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Magnitude and probable etiologies of neonatal seizure among neonates admitted to neonatal intensive care unit of Ayder comprehensive specialized hospital, Mekelle, Ethiopia.

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Abstract

Background

Neonatal Seizure is defined as a sudden uncontrolled surge of electrical activity in the brain manifesting as physical convulsion, autonomic changes and mental status changes or combination of any of those symptoms diagnosed by a clinician who observed the seizure semiology or by EEG. The incidence of seizures is higher in the neonatal period than in any other period of life and is estimated to be approximately 3 per 1000 live births worldwide. The higher rates of neonatal encephalopathy, neonatal sepsis and premature births in developing countries suggest that the incidence may be much higher than that reported in the West.

Objective

The objective of the study was to assess the magnitude of neonatal seizure, and its probable etiologies among neonates admitted to Neonatal Intensive Care Unit (NICU) of Ayder Comprehensive Specialized Hospital (ACSH) in Mekelle, Tigray.

Methods

Hospital based cross sectional study design with retrospective data collection was conducted among neonates admitted to neonatal intensive care unit of Ayder Comprehensive Specialized Hospital. Trained data collectors did the data collection process. After data was retrieved and collected from patient charts, it was cleaned, edited and entered to IBM SPSS version 25. Descriptive statistics was performed.

Results

Of those 1622 neonates admitted to NICU in the year 2018/2019, 155 neonates (9.6%) had a diagnosis of neonatal seizure. Of those 155 neonates with seizures, 62(40%) had birth asphyxia/hypoxic-ischemic encephalopathy (HIE), 26 (16.8%) had sepsis with Meningitis, 19 (12.3%) had Jaundice with acute bilirubin encephalopathy (ABE), 14 (9%) neonates had intracranial hemorrhage, 13 (8.4%) had hypoglycemia, 12 (7.7%) had respiratory distress (MAS & HMD), and 4 (2.6%) neonates had electrolyte abnormalities. Three (1.9%) had congenital malformation of the central nervous system and 2 (1.3%) neonates had no identified etiology on evaluations and investigations performed.

Conclusions

Neonatal seizure was found to be a common neonatal neurological disorder among neonates visiting the tertiary hospital of ACSH in Tigray Region of Ethiopia and was found in about 9.6% of all neonatal admissions. Birth asphyxia was the commonest etiology found in neonates with seizure, followed by sepsis with meningitis, jaundice with ABEs and intracranial hemorrhage.

Keywords: Neonatal seizure, magnitude, probable etiologies, Mekelle, Tigray, Ethiopia.

Introduction

Neonatal seizures are usually an acute manifestation of disturbance of the developing brain and common in early weeks of life [1, 2]. Although neonatal seizures are a common problem in hospitalized neonates in the African region few African studies have examined the burden, etiologies and the outcomes of treatment [3, 4]. The incidence of seizures is higher in the neonatal period than in any other period of life and is estimated to be approximately 3 per 1000 live births worldwide [5, 6]. The higher rates of neonatal encephalopathy, neonatal sepsis and premature births in developing countries suggest that the incidence may be much higher than that reported in the West [7, 8]. A prospective, observational study conducted on etiology and short term outcomes of neonatal seizure in the neonatal care unit and general wards of Babylon Gynecology and Pediatrics teaching hospital showed that from total of 3154 neonates admitted to the neonatal care unit and general wards during the study period, 122 (3.9%) neonates (term and preterm) developed clinical seizures [9]. Another prospective descriptive study on Pattern of neonatal seizures in Osogbo, Nigeria Special Care Baby Unit, Ladoke Akintola University of Technology Teaching Hospital showed that seizures were reported in 59 neonates (6.8%) out of 866 neonatal admissions. Despite the tremendous development in medical sciences and improvement of global medical health in recent decades, neonatal seizure is still a common phenomenon in neonates and is associated with high rate of morbidity and mortality [11, 12, 13].

Neonatal seizure is caused by various disorders which are broadly categorized as follows: Brain insults (hypoxic ischemic encephalopathy, intracranial infections, intracranial hemorrhage, cerebrovascular infarction and structural malformation of brain), metabolic disorders (hypocalcemia, hypoglycemia, hypernatremia, hyponatremia and pyridoxine deficiency), inborn error of metabolism (urea cycle disorder, aminoacidopathies, biotinidase deficiency, mitochondrial disorder, defects in beta oxidation, glucose transporter deficiency, peroxisomal disorder, pyridoxine deficiency and non ketotic hyperglycinemia), neonatal epileptic syndromes (benign idiopathic neonatal seizures, benign familial neonatal seizures, early myoclonic encephalo-

pathy and Ohtahara's syndrome [14, 15, 16]. A prospective cross sectional study conducted in NICU of PBM Hospital, Bikaner, India to determine Clinico etiological profile and outcome of neonatal seizures showed that the Most common etiologic diseases with neonatal seizures were perinatal asphyxia 80 (53%) followed by metabolic causes 24 (16%), infections 15(10%), intracranial hemorrhage in 7 (4.66%), meconium aspiration syndrome (MAS) 5 (3.33%), bilirubin encephalopathy and polycythemia 2 (1.33%) each and 12 (8%) had undetermined diagnosis [17]. Another prospective cross-sectional descriptive study conducted at Hayatabad Medical Complex, Peshawar, Pakistan from January to December 2011 to determine incidence and etiology of neonatal seizure showed that Hypoxic Ischemic Encephalopathy was found to be the commonest cause (44%) of neonatal seizures, followed by hypoglycemia (18.8%) and hypocalcaemia (12.5%) [18]. Similarly another hospital-based prospective observational cohort study conducted in the neonatal intensive care unit of Gondar University Specialized Comprehensive Hospital from October 1, 2016, to September 30, 2018 on assessments of patterns, probable etiology, and short-term Outcomes of neonatal seizures showed that the most common causes of seizure in neonates were perinatal asphyxia (PNA) with hypoxic-ischemic encephalopathy (HIE; 74.4%) followed by electrolyte disturbances (12.8%) [19]. Recognition of the contributory diseases towards neonatal seizure would enable us to identify the quantum of a problem in our circumstances and devise effective treatment/preventive strategies. Knowing the burden and underlying causes for the development of neonatal seizure makes it clear on which factors to act to significantly decrease this disabling and fatal neonatal neurologic disorder.

Methods

Study area

Ayder Comprehensive Specialized Hospital is a teaching referral hospital found in Tigray region Mekelle city, which is around 778 km from the capital city Addis Ababa Ethiopia. It is the second largest hospital in the nation and has 500 inpatient beds in the four major departments and other specialties. Department of pediatrics and child health is one of the major specialties under ACSH.

One of the units in this department is pediatric neonatology unit. It offers outpatient services with Emergency neonatal evaluation & high risk infant follow up clinic. As in-patient service it offers neonatal intensive care, maternity room neonatal care and KMC services.

Study period

The study was conducted at ACSH neonatal intensive care unit from March 2020 to July 2020.

Study design

Hospital based Cross sectional study design with retrospective data collection was used to determine the magnitude of neonatal seizure and its possible etiologies in newborns admitted to neonatal intensive care unit of Ayder comprehensive specialized hospital.

Source population

All neonates who got admitted to Ayder Comprehensive Specialized Hospital.

Study population

All neonates who get admitted to neonatal intensive care unit of Ayder Comprehensive Specialized Hospital during the study period.

Inclusion and exclusion criteria

Inclusion criteria

All neonates who get admitted to Neonatal intensive care unit of ACSH for more than 24 hours during the study period

Exclusion criteria

- Neonatal visits staying < 24 hours
- Neonatal admissions with lost charts and incomplete documentations

Sample size determination

Sample size was calculated using population proportion formula from Mwaniki et al study [20] done in Kenyan district hospital which showed seizures were reported in 142 out of 1572 neonatal admissions i.e. 9%, hence $n = p(1-p) / [z^2/d^2]$, $n = 126$, but we studied all neonatal admissions over a time frame of one year i.e. from September 1, 2018 to August 30, 2019 GC. Hence all 155 neonates with seizure who get admitted to Neonatal intensive care unit of Ayder Comprehensive Specialized Hospital from September 1, 2018 to August 30, 2019

GC Were included.

Data collection Tools and procedures

Data collection method and procedure

Locally developed data abstraction format by record review technique was used to collect data from patient's chart reviews. During one year September 2018 to August 2019 NICU service a total of 6 registration books were used for registration of all neonatal admissions. From these all registration books a total of 1694 neonatal admissions were found registered. The card room workers retrieved 1622 charts that were available; the remaining 72 charts were not found due to different reasons. A total of 155 charts with a diagnosis of neonatal seizure were found out of all 1622 charts available for September 2018 to August 2019 year neonatal admissions.

Operational definitions

Clinical Seizure is defined as:

A sudden uncontrolled surge of electrical activity in the brain manifesting as physical convulsion, autonomic changes, cognitive changes or combination of any of those symptoms diagnosed by a physician.

Poor outcome: Neonates with seizure that died or discharged/left against medical advice with severe neurologic deficit.

Incomplete documentation of history, physical examination, diagnosis, investigations and treatments; means missing of any of the required history, physical examination, diagnosis, investigations and treatments on the chart of a patient.

Lost chart/medical record: when a patient's chart/medical record couldn't be retrieved from medical record store of the hospital.

Birth asphyxia: when a physician has diagnosed birth asphyxia and documented it or when there are documented history evidences like delayed cry after delivery and prolonged labor or brain MRI (abnormal signal intensity in the basal ganglia and thalami, corticospinal tract, white matter, and cortex) has shown consistent results.

Bacterial meningitis: when the neonate had documented diagnosis and treatment for meningitis by physician with evidences from history, physical examination and investigations with CSF analysis or imagings with Cr US/MRI.

Intracranial hemorrhage: documented Neuroimaging findings of bleeding in to any of the intracranial spaces/tissues.

Hypoglycemia: physician diagnosed abnormally low serum level of glucose that resulted in disease manifestations.

Hypонатremia: physician diagnosed abnormally low serum level of Sodium that resulted in disease manifestations.

Hypernatremia: physician diagnosed abnormally high serum level of Sodium that resulted in disease manifestations.

Macrosomic Neonate: A new born delivered with birth weight of more than 4000 grams.

Data quality assurance

To assure the quality of data, the following measures were undertaken. Locally developed data abstraction instrument by record review technique was used. The data abstraction instrument was pretested in 5% of the retrieved charts. At the end of each data collection days, the principal investigator checked the completeness of filled questionnaires and whether recorded information makes sense to ensure the quality of the data collected. Regular meetings were being held with the

data collectors to clear any ambiguity. The diagnosis of neonatal seizure was made by the NICU team managing physicians lead by a neonatologist. Pediatric neurologist was being consulted if needed during the diagnosis, investigation and management of neonates with seizure.

Data processing and analysis

Data coding, cleaning and editing was done before entry into SPSS, then data was entered into IBM Statistical package for Social Science (SPSS) version 25 for analysis. Then a descriptive statistical analysis was done to determine the magnitude of neonatal seizure and its etiologies.

Results

Socio-demographic characteristics results of Neonates and their parents

A total of 155 neonates with seizure were included in the study. The demographic data revealed that the number of male and female patients were 84 and 71 respectively. Majority of study participants (80.6%) were term babies and the remaining 18.1 and 1.3% were preterm and post term deliveries respectively [Table1].

Table 1: Socio-demographic characteristics of Neonates with seizure and their mothers, ACSH, September 2018 to August 2019 (n=155).

Variable	Frequency	Percentage
Age of Neonate at admission		
<24hours	70	45.2
25-72 hours	49	31.6
72 hours and above	36	23.2
Gestational age at delivery		
Term	125	80.6
Preterm	28	18.1
Post term	2	1.3
Birth weight		
Normal birth weight	105	67.7
Low birth weight	20	12.9
Macrosomia	4	2.6
Unknown birth	26	16.8
Maternal educational status		
Primary	59	38.1
Secondary	29	18.7
Higher Education	19	12.3
Illiterate/None	48	31
Family's residence		

Variable	Frequency	Percentage
Mekelle City	45	29
Tigran towns out of Mekelle	58	37.4
Rural areas of Tigray	41	26.5
Out of Tigray	11	7.1
Weight for gestational age		
AGA	139	89.7
SGA	10	6.4
LGA	6	3.9
Sex of neonate		
Male	84	54.2
Female	71	45.8

Perinatal Characteristics results of mothers and Neonates with Neonatal Seizure

The perinatal condition findings of this study revealed that 16 to 21% neonates were delivered from mothers with morbidity during pregnancy, these include 21% of neonates were delivered from mothers with pregnancy induced hypertension, 19% of

neonates were delivered from mothers with fever and 16% of neonates were delivered from mothers with offensive vaginal discharge. Other perinatal conditions in this study include delayed cry after delivery, prolonged labor, low APGAR score and neonatal jaundice were present in 42.6%, 35.5%, 34.9% and 23.2%, respectively [Table 2].

Table 2: Perinatal characteristics results of Neonates with seizure and their mothers, ACSH, September 2018 to August 2019 (n=155).

Perinatal characteristics	Findings/measurements in this study		
APGAR Score:	Low = 54(34.9%)	Normal 66(42.6%)	UK 35(22.6%)
Delayed cry after delivery:	Yes = 66(42.6%)	No = 89(57.4%)	-
Presence of prolonged labor:	Yes = 55(35.5%)	No = 100(63.5%)	-
Yellowish discolorations of the body in the neonate:	Yes = 36(23.2%)	No = 119(76.8%)	-
Birth trauma involving the Scalp/Brain:	Yes = 18(11.6%)	No = 137(88.4%)	-
Instrumental delivery:	Yes = 20(12.9%)	No = 135(87.1%)	-
Maternal fever during pregnancy	Yes = 19(12.2%)	No = 136(87.8%)	-
Maternal hypertension during pregnancy:	Yes = 21(13.5%)	No = 134(86.5%)	-
Maternal offensive vaginal discharge:	Yes = 16(10.3%)	No = 139(89.7%)	-

Laboratory and Clinical Findings/measurements in Neonates with Seizure

The commonest laboratory evaluations done in neonates with seizure include: CSF analysis, brain imaging, CBC, random blood sugar and serum electrolytes. Almost in all of them CBC was done and the result shows normal in 59.4%, sepsis in 34.2% and anemia in 6.5% of neonates. CSF analysis was performed in 86.5% of neonates and the results showed Normal in

102(65.8%), meningitis in 22(14.2%) and traumatic in 10(6.5%) of neonates. Brain scanning was done similarly in 86.5% of neonates with seizure and the commonest abnormality detected was intracranial hemorrhage (12.3%) followed by hydrocephalus & subdural effusions 15(9.7%). Congenital CNS malformations were detected in 3(1.9%) neonates only. Hypoglycemia was detected in 13(8.4%) of neonates only, in majority of them (85.2%) the random blood sugar was within normal range, [Table 3].

Table 3 : Clinical and Laboratory Characteristics findings of Neonates with Seizure, ACSH, September 2018 to August 2019 (n=155).

Laboratory and Clinical Findings/measurements in Neonates with Seizure					
Variables			Results/Findings		
Brain imaging (US/MRI/CTScan)	Normal = 97(62.6%)	ICH = 19(12.3%)	Hydrocephalus/ Effusions = 15 (9.7%)	Congenital malformations = 3 (1.9%)	Not done =21(13.5%)
Random blood sugar	Normal = 132(85.2%)	Hypoglycemia = 13 (8.4%)	Hyperglycemia = 3 (1.9%)	Not done = 7(4.5%)	-
CBC	Normal = 92(59.4%)	Shows sepsis = 53 (34.2%)	Shows anemia = 10(6.5%)	Not done = 0	-
Serum electrolytes	Normal = 118(76.1%)	Abnormally low = 6 (3.9%)	Abnormally high = 7(4.5%)	Not done =24 (15.5%)	-
Total bilirubin	Normal = 24(15.5%)	Abnormally high =21 (13.5%)	Not done = 110 (71%)	-	-
CSF analysis	Normal = 102(65.8%)	Shows meningitis = 22 (14.2%)	Was traumatic = 10(6.5%)	Not done = 21 (13.5%)	-
APGAR Score	Normal (>7) = 66(42.6%)	Moderate Asphyxia (3-6) =37(23.9%)	Severe Asphyxia (<3) = 17(11%)	Unknown = 35(22.6%)	-
General appearance	Well looking = 15 (9.7%)	Acutely sick looking = 140(90.3%)	-	-	-
Weight for Gestational age	AGA = 139(89.7%)	SGA = 10(6.5%)	LGA = 6(3.9%)	-	-
HC for Age	Normal = 126(81.3%)	Macrocephaly = 27 (17.4)	Microcephaly = 2 (1.3%)	-	-
Respiratory condition	Normal = 24(15.5%)	In distress = 100 (64.5%)	Apnea = 31(20%)	-	-
Skin condition	Normal = 100(64.5%)	Jaundice = 33(21.3%)	Pallor = 18(11.6%)	Rashes = 4 (2.6%)	-
Mental status	Alert = 9(5.8%)	Lethargic = 110(71%)	Comatose = 36 (23.2%)	-	-
Moro reflex	Complete= 6(3.9%)	Incomplete = 113 (72.9%)	Absent = 36 (23.2%)	-	-
Suckling reflex	Sustained =19(12.3%)	Unsustained = 101 (65.2%)	Absent = 35 (22.5%)	-	-
Grasp reflex	Strong = 8(5.2%)	Weak = 113(72.9%)	Absent = 34 (21.9%)	-	-
Tone	Normal = 42(27.1%)	Hypotonic = 87(56.1%)	Hypertonic = 26 (16.8%)	-	-

Of those 155 neonates with seizure, 46 (29.7%) were born in ACSH, 50(32.3%) were born in general hospitals, 30(19.4%)

were born in primary hospitals, 16(10.3%) in health centers and 13(8.3) were born at home [Table 4].

Table 4: showing the different places of delivery for the neonates with neonatal seizure, ACSH, September 2018 to August 2019 (n=155).

Where was the Place of delivery of the neonate with seizure?	Frequency	Percent
General hospital	50	32.3
Specialized hospital	46	29.7
primary hospital	30	19.4
health center	16	10.3
Home	13	8.3
Total	155	100.0

Magnitude of Neonatal Seizure

Of those 1622 neonates admitted to NICU in the year

September 2018 to August 2019, 155 (9.6%) had a diagnosis of neonatal seizure [Table 5].

Table 5: showing the magnitude of neonatal seizure, ACSH, September 2018 to August 2019 (n=155).

Does the neonate have a diagnosis of seizure?	Frequency	Percent
Yes	155	9.6
No	1467	90.4
Total	1622	100.0

Etiologies of Neonatal Seizure

Of those 1622 neonates admitted to NICU in the year 2018/2019, 155 (9.6%) had a diagnosis of neonatal seizure. Of those 155 neonates with seizures, 62(40%) neonates had birth asphyxia/HIE, 26(16.8%) neonates had sepsis with Meningitis, 19(12.3%) neonates had Jaundice with acute bilirubin encephalopathy, 14(9%) neo-

nates had intracranial hemorrhage, and the remaining 34(21.9%) neonates had: 13(8.4%) neonates had hypoglycemia, 12(7.7%) neonates had respiratory distress (MAS & HMD), and 4(2.6%) and electrolyte abnormalities. Three (1.9%) had congenital malformation of the central nervous system and 2 (1.3%) neonates had no identified etiology on evaluations and investigations performed [Table]).

Table 6: showing the commonest etiologies identified in neonates with seizure, ACSH, September 2018 to August 2019 (n=155).

What was the probable etiology of the seizure?	Frequency	Percent
Birth asphyxia/HIEs	62	40
Sepsis with Meningitis	26	16.7
Jaundice/ABEs	19	12.3
Intracranial hemorrhage/ICH	14	9
Hypoglycemia	13	8.4
RDs (HMD, MAS)	12	7.7
Others (electrolyte abnormalities and CNS congenital malf.)	7	4.5
No treatment for other diseases	2	1.3
Total	155	100.0

Discussion

In our study it was found that the magnitude of neonatal seizures was 9.6%, which is comparable to the done elsewhere [20-23]. The explanation for this slightly low incidence compared to those studies can be because we didn't practice diagnostic EEG recording for neonates who are at risk of seizure (PNA, meningitis, ABEs and ICH neonates) who didn't manifest clinically observable seizures which was done in those studies hence this can be due to the fact that we were only able to document seizures that were clinically obvious hence possibly missed subclinical seizures.

The most common etiologies of neonatal seizure in our study were; 62(40%) neonates had birth asphyxia/HIE, 26(16.8%) neonates had sepsis with Meningitis, 19(12.3%) neonates had Jaundice with acute bilirubin encephalopathy, 14(9%) neonates had intracranial hemorrhage, and the remaining 34(21.9%) neonates had: 13(8.4%) neonates had hypoglycemia, 12(7.7%) neonates had respiratory distress (MAS & HMD), and 4(2.6%) neonates had electrolyte abnormalities. Three (1.9%) had congenital malformation of the central nervous system and 2 (1.3%) neonates had no identified etiology on evaluations and investigations performed. This finding was similar to studies done in Pakistan which showed Hypoxic Ischemic Encephalopathy was found to be the commonest underlying etiologies of 44% of all neonatal seizures, followed by hypoglycemia (18.8%) and hypocalcemia (12.5%) [18], and a study in Iraq showed the main etiologies of neonates with seizures was hypoxic-ischemic encephalopathy (HIE) (23.9%) and hypoglycemia (10.22%) [11].

Another similar study in Gondar University showed the most common etiologies of seizure were perinatal asphyxia (PNA) with hypoxic-ischemic encephalopathy (HIE;74.4%) followed by electrolyte disturbances (12.8%) [19], which was similar to our study. Another study again in France showed among 243 neonates admitted with seizure the frequencies of underlying diseases with neonatal seizures were: hypoxic-ischemic encephalopathy (HIE) 91(37%), ischemic infarction 36(15%), intracranial hemorrhage 29(12%), intracranial infection 19(8%), metabolic or electrolyte disorders 9(3%), inborn errors of metabolism 5(2%), congenital malformations of the central

nervous system 11(5%), epileptic syndromes 27(12%) and unknown 16(7%) [13], which was also similar to our study again.

Another Similar studies on etiology to our study include: a study in Thailand showed the most common etiologic diseases found in neonates with seizure were hypoxic ischemic encephalopathy (n=69, 59%), followed by infection (n=20, 17.09%), and metabolic disturbances (n=16, 13.7%)[15]), a study in India showed the Most common underlying comorbidities associated with neonatal seizures were perinatal asphyxia 80 (53%) followed by metabolic causes 24 (16%), infections 15(10%), intracranial hemorrhage in 7 (4.66%), meconium aspiration syndrome (MAS) 5 (3.33%), bilirubin encephalopathy and polycythemia 2 (1.33%) each and 12 (8%) had undetermined diagnosis[17]). A study in Babylon showed the most common underlying diseases associated with neonatal seizures were hypoxic ischemic encephalopathy 41(33.6%) of 122 neonates, followed by metabolic disturbances collectively constitute 36(29.5%) neonates, infections were found in 20 (16.4%) neonates, intracranial hemorrhage, hyperbilirubinemia encephalopathy (Kernicterus), brain malformation and unknown disease each accounted for 13(10.7%), 5 (4.1%), 5 (4.1%) and 2 (1.6%) respectively [9].

Additional other studies by Sahana et al and Sabzehei et al also showed that perinatal asphyxia/HIE was the most common underlying comorbidity found in neonates with seizure constituting about 57.8% and 34.3% of neonates with seizure respectively [3,16]. While another study from Kenya: A 4 years prospective cohort study in Kenyan district hospital showed the main diagnoses in neonates with seizures was sepsis in 85 (60%) of neonates with seizure [21], this may be a reflection of early use of antibiotics in our neonatal intensive care unit while the Kenyan study didn't use antibiotics for asphyxiated neonates unless there is evidence from blood culture unlike our set up study that used IV antibiotics for almost all neonates with asphyxia.

Limitations of the Study

Since neonatal seizures are often subclinical, EEG recording of electrographic seizures in high risk neonates is crucial for estimation of true seizure burden of seizure which was not done in our study due to the study being

Conclusions and Recommendations

Conclusions

Neonatal seizure was found to be a common neonatal neurological disorder among neonates visiting the tertiary hospital of ACSH in Tigray Region of Ethiopia and was found in about 9.6% of all neonatal admissions. Birth asphyxia was the commonest etiology found in neonates with seizure, followed by sepsis with meningitis, jaundice with ABEs and intracranial hemorrhage.

Recommendations

The major underlying etiologies with neonatal seizures and the deaths and neurological deficits ascribed are potentially preventable hence comprehensive and vigorous efforts are needed to achieve safe delivery, prevent birth asphyxia and improve care and transport of sick neonates at primary, secondary and tertiary levels of care for early treatment and achievement of better outcomes.

Declarations

Ethical considerations

Ethical clearance was obtained from the Institutional Review Board of the College of Health Sciences of Mekelle University with MU-IRB reference number of 1640/2020. Permission from the dataset owner (Ayder Comprehensive Specialized Hospital clinical director's offices) and a support letter from the chief clinical director were obtained before the commencement of the study. Data were taken from patient records. Confidentiality of the data was kept safely and the data were only used for our current study.

Abbreviations and Acronyms

ABE:- Acute Bilirubin Encephalopathy; ACSH:- Ayder Comprehensive Specialized Hospital; AGA:- Appropriate for Gestational Age; ANC:- Antenatal Care; APGAR score:- Appearance, Pulse rate, Grimace, Activity, Respiratory rate; CNS:- Central Nervous System; Cr U/S:- Cranial Ultrasound; CSF:- Cerebro-Spinal-Fluid; CT

scan:- Computed Tomography scan; EDHS:- Ethiopian Demographic and Health Surveys; EEG:- Electroencephalography; GABA:- Gamma Amino Butyric Acid; HIE:- Hypoxic Ischemic Encephalopathy; ICH:- Intracranial Hemorrhage; IVH:- Intraventricular Hemorrhage; KMC:- Kangaroo Mother Care; LGA:- Large for Gestational Age; MAS:- Meconium Aspiration Syndrome; MICHU:- Maternal Infant and Child Health Unit; MMC:- MeningoMyelo-Cele (Neural tube defects); MRI:- Magnetic Resonance Imaging; MU:- Mekelle University; NICU:- Neonatal Intensive Care Unit; PICU:- Pediatric Intensive Care Unit; PNA:- Perinatal Asphyxia; RD:- Respiratory Distress; SGA:- Small for Gestational Age;

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Data availability

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

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Fund was obtained from Mekelle University College of Health Sciences and World-Wide Fistula.

Conflicts of interest

There is no conflict of interest.

Authors' contributions

K.W.G. participated in the conception of ideas, writing up the protocol, developing methodologies, analyses and write-up of the article and drafted the manuscript and A.H.B. contributed to the write up of the study, S.N.W. had higher role in editing of the manuscript and contributed to the write up of the study. M.H.B. took his part in developing methodologies and made a critical revision to the paper and manuscript.

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