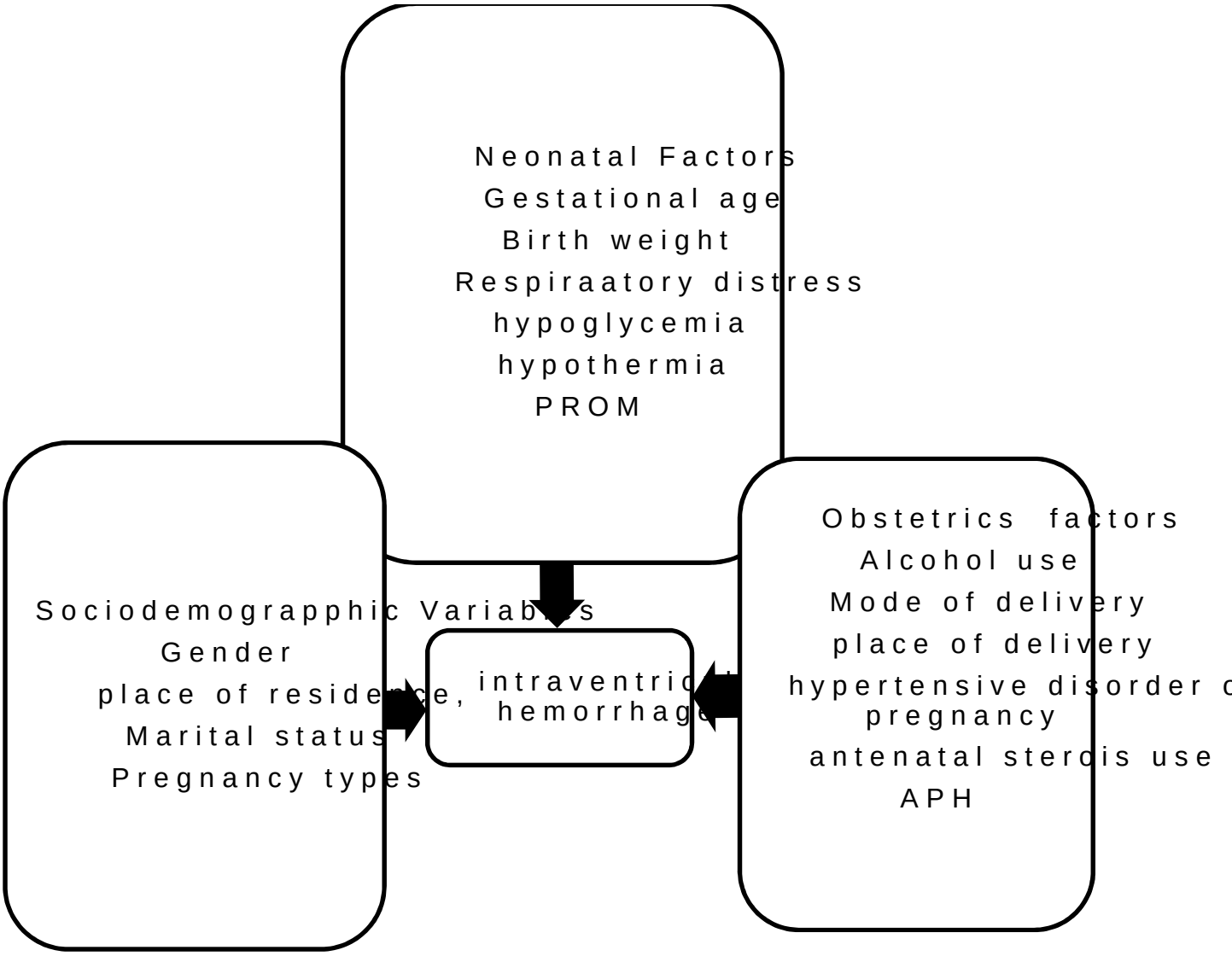

Figure 1 conceptual frame work that shows the relationship between IVH and other independent variable.

3. Objectives

3.1. General objectives

To determine the magnitude and associated factors of IVH in preterm neonates admitted to Tibebe Ghion Specialized hospital during study period from March 1-August 30, 2022 EC.

3.2 Specific objectives

- To determine magnitude of IVH in preterm neonates admitted to Tibebe Ghion Specialized hospital
- To identify factors associated with of IVH in preterm neonates admitted to Tibebe Ghion Specialized hospital

4. METHODS

4.1 Study area and study period

The study was carried out in the Tibebe Ghion specialty hospital between March 2022 and August 2022. The hospital is situated in Bahir Dar, 552 kilometers northwest of Addis Ababa. It was founded in 2019 and is owned by Bahir Dar University. The hospital is a specialized teaching hospital of Bahir Dar University and currently provides various clinical services to more than 6 million people in its catchment region. With a total of 539 doctors representing 12 subspecialists, 126 specialists, 23 general practitioners, 252 residents, and 126 interns. The hospital offers a variety of clinical services and becomes one of the most renowned institutions in the country for specialty training. The NICU is one of the busiest areas in this hospital. Over the course of six months around 400 premature newborns are admitted to the hospital's NICU unit. (NICU report)

4.2, Study Design

Institutional based Cross sectional study design was used.

4.3. Population

4.3.1. Source Population

All preterm neonates admitted to the hospital during study period

4.3.2, Study population

Preterm neonates that selected systematically and whose parents gave consent to be enrolled to the study

4.4, Sample size determination

Neonates filling inclusion criteria during study period was studied. Preterm neonates who meet the inclusion criteria were enrolled to the study by census methods until the sample size of 196 is reached.

The sample size is calculated using the formula

$N = z^2 (p) (1-p)/d^2$

Assuming the global 50% IVH prevalence in the preterm neonates and

95% confidence level.

Where N = required sample size,

z = 1.96

p = assumed IVH prevalence

d= was the desired width of confidence interval (0.05).

N= 385, but, the source population size in NICU in 06 month is 400,

Using adjusted formula (finite population correction) n=196 and adding 5 %(10) non response rate, 206 is considered the minimum sample size required for the study.

4.5. Sampling technique.

Systematic random sampling was used with (k=2) (400/206) and the first neonate was selected by lottery method and the others taken every second interval.

4.6. Inclusion and Exclusion criteria

4.6.1. Inclusion criteria

All preterm neonates (GA, 28-37 weeks) admitted to Tibebe Ghion specialized hospital during study period included.

4.6.2. Exclusion criteria

Preterm neonates with known genetic disease congenital anomalies were excluded.

4.7. Study variables

4.7.1. Dependent variables

-Intraventricular hemorrhage

4.7.2. Independent Variables

-Gender
-Place of residency
-Marital status
-Place of delivery
-Alcohol use during pregnancy
-Gestational age
-Birth weight
-Mode of delivery
-Steroid use
-PROM
-APH
-Hypertensive disorder of pregnancy
-Types of pregnancy
-Respiratory distress
-Hypoglycemia
-Hypothermia

4.8. Definitions of terms

1. Intraventricular hemorrhage- is those having intraventricular hemorrhage showing echogenic regions close to the caudothalamic groove extending along the floor of the frontal horn of the lateral ventricle on cranial sonographic study.
2. Germinal matrix- a densely cellular and vascular tissue serve as site of glial and neuronal differentiation that easily ruptures and bleeds in perinatal stresses.
3. Ventricular system- is part of brain system that serves as site of collection of CSF and drainage to subarachnoid system.
4. Trans-fontanel- is a window for sonographic scan of neonatal brain via skull bone defect that normally allows skull bone to expand for brain growth.
5. Preterm- birth that occur between 28-37 weeks of gestation.
6. Gestational age- duration in weeks found between last normal menstrual period and birth
7. Low birth weight- birth weight 2000gm-2499gm.
8. Very low birth weight- birth weight 1500gm-1999gm.
9. Extreme low birth weight- birth weight of 1000-1499gm.
10. Duration of labor- is a time found between onset of regular uterine contraction and birth.
11. Place of delivery- The place either health institution or home where the baby borns,
12. Mode of delivery- it is the route the baby comes out from his maternal uterus and shows if any intervention done.
13. Neonates- babies born after 28 weeks of gestation and less than 28 days old.
14. NICU- is the hospital center where neonates get admitted for the help they need.

4.9. Data collection methods and procedures

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. Using a Siemens ultrasound scanner (ACUSON, Germany, 2021) outfitted with both a curved probe (5 MHz) and a linear probe (8 MHz), the lead investigator made the IVH diagnosis. To look for the ventricular system and brain parenchyma, a sonographic examination was conducted using the anterior fontanelle as an acoustic window in sagittal, axial, and coronal perspectives. The scan was performed at the patient's bedside in NICU ward, for newborns between fourth and seventh postnatal days. Senior radiologists were consulted when problems interpreting the results arose.

During a head ultrasound, 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. Medical gel will be applied to the scanning zone, hence newborns have been placed supine on the scan table or neonatal bed and the fontanels have been identified. We can obtain high-quality images of the brain by moistening the area with gel that removes air b/n probe, skin, and skull. The scan may take 10–15 minutes, and we can adjust the probe's location and angle until we achieve the desired image quality.

The brain's inner structure, including the ventricles and blood vessels, is depicted in black-and-white pictures. When cranial sonography revealed echogenic portions at the caudothalamic groove extending along the floor of the frontal horn of the lateral ventricle, we diagnosed the neonate as having IVH and graded this condition using the papile grading system after observing the anatomic region to which these echogenic contents expand.

4.10. Data analysis and interpretation

After being cleaned and validated as complete, the collected data is loaded into the EPI info 7.2.5 software and exported to SPSS version 23 for analysis. Descriptive statistics are employed and provided as frequency and percentage for demographic and clinical data of categorical variables. With a 95% confidence interval (CI), binary logistic regression model was employed to see the relationship between IVH and additional clinical and sociodemographic parameters. IVH is used as a binary dependent variable (IVH/No IVH). Furthermore, other independent variables were instituted in to logistic regression first as a variable and later as multivariable (those with P<0.25 on Bivariable). This analysis for gestational age and birth weight was done as categorical variables using WHO classification for Gestational age (very preterm <28, 28-32weeks, moderate to late preterm 32-37weeks) and Birth weight (extreme very low birth weight <1000gm, Very low birth weight, 1000-1499 gm., low birth weight, 1500-2500gm). Our newborns have birth weight between 1000-2000gm and gestational age between 28-36 weeks. The results are presented using text, tables, and diagrams.

4.11. Quality control measures

The cerebral ultrasound scan method and data collection questions were reviewed with Neonatologists working in NICU who participated in data collection. Radiologists were consulted when it was difficult to decide on the sonographic scan's findings.

4.12. Ethical consideration

Prior to the commencement of data gathering, the institutional review board of Bahir dar university medical college and health science granted ethical approval. The family was informed of the study's purpose prior to the commencement of data collection. We also got verbal informed permission. The examination's findings were kept private and accountable, and only the investigator and the medical professionals who were caring for the newborn used the data. The inspection is carried out in a temperature-controlled setting. The treating physicians were informed of incidental findings with clinical value and those with positive IVH findings during the data collection phase.

4.13. Dissemination plan

The study's conclusions were written up and sent to the pediatric and child health departments, as well as the radiology department. Additionally, the findings will be published in a peer-reviewed journal.

5, RESULTS

5.1 Sociodemographic and clinical characteristic of neonates

The response rate was 95% and study contains 196 preterm neonates admitted to Tibebe Ghion specialized hospital throughout the study period, of which 105 (53.6%) are male and 91 (46.4%) are female.

Majority of the preterm birth women live in metropolitan areas (46.4%), while rural areas make up 34.2%. semi urban population accounts for 19.4% of IVH. The majorities of mothers (accounts 98% of the sample) are married and live with their spouse.

Among neonates enrolled in the study 61.7% of them are singletons and 37.2% of them are twin. A hospital was used in 87.2% of deliveries, with SVDs accounting for 61.2% of all deliveries Deliveries through caesarean section account for 38.8% of all births and contribute 8.7% of total IVH.

Most of the neonates in the study have birth weights between 1500 and 2000 gram (60.7%) and contribute less to total IVH (10.7% out of 27.04% total). 38.3% of babies born before 32 weeks of gestation and holds most of IVH (15.8%) of total IVH.

There were variety of neonatal problems and of 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.

For further information see Table 2 below.

Table2Descriptive data on sociodemographic and clinical traits of preterm newborns admitted to Tibebe Ghion specialized hospital, Bahardar, Ethiopia, in 2022 with IVH status.

Variables	Frequency(%)
Place of residency	
Rural	67(34.2%)
Semi urban	38(19.4%)
Urban	91(46.4%)
Gender	
FemaleNo. (%)	91(46.4)
Male No. (%)	105(53.6)
Place of delivery	
Health center	25(34.2)
Hospital	171(87.2)
GA (weeks)	
28 to32	75(38.3)
32 to 37	121(61.7)
Birth weight (gm.)	
1000 to 1500	75(38.3)
1500 to 2000	121(61.7)
Pregnancy	
Singleton	121(61.7)
Twins	73(37.2)
Triplets	2(1)
Mode of delivery	
SVD	120(61.2)
Caesarian 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)

5.2. Obstetric problems.

Numerous obstetric problems occurred during births of these premature infants. Of this mother who gave preterm birth, 20.9% of them given steroid injection to accelerate fetal lung maturity. 23.5% of mothers has one of hypertension disorders of pregnancy and they contributed for 6.1% of total IVH. Preeclampsia affects the majority of women with hypertension, 3.3% of total hypertension, 23.5%. Results of a study on alcohol usage, late pregnancy problems like APH, PROM, and labor anomalies shown in table 2.

Table3 showing distribution of common obstetric disorder of preterm neonates admitted to Tibebe Ghion specialized hospital, bahardar, Ethiopia2022

Factors	Value		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)
		Super imposed preeclamsia	6(3.1)
		Total	46(23.5)
	No hypertension		150(76.5)
Alcohol use	No alcohol		179(91.3)
	Alcohol		17(8.7)
APH	No APH		184(93.9)
	APH		12(6.1)
PROM	No PROM		173(88.3)
	PROM		23(11.7)
Spontaneous labor	Yes		174(88.8)
	No		22(11.2)
Labor induction	Yes		12(6.1)
	No		184(93.9)

5.3. Sonographic study

The overall magnitude of IVH in preterm newborns (28-37 weeks) admitted to this hospital is found to be 27.04% (95% CI; 20.9%-32.2%) (fig. 2), and the magnitude is 42.6% for very preterm (28-32 weeks) and 41.3% for VLBW (1000-1500gm.). Applying the papile grading system of IVH, grade I is the most observed (12.24%) and the severe form of IVH (grade IV) accounts 0.5% only (Table 4).

Figure 2 Showing magnitude of intraventricular hemorrhage among preterm neonates admitted to Tibebe Ghion specialized hospital, bahardar, Ethiopia, 2022.

Table 4 Grading of severity of IVH in preterm neonates admitted neonates admitted to Tibebe Ghion specialized hospital, bahardar, Ethiopia, 2022.

Grading	Frequency	Percentage (%)
Grade I	24	12.24
Grade II	19	9.7
Grade III	9	4.6
Grade IV	1	0.5
TOTAL	53	27.04%

5.4. Factors Associated with Intra ventricular hemorrhage 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 <0.25 were then entered into multivariable logistic regression.

Hosmer and Lemeshow test was run and it indicates that the model has good fit.

Multivariable logistic regression analysis has identified factors that are associated with IVH (P-values <0.05). These were gestational age and birth weight of the preterm neonates. The odds of IVH was low among preterm neonates with birth weight between 1500-2000gm than neonates having birth weight between 1000-1499gram (AOR:0.38, 95% CI:0.18-0.79). The odds of IVH was high among women who had gestational age between 28-32 weeks than those women of gestational age between 33-36 weeks (AOR: 2.14, 95% CI: 1.04-4.41).

Findings indicate that newborns that were very preterm (28 to 32 weeks) develop IVH two times more than moderate to late preterm (33 to 36 weeks) (AOR: 2.14, 95% CI: 1.04-4.41).
And Compared to newborns with VLBW (1000-1499gm), LBW neonates (1500-2000gm) have a 62% lower risk of developing IVH (AOR: 0.38, 95% CI 0.18-0.79). See Table 4.

Table 5 Bivariable and Multivariable logistic regression results of factors associated with Intraventricular hemorrhage in preterm neonates admitted to Tibebe Ghion specialized hospital, bahardar, Ethiopia, 2022

Factors	Category	IVH status		Bivariable L.R	Multivariable L.R
		No IVH	IVH	COR (95% CI)	AOR (95% CI)
Birth weight(gm.)	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)*
Mode of delivery	SVD	84(42.9%)	36(18.4%)	0.67(0.34,1.30)	0.92(0.44, 1.92)
	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)
	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)
	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)*
	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)
	Distress	74(37.8%)	37(18.9%)	1	1
PROM	No PROM	122(62.2%0	51(26.0%)	4.39(0.99,19.41)	4.20(0.90, 19.54)
	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)
	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)
	Yes	17(8.7%)	1(0.5%)	1	1

* P „ 0.05, AOR= adjusted odds ratio COR = crude odds ratio, CI = confidence interval

6, DISCUSSIONS

This study is one of the few studies of IVH in preterm neonates in Sub-Saharan Africa and the first in Ethiopia for using cranial sonography to know status of IVH.

In this institutional based study in which 196 preterm neonates were included magnitude of IVH is determined as 27.04% for GA< 36 weeks and it more than 40% for those neonates gestational age< 32 weeks and birth weight<1500gm. regarding the severity of IVH occurance 81% of total IVH is mild(I&II) and severe(III &IV) accounts 19%.

Our investigation revealed a higher incidence of IVH compared to a study conducted in the United States, which reports a prevalence of 22.5%. The elevated rate may have been caused by the fact that our study population included newborns who were hospitalized and had neonatal problems with documented risk factors for IVH, 60-70% (20-30% in USA) (respiratory distress, and neonatal infections) [17].

Compared to study done in Germany our finding is comparable for preterm births with Either SVD (26.6%) and emergency C/S(31.1%) and higher than those done with elective Cesarean section(17.7%) This disparity showed the preventive effect of elective C/S, which removes the baby's exposure to the second stage of labor when its exposure is already known to increase the risk of IVH. and most of neonates in our study is already exposed to second stage of labor (61.2%) [41].

Our data point to a marginally lower prevalence when compared to studies done in two other African nations (Uganda and Zambia) (27.02% vs. 34% in both). The main distinction is that while both of their sample populations included higher risk categories with GA<32 weeks, our study included all preterm newborns [22, 37].

Our study found a reduced prevalence (27.04% versus 32%) when compared to research conducted in Ethiopia 20 years prior. The reason for the discrepancy could be because the neonates in this study were already deceased, suggesting they have had serious problems that increased their likelihood of developing IVH, and that the diagnosis method employed was autopsy, which is more sensitive to IVH than the sonographic study [38]

In line with prior studies, we discovered that infants who are born weighing more than 1500 g experience less IVH than those who do not (AOR=0.38, CI(0.18,0.79)) and babies born after 32 weeks of gestation experience less IVH than those born before 32 weeks (AOR=2.14, CI(1.04,4.41)). [20, 22, 37, 39, 40]

Only the estimated gestational age and birth weight were significantly correlated, whereas the modes of delivery, place of delivery, Gender, and the use of steroids were not.

In studies conducted in various locations, vaginal delivery is linked to a higher risk of IVH than elective C/S delivery; however, in our cases, there was no 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 didn't separate emergency from elective C/S deliveries. [24, 37, 41]

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 moms who received steroids during pregnancy (20.9% vs. 57% of steroid usage). [21]

In this study we have found that Birth weight and gestational age were found to have a substantial impact on the incidence of IVH in preterm babies. Given that IVH substantially reduces the quality of life for affected neonates who survive; this study will be a crucial contribution to preventative initiatives in target groups.

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

7, CONCLUSIONS AND RECOMMENDATIONS

7.1. Conclusion

The study revealed that the magnitude of IVH in preterm neonates was high (27.04%). The magnitude is greater in newborns who were born very early and in infants who had very low birth weight, showing having smaller birth weight and earlier gestational age increased the risk of IVH. The magnitude of IVH is little higher than what has been reported globally and from some African nations likely because of neonates in our study are those who were admitted to NICU wards and have a greater number of known risk factors for IVH than neonates in our reference Mild IVH accounts for 80% of all IVH cases. Prenatal steroid use, mode of delivery, or place has no significant effect on the occurrences of IVH in our sample.

7.2. Recommendations

- 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.
- Formal risk assessments that are started at the first visit and continued periodically throughout the pregnancy should be a part of prenatal care in order to identify potential challenges.
- Expanding the use of ultrasound imaging early in pregnancy will improve the accuracy of pregnancy dates.
- Pregnant Mothers should be strict to attend ANC follow-up appointments to identify pregnancy problems that may have contributed to the development of IVH early on
- To effectively manage affected newborns, the neonatal intensive care unit must be furnished with appropriate equipment.
- Clinicians and nurses need to be conscious of the severity and difficulties linked to IVH.
- To learn more about the contributing factors, in-depth research using a case-control or cohort should be carried out

Annex 1

Questionnaire

This is a format prepared in order to collect information on the magnitude and associated factors of IVH in preterm neonates admitted to Tibebe Ghion specialized hospital, Bahir Dar, Ethiopia.

- Inclusion criteria ƒ Preterm neonates (GA= 28 wk) admitted to TGSH NICU.

1, Demographic data

1. Maternal Age_____
2. Place of residency
   - I. ☐ Urban
   - II. ☐ Semi urban
   - III. ☐ Rural
3. marital status
   - I. ☐ Married
   - II. ☐ Single
   - III. ☐ widowed

2, Neonatal conditions

1, Pregnancy
1, ☐ Singleton
2, ☐ Twins
3, ☐ Triplets

2, place of delivery
1, ☐ Home
2, ☐ Hospital
3, ☐ health center

3, mode of delivery
1, ☐ SVD
2, ☐ Cesarean section
3, ☐ Instrumental

4, Duration of labor: _____in hours

5,Post Natal dates_____

6,Sex
1, ☐ Male
2, ☐ Female

7, best gestational age in weeks: ____ wks

8, Birth weight: _____gm

9. Apgar Score at 0 and 5 mints: ___,___|

10, is there antenatal corticosteroid used?
1, ☐ Yes
2, ☐ No

11. IF yes at which GA?_____

12. Diagnosis of the neonate (tick all that apply)

1. ☐ Respiratory Distress Syndrome
2. ☐ neonatal infections, sepsis, meningitis
3. ☐ Perinatal asphyxia
4. ☐ Hypoglycemia
5. ☐ Hypothermia
6. ☐ Other, specify:_____

3. OBSTETRIC DISORDERS

12.1 Hypertensive disorders of pregnancy 1☐ Yes 2☐ No

12.2 Alcohol use during pregnancy 1☐ Yes 2☐ No

12.3 If yes, check type (TICK ALL THAT APPLY):

1☐ Pre-eclampsia 3☐ Superimposed pre-eclampsia

2☐ Eclampsia 4☐ Chronic hypertension

12.4 Antepartum hemorrhage (APH): 1☐ Yes 2☐ No

12.5 Other maternal illnesses 1☐ Yes 2☐ No

12.6 If yes specify_____

INTRAPARTUM AND IMME DIATE POSTPARTUM

12.7 Spontaneous labor 1☐ Yes 2☐ No

12.8 PROM 1☐ Yes 2☐ No

12.9 Induction of labor 1☐ Yes 2☐ No

4. Sonographic finding
13.1 Is there evidence of IVH? 1,☐Yes 2,☐ No
13.2 If yes what is the grade of IVH? 1, ☐Grade I (confined to the germinal matrix) 2, ☐GradeII („ 50% of the lateral ventricle volume) 3, ☐GradeIII (… 50% of the lateral ventricle volume) 4, ☐GradeIV (periventricular infarction/hemorrhage)
13.3. is there incidental congenital brain anomaly seen? 1,☐Yes 2,☐ No
13.3.1. if yes, specify_____

Thank you!

References

1. March of Dimes, P., Save the Children W. World Health Organization born too soon, vol. 126;2012.Availablefrom:
2. Howson, C.P., et al., Born too soon: preterm birth matters. 2013. 101(1): p. 1-9.
3. Muhe, L.M., et al., Major causes of death in preterm infants in selected hospitals in Ethiopia (SIP): a prospective, cross-sectional, observational study. 2019. 7(8): p. e1130-e1138.
4. Howson, C., M. Kinney, and J.J.G.W.H.O. Lawn, PMNCH, save the children, born too soon: the global action report on preterm birth. 2012.
5. Baumert M, B.G., Paprotny M, Walencka Z, Sodowska H, Cnota W and Sodowski K. Epidemiology of peri/intraventricular haemorrhage in newborns at term. J Physiol Pharmacol 2008; 59 Suppl 4: 67-75.
6. Dr Bahman Rasuli , A.P.F.G.e.a., Germinal matrix hemorrhage. Radiopedia.org, 2021.
7. Kuperman AA, K.G., Papadakis E, Brenner B. , Intraventricular hemorrhage in preterm infants: Coagulation perspectives. Semin Thromb Hemost, 2011(37): p. 730-6.
8. Brouwer, A., et al., Neurodevelopmental outcome of preterm infants with severe intraventricular hemorrhage and therapy for post-hemorrhagic ventricular dilatation. 2008.152(5): p. 648-654.
9. Paneth, N., et al., Incidence and timing of germinal matrix/intraventricular hemorrhage in low birth weight infants. 1993.137(11): p. 1167-1176.
10. LeFlore JL, B.R., Pritchard MA and Engle WD. Value of neurosonography in predicting subsequent cognitive and motor development in extremely low birth weight neonates. J Perinatol 2003; 23: 629-634.
11. Papile LA, B.J., Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr. 1978;92(4):529-534.
12. A.M. Heuchan, N.E., D.H. Smart, J.M. Simpson, Perinatal risk factors for major intraventricular hemorrhage in the Australian and New Zealand Neonatal Network,. Arch Dis Child Fetal, 1995-97. 86.
13. Ethiopian Public Health Institute (EPHI) [Ethiopia] and ICF. 2019. Ethiopia Mini Demographic and Health Survey 2019: Key Indicators. Rockville, Maryland, USA: EPHI and ICF.
14. Brouwer AJ, G.F., Benders MJNL, De Vries LS. Early and late complications of germinal matrix-intraventricular haemorrhage in the preterm infant: what's new? Neonatology. 2014;106(4):296-303.
15. Hinson, H.E., et al., Management of intraventricular hemorrhage. 2012. 101(2): p. 73-82.

16. Adegoke S, O.A., Bankole K, Tinuade O. Intraventricular hemorrhage in newborns weighing <1500 g: Epidemiology and short-term clinical outcome in a resource-poor setting. Ann Trop Med Public Health. 2014;7(1):e54. Available from:
17. McCrea, H.J. and L.R. Ment, The diagnosis, management, and postnatal prevention of intraventricular hemorrhage in the preterm neonate. Clinics in perinatology, 2008. 35(4): p. 777-vii.
18. Mancini, M.C., et al., Intraventricular hemorrhage in very low birth weight infants: associated risk factors and outcome in the neonatal period. 1995. 54(9): p. 151-154.
19. Kadri, H., A.A. Mawla, and J.J.C.s.N.S. Kazah, The incidence, timing, and predisposing factors of germinal matrix and intraventricular hemorrhage (GMH/IVH) in preterm neonates. 2006. 22(9): p. 1086-1090.
20. Stoll BJ, H.N., Bell EF, Shankaran S, Laptook AR, Walsh MC, et al. Neonatal outcomes of extremely preterm infants from the NICHD neonatal research network. Pediatrics. 2010;126(3):443-56.
21. Sajjadian, N., H. Fakhrai, and R.J.A.M.I. Jahadi, Incidence of intraventricular hemorrhage and post hemorrhagic hydrocephalus in preterm infants. 2010: p. 260-262.
22. Mulindwa M. J. , S.S., Chomba E., The Prevalence of Intraventricular Haemorrhage and Associated Risk Factors in Preterm Neonates in the Neonatal Intensive Care Unit at the University Teaching Hospital, Lusaka, Zambia. Medical Journal of Zambia, 2012. 39.
23. Abolfotouh, S.A.S., W.A. Altwaijri, M.A. Al Rowaily, Prospective study of early and late outcomes of extremely low birthweight in Central Saudi Arabia. Bmc pediatrics, 2018. 18: p. 280.
24. Alotaibi, Wafa Sattam M et al. •Reduction of severe intraventricular hemorrhage, a tertiary singlecenter experience: incidence trends, associated risk factors, and hospital policy., Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery vol. 36,12 (2020): 2971-2979.
25. Al Yazidi, G., Boudes, E., Tan, X. et al. Intraventricular hemorrhage in asphyxiated newborns treated with hypothermia: a look into incidence, timing and risk factors. BMC Pediatrics 15, 106 (2015).26. Volpe, J.J., Neurology of the newborn. E-Book. 2008.
27. Boal, D., et al., Optimal cost-effective timing of cranial ultrasound screening in low birth-weight infants. 1995. 25(6): p. 425-428.
28. Sauve, R., Fetus, and N.C.J.P.C. Health, The neurodevelopmental outcome of preterm screening cranial ultrasound examinations for the prediction of long term neurodevelopmental outcomes in preterm infants. 2001. 6(1): p. 39-52.
29. Han, R.H., et al., Predictors of mortality for preterm infants with intraventricular hemorrhage: a population-based study. Childs Nerv Syst, 2018. 34(11): p. 2203-2213.
30. Whitaker, A.H., et al., Neonatal cranial ultrasound abnormalities in low birth weight infants: relation to cognitive outcomes at six years of age. 1994. 94(6): p. 719-729.

31. Pinto-Martin, J.A., et al., Relation of cranial ultrasound abnormalities in low-birthweight infants to motor or cognitive performance at ages 2, 6, and 9 years. 1999. 41(12): p. 826-833.
32. Ment, L., et al., Practice parameter: Neuroimaging of the neonate [RETIRED]: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. 2009. 58(12): p. 1726-1738.
33. Ment, L.R., et al., Indomethacin promotes germinal matrix microvessel maturation in the newborn beagle pup. 1992. 23(8): p. 1132-1137.
34. Volpe, J.J.J.C.i.p., Brain injury in the premature infant: neuropathology, clinical aspects, pathogenesis, and prevention. 1992. 27(3): p. 567-587.
35. Wells, J.T. and L.R. Ment, Prevention of intraventricular hemorrhage in preterm infants. Early Hum Dev, 1995. 42(3): p. 209-33.
36. Ballabh, P., Pathogenesis and prevention of intraventricular hemorrhage. Clinics in perinatology, 2014. 41(1): p. 47-67.
37. R. MacLeod, J.N.P., N. Okalany, Intraventricular haemorrhage in a Ugandan cohort of low birth weight neonates: the IVHU study. BMC PEDIATRICS, 2021.
38. Worku, B., T. Tilahun, and J. Schneider, Occurrence of intraventricular hemorrhage among preterm infants admitted in Tikur Anbessa Hospital, Ethiop Med J, 2004. 42(2): p. 109-14.
39. Egwu C C, Ogala W N, Farouk Z L, Tabari A M, Dambatta A H. Factors associated with intraventricular hemorrhage among preterm neonates in Aminu Kano teaching hospital. Niger J Clin Pract 2019;22:298-304
40. Basiri B, Sabzehei MK, Shokouhi Solgi M, Khanlarzadeh E, Mosheiri M. The Frequency of Intraventricular Hemorrhage and its Risk Factors in Premature Neonates in a Hospital's NICU. Iran J Child Neurol. 2021 Summer; 15(3):109-118.
41. Humberg, A., Härtel, C., Paul, P., Hanke, K., Bossung, V., Hartz, A., Fasel, L., Rausch, T. K., Rody, A., Herting, E., Göpel, W., & German Neonatal Network (GNN) (2017). Delivery mode and intraventricular hemorrhage risk in very low-birth-weight infants: Observational data of the German Neonatal Network. European journal of obstetrics, gynecology, and reproductive biology, 212, 144–149.