Magnitude and Predictors of Mortality Among Neonates Admitted with Perinatal Asphyxia at Asella Teaching and Referral Hospital

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ABSTRACT

Introduction: The term "perinatal asphyxia" describes a condition that occurs in the first and second stages of labor when fetal acidosis, hypoxemia, and hypercarbia are caused by impeded gas exchange. Seventy-five percent of neonatal deaths happen in the first week of life, and one million babies pass away in the first twenty-four hours. The overall mortality rate of perinatal Asphyxia is approximately 20%. The outcome of Hypoxic ischemic encephalopathy, ranges from complete recovery to death. Prolonged labor, low birth weight; meconium-stained amniotic fluid and instrumental delivery were the determinant factors of perinatal asphyxia in Ethiopia

Objectives: To Asses magnitude and predictors of mortality among neonates admitted with perinatal asphyxia at Asella teaching and referral hospital.

Method: Institution-based retrospective cohort study was conducted on asphyxiated neonates admitted in the NICU of Asella teaching and referral hospital. A sample of 217 neonatal records was included in the study. Data was analyzed using SPSS version 27. Descriptive analysis was carried out to describe the patient's baseline characteristics. A descriptive survival time analysis using the duration of illness from confirmed perinatal asphyxia onset until event was carried out. Cox regression model with 95% CI and Adjusted Cause- Specific Hazard Ratios was used to report statistically significance at P-value < 0.05.

Result: In this study, out of 217 asphyxiated neonates, 29(13.3%) neonates have died and 25(86.2%) of the death of neonates occurred during the first 7 days. The survival probability was 86%, 82 %, and 73% at the first, second, and third weeks of life, respectively. Stage III HIE (AHR 4.09(1.283-13.057)) male sex (AHR 4.8(1.232 - 19.47)), convulsion and use of anticonvulsants (AHR 14(1.54-133.26)) were independent predictors of mortality.

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Conclusion: The survival status of newborns admitted with perinatal asphyxia was low. In addition, being male; stage III HIE, newborn history of convulsion and use of Anticonvulsants were the independent predictors of mortality. Therefore, special attention should be given to asphyxiated neonate with male sex and those who have seizure.

Keywords: Perinatal Asphyxia, Mortality, Mortality Predictors

ABBREVIATIONS

ATRH: Asella Teaching and Referral Hospital

ANC: Antenatal care

CI: Confidence Interval

CP: Cerebral Palsy

CPR: Cardiopulmonary Resuscitation

HIE: Hypoxic Ischemic Encephalopathy

NICU: Neonatal Intensive Care Unit

NR: Non response rate

PNA: Perinatal Asphyxia

PROM: Premature Rupture of Membrane

WHO: World Health Organization

INTRODUCTION

Background

orld health organization (WHO) defines Birth asphyxia as a failure to initiate and sustain breathing at birth [1]. Perinatal Asphyxia refers to a condition during the first and second stage of labor in which impaired gas exchange leads to fetal acidosis, hypoxemia, and hypercarbia [2].

Worldwide 2.3 million children died in the first 20 days of life in 2022. There are approximately 6500 newborn deaths every day, amounting to 47% of all child deaths under the age of 5 years. Seventy-five percent of neonatal deaths happen in the first week of life, and one million babies pass away in the first twenty-four hours. Neonatal infections, congenital anomalies, birth complications (birth asphyxia/trauma), and premature birth are the main causes of death for newborns, which together account for almost 4 in every 10 deaths in children under 5 years of age [1].

The Sustainable Development Goals were adopted by the United Nations in 2015; with the aim of reducing neonatal mortality to fewer than 12 per 1000 live births by 2030. In order to accomplish this goal, the Ethiopian government has also implemented a number of policies, such as encouraging the growth of emergency obstetric and newborn care services in order to enhance the health of mothers and newborns [3].

The overall mortality rate of perinatal Asphyxia is approximately 20%. The frequency of neurodevelopmental sequelae in surviving newborns ranges from 30% to 50%. In contrast to the 0.2% risk in the general population, survivors of prenatal asphyxia have a 5% to 10% chance of developing cerebral palsy [4].

A systematic review and meta-analysis done in Ethiopia shows the overall prevalence of perinatal asphyxia in Ethiopia was 24.06%. prolonged labor, low birth weight; meconium-stained amniotic fluid and instrumental delivery were the determinant factors of perinatal asphyxia in Ethiopia [5].

The outcome of Hypoxic Ischemic Encephalopathy (HIE) varies from full recovery to death and is correlated with the timing and intensity of the injury. Low (0–3) 10 min Apgar score, need for Cardiopulmonary Resuscitation (CPR) in the delivery room, Delayed onset (≥20 min) of spontaneous breathing, Severe neurologic signs (coma, hypotonia, hypertonia), Seizures onset ≤12 hr or difficult to treat, Oliguria/anuria >24 hr. Abnormal neurologic exam ≥14 day are associated with increased risk for death or impairment [6].

Statement of Problem

Perinatal asphyxia, a condition characterized by oxygen deprivation during labor and delivery, remains a significant cause of neonatal morbidity and mortality globally.

An estimated 4 million newborns die within the first four weeks of life each year. First week deaths account for 75% of newborn deaths, with the first day of life carrying the highest risk of death. Nearly all (99%) newborn fatalities occur in low- and middle-income countries. Countries in south-central Asia and sub-Saharan Africa have the highest rates of newborn mortality. Globally, the main causes of neonatal death are preterm birth (28%), infections (26%), and asphyxia (23%) [7].

In the western world, asphyxiated newborns have a higher chance of survival because of improved perinatal care, ongoing fetal monitoring throughout intrapartum, early newborn presentation in Neonatal Intensive Care Unit (NICUs),

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and several treatment methods. But in developing countries, where mortality rates are high and recovery times or average hospital stays are protracted due to multiple predictors, this was not the case [8].

In low- and middle-income nations, 80% of developmental delays in children under five are caused by a neurologic problem associated with prenatal hypoxia [9].

Stage I cases of HIE can improve within a day of treatment, but patients with stage II and III will need to stay in the hospital for days to weeks because of complications. Around 15 to 20% of newborns who experience perinatal asphyxia will not survive, while 25% will live with lasting neurological issues [10].

A research conducted in southern Ethiopia showed that certain conditions like pregnancy-induced hypertension, cord prolapse, iron deficiency anemia, and convulsions can increase the likelihood of neonatal death in babies with perinatal asphyxia [11].

In low- and middle-income countries like Ethiopia, the burden of perinatal asphyxia is particularly high, often due to limited access to quality maternal and newborn healthcare.

Asella Teaching and Referral Hospital (ATRH), a major referral center for newborns in the southeast Oromia Region, Ethiopia, witnesses a significant number of neonates admitted with perinatal asphyxia. However, the specific outcomes and predictors of mortality in this population remain poorly understood.

This lack of understanding hinders the development of effective strategies for improving neonatal care and reducing mortality rates associated with perinatal asphyxia at ATRH.

Significance of the Study

This research on the magnitude and predictors of mortality among neonates admitted with perinatal asphyxia at ATRH holds significant value for various stakeholders, contributing to improved neonatal care and reduced mortality rates.

The study will provide crucial insights into the factors associated with mortality in neonates with perinatal asphyxia. This information will guide healthcare professionals at ATRH in identifying high-risk newborns, providing timely and targeted interventions, and optimizing their care strategies.

Identifying predictors of mortality will enable early identification of neonates at increased risk. This will allow for prompt interventions, such as resuscitation, supportive care, and management of complications, ultimately improving their chances of survival.

Literature Review

Magnitude of Perinatal Asphyxia

Birth asphyxia is one of the leading causes of early neonatal mortality, and accounts for an estimated 900,000 deaths worldwide each year[1]. It is estimated that birth asphyxia is responsible for almost 23% of all newborn deaths globally [12].

The estimated frequency of severe prenatal asphyxia in a research conducted from 2004 to 2014 at a single hospital in Switzerland ranged from 5 to 8 per 1000 live births. The incidence of hypoxic-ischemic encephalopathy (HIE) was approximately 1 per 1000 live births [13]. In a population-based study from Sweden that analyzed data from >3 million singleton live births from 1988 through 2018, the incidence of perinatal asphyxia was 11 per 1000 live births [14].

Birth asphyxia is the leading cause of neonatal mortality in low and middle-income countries, and it is also the primary cause of long-term neurodevelopmental disorders [15]. The incidence of birth asphyxia has decreased significantly in most industrialized countries and accounts for less than 0.1% of newborn infant deaths. However, in developing countries, the rate of birth asphyxia is much higher, and the case fatality rate is > 40%.

In East Africa, the neonatal mortality rate ranges from 11–102 per 1000 live births, and birth asphyxia was the primary cause of neonatal death in 2015 (31.6%) [12]. Another study done at Cameron shows 9.7% neonates had perinatal asphyxia and most of the asphyxiated neonates were males (sex ratio 1.4), 86.1% weighed between 2500-3999g, and 58.3% mothers were in the age group between 18-29 years. risk factors for birth asphyxia included: were, mothers who had urinary tract infection in pregnancy, prolonged rupture of membranes, prolonged labor and mothers who delivered by emergency caesarian section. Among the asphyxiated neonates, 20.8% died. Eighty-eight percent of asphyxiated neonates developed hypoxic ischemic encephalopathy, of which, 54.7% were Sarnat's stage I, 15.6% stage II and 29.7% stage III [16].

In Ethiopia, birth asphyxia ranks fourth in terms of causes of death for children under five (11.3%), and it is the second most common cause of newborn mortality (26.7%).

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Risk Factors for Death in Perinatal Asphyxia

A Population-based study of neonatal deaths associated with perinatal asphyxia in São Paulo State, Brazil, shows absence of prenatal visits and 1st minute Apgar score 0–3, were found to be associated with increased mortality. Whereas Cesarean delivery compared to vaginal was protective against death with perinatal asphyxia for infants at 28–36 weeks [17].

A study conducted in Sri Lanka found that Neonates presenting with convulsions and neonates in HIE stage III were risk factors for mortality in asphyxiated neonates [18].

A study conducted in Nigeria found that 25.3% of asphyxiated neonates died. The study showed that majority of the infants with HIE were out born and that most of the babies delivered at home or in a traditional birth attendant's place, who presented with HIE, died [19]. A finding of a study conducted in, Kenya, and Tanzania indicates that having acute kidney injury was associated with a higher risk of neonatal mortality [20,21].

A retrospective cohort study done at Jimma University Medical Center, showed, among asphyxiated neonates, 22.52% of neonates have died. Neonates in stage III HIE were 3.46 as likely to die as those in stage I adjusting for other factors [22].

Another study done at Dessie comprehensive specialized hospital, showed 32% of asphyxiated newborns admitted to the NICU died. Asphyxiated neonates weighing <2500g at admission had a 1.72 times higher risk of death than their counterparts. Likewise, the risk of death was 1.52 times higher among asphyxiated newborns with seizures compared to those without seizures [23].

Retrospective follow-up study conducted in west Oromia region referral hospitals revealed that neonates who had low APGAR score (< 3) at the fifth minute of birth were more likely to die when compared with those with greater than three. Furthermore, asphyxiated neonates who were treated with CPAP had a better probability of survival compared with new-born that were treated with direct oxygen. Moreover, asphyxiated neonates who had been diagnosed with stage III hypoxic ischemic encephalopathy had a lower survival probability compared with those diagnosed with stage I and stage II HIE [4].

Study done in NICU of West Shewa Zone Public Hospitals showed maternal-related factors such as age, history of chewing khat, ANC follow-up, obstructed labor, place of delivery, and neonatal related factors such as: age at admission, having comorbidity, birth injury, APGAR score at first minute, hypothermia, blood sugar and MAS were found to be the significant predictors of neonatal mortality among asphyxiated neonates. Asphyxiated newborns whose mothers chewed chats had a 2.21-fold increased risk of mortality. Similarly, compared with mothers who gave birth in healthcare facilities, the risk of death was 1.45 times higher for asphyxiated newborns whose mothers gave birth at home. Additionally, the risk of death was 1.44 times higher among asphyxiated neonates whose mothers didn't have ANC compared with their counterparts. Likewise, when compared with their counterparts, asphyxiated neonates that developed hypothermia had a 1.56 times higher risk of mortality. Moreover, the risk of death was 2.23 times higher among neonates with hypoglycaemia. Finally, the risk of mortality was 1.4 times higher among asphyxiated neonates whose mothers developed obstructed labour during delivery [24].

Conceptual Frame Work of the Study

This is a conceptual framework for the mortality of a neonate admitted with perinatal asphyxia. This was adapted and modified after reading different literature [11,19,22].

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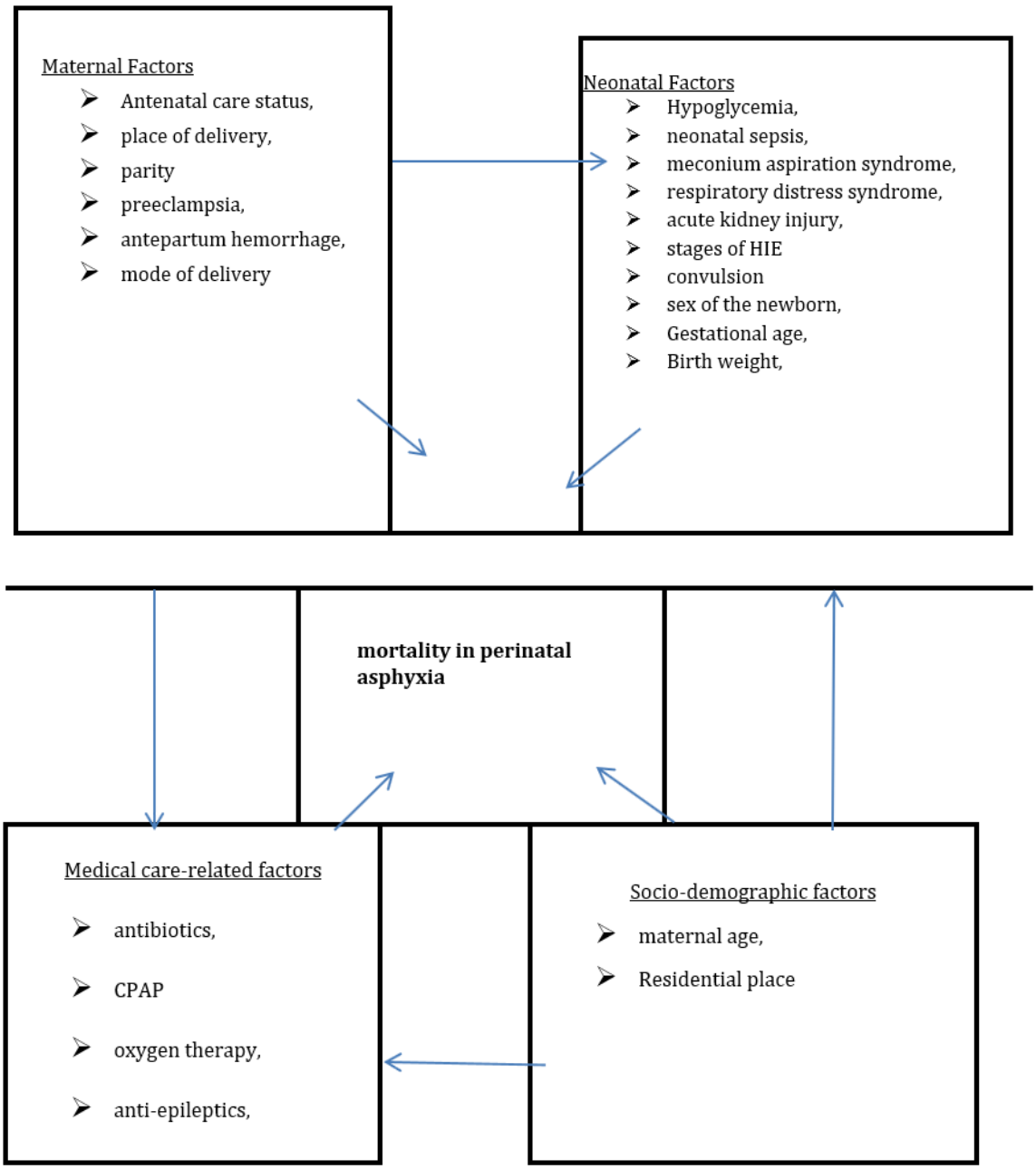

Figure 1: Conceptual frame work about Outcome and predictors of mortality among neonates admitted with perinatal asphyxia at Asella teaching and referral hospital, from January 2023 - June 2024 Asella Southeast Ethiopia.

Objectives

General objective

- To Asses magnitude and predictors of mortality among neonates admitted with perinatal asphyxia at Asella teaching and referral hospital.

Specific objectives

- To determine the mortality rate among neonates admitted with perinatal asphyxia at ATRH.
- To identify predictors of mortality in neonates admitted with perinatal asphyxia at ATRH.

METHODS AND MATERIALS

Study Period and Area

The study was conducted at Asella teaching and referral hospital (ATRH), from September – October 2024. ATRH is located in Asella town, Arsi zone, Oromia Regional State, Ethiopia. Asella town is located at 165 KM to southeast of Addis Ababa, the capital city of Ethiopia. The hospital has

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321 beds with more than 6 departments (Pediatrics and Child Health, Gynecology and Obstetrics, Internal Medicine, Surgery, Orthopedics and Oncology) and involved in training undergraduate and postgraduates in different specialties in 04 major departments (Pediatrics and Child Health, Gynecology and Obstetrics, Internal Medicine, and Surgery).

The department of Pediatric and Child health is one of the major units of the hospital delivering services under four main sub-units with 106 beds for the pediatric ward (42 NICU, 54 Pediatrics ward and 9 for emergency pediatric ward).

Annually more than 1,200 neonates are admitted to this hospital at NICU ward. Around 70% of them are admitted from this Hospital obstetric ward, 18% from other health facility, and 12% from Home.

The department has 12 seniors, 28 residents of different level, 03 General Practitioners and there are 21 nurses in NICU ward, among which 10 of them have specialty in neonatology.

Study Design

Institution-based retrospective cohort study was conducted on asphyxiated neonates admitted in the neonatal intensive care unit of Asella teaching and referral hospital.

Population

Source population: All asphyxiated neonates admitted in the neonatal intensive care unit of Asella teaching and referral hospital.

Study population: All randomly selected records of asphyxiated neonates admitted in the neonatal intensive care unit of Asella teaching and referral hospital from January 2023 - June 2024 and that met the inclusion criteria.

Inclusion and Exclusion Criteria

Inclusion criteria

All records of asphyxiated newborns who were admitted in NICUs of Asella teaching and referral hospital from January 2023 – June 2024.

Exclusion criteria

✓ Asphyxiated babies whose chart is lost.

✓ Asphyxiated babies who are self-discharged.

Sample Size and Sampling Technique

Sample size determination: The single population proportion formula is used to calculate sample size.

$$n = z_{\alpha/2}^2 \frac{\rho(1-\rho)}{d^2}$$

Where: -

n= sample size

Z = standard normal distribution corresponding to significance level at α = 0.05

P = proportion of mortality among neonates admitted with perinatal asphyxia

D= is the margin of error of 5%

"P" is taken from a study done at Jimma University Medical Center, which shows mortality rate of 22.5%[22].

So using this proportion with 95% CI and 5% marginal error, the calculated sample size will be

Where n- sample size, p= 0.225 z= 1.96 d=0.05

n = (1.96)2*0.225(1-0.225)/ (0.05)2 =268

The calculated sample size = 268

Since study population is <10,000

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$$n = \left(\frac{n_0}{1 + \frac{n_0}{N}} \right)$$

n= corrected sample size

n0= Initial sample size (268)

N= Source population size (242 neonates were admitted with the diagnosis of PNA from January 2023 - June 2024)

So the corrected sample size will be 127

- After calculating a 10% non-response rate (13), the final sample size becomes 127+13 = 140.

Since it is manageable, all eligible records of asphyxiated neonates found during the study period was included in the study.

For second objective the sample size was calculated using the double population formula by Epi info considering the following assumptions: Z (1-α/2) at 95%, CI: 1.96; 80% power; 1:1 ratio of unexposed to exposed; anticipated proportion of mortality rate among neonates who do have maternal antepartum Hemorrhage (p1 = 3.2%) ; neonates who did not have maternal antepartum Hemorrhage (p2 = 19.3%); adjusted hazard ratio of (AHR=7.2) which was taken from a previous study done in Jimma University medical center[22]. After adding 10% for incomplete records, the minimal sample size was 158 neonates. Since it is manageable, all eligible neonates found during the study period was included in the study.

Sampling Procedures

All medical records for neonates who admitted with the diagnosis of PNA in Asella Teaching and Referral Hospitals NICU ward from January 2023 - June 2024 was listed based on the sequence of their card numbers from registration book, and census of those meet inclusion criteria during the study period was included in the study and data was collected from their medical records history, physical examination, laboratory investigation, and diagnosis, entered into the checklist.

Total number admission (newborn with perinatal asphyxia) during the study period (N) is 242 from January 2023 - June 2024.

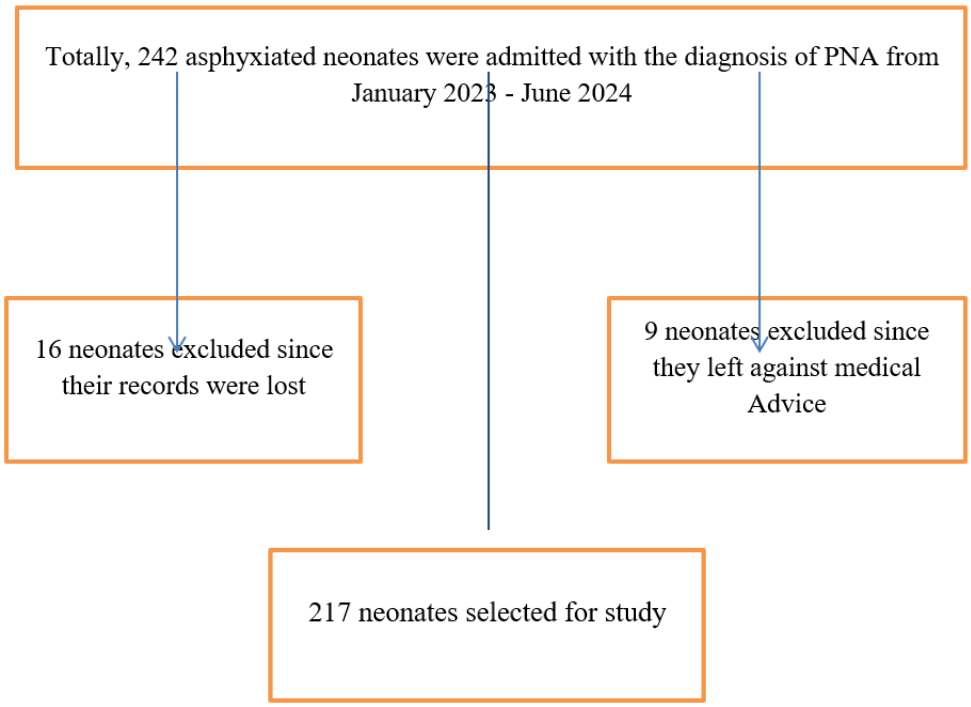

Figure 2: Case selection flow diagram of magnitude and predictors of mortality among neonates admitted with perinatal asphyxia at Asella teaching and referral hospital, from January 2023 - June 2024 Asella Southeast Ethiopia.

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Measurement

Variables

Dependent variable

- Incidence of mortality from perinatal asphyxia

Independent variables

- Socio-demographic factors: sex of the newborn, Gestational age, Birth weight, place of residence,
- Medical care-related factors: antibiotics, oxygen, CPAP anti-epileptics,
- Neonatal related factors: Hypoglycemia, neonatal sepsis, meconium aspiration syndrome, respiratory distress syndrome, acute kidney injury, stages of HIE, convulsion
- Maternal factors: Antenatal care status, place of delivery, parity, preeclampsia, antepartum haemorrhage, mode of delivery.

Operational Definition

Perinatal asphyxia: - is considered when the 5th minute APGAR score is <7. Perinatal asphyxia was diagnosed when the newborn had at least one of the following signs: not breathing or gasping, < 30 breaths per minute, or < 7 APGAR score, had neonatal neurologic sequelae (seizures, coma, and hypotonia), or multiple organ involvement (kidney, lungs, liver, heart, and intestines).

Event (death):- Neonate died in the hospital and death summary written on a chart due to PNA.

Censored: Newborns with PNA who did not develop the outcome of interest(death) until the end of follow-up period or lost to follow-up, recovery from illness, discharged against medical advice or transfer out to other health institutions without knowing the outcome.

Stages of HIE: HIE stages were determined based on saranat's classifications of the clinical diagnosis made by a health care provider (stage I, stage II, and stage III).

Survival - newborns who become well (becoming free of clinical features of asphyxia, declared recovered from PNA and/or discharged from NICU due to completion of their management).

Survival time: The time in days from admission to the development of outcome variable (Death) within follow-up time.

Co-morbidities: newborns with PNA and other medical problems.

Incomplete chart: a medical record or document that lacks necessary information or documentation.

Data Collection Procedure

Data was collected using check list from medical record of the neonate. Four nurses from medical ward was selected from Arsi University, College of Health Science School of medicine for data collection since they have a medical background. A total of 2 days of training was given to all data collectors. Information regarding demographic characteristics of the neonate, maternal factor, neonatal information, and perinatal factor was gathered from the sampled individual patient's card.

Data Quality Management

The adapted checklist was approved by the advisors, and data collectors received two days of training on the study's objectives and the eligibility criteria for the study population prior to data collection. Additionally, a pre-test was conducted with 20 neonates who were treated before January 2023, at ATRH (neonates treated before the commencement of the study period). Further modifications were made to the sequence of questions and the content of the checklist. The principal investigator ensured the collected data was stored after verifying its completeness and consistency to minimize the risk of data loss. Furthermore, the pre-test data were excluded from the final analysis.

Data Processing and Analysis

Data was recoded and entered into EPI-INFO version 6.2, and then exported to Statistical Package for Social Sciences (SPSS) version 27 for analysis. A descriptive survival time analysis using the duration of illness from confirmed perinatal asphyxia onset until event was carried out and survival estimates were computed. The mean, standard deviations and inter quartile range (IQR) were reported for continuous variables, while frequencies, and proportions for categorical variables. Days were used as time scale to calculate median time to event. A survival time analysis was conducted for in-hospital neonatal death to predict the effect of risk factors on

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the outcome of interest, and an adjusted cause specific hazard ratio was reported. Multivariable Cox regression model with 95% CI and Adjusted Cause- Specific Hazard Ratios was used to report statistically significance at P-value < 0.05. The results were presented in the form of table, figures and text.

Ethical Considerations

Ethical clearance was obtained from Arsi University, Asella Teaching and Referral and Hospital Institutional Review Board to conduct the research. Permission request letter was written to ATRH administration to get access to neonatal charts. The study was conducted through a review of records. To ensure confidentiality, the name and other identifiers of patients, physicians, and other health care members who examine the patient was not recorded on the data extraction format.

Dissemination Plan

After research completion and finalizing report, this study will be presented to the department of pediatrics and child health and public health, as part of pediatrics and child health specialty thesis at Arsi University and submitted to post graduate programs coordinating office of college of health sciences of Arsi University and other stake holders for possible application and publication of the study.

RESULTS

Socio-demographic Characteristics

In this study a total of 217 newborns were involved, of which 148(68.2%) of them were males and 69(31.8) of them were females. At birth, 180 (82.9%) weigh 2500 to 3999 grams and 33 of neonate's birth weight was less than 2500 grams.

Furthermore, 2(100%) and 23(12.7%) neonates with birth weight <1500 and 2500-3999g respectively, have died. On the other hand, 4(57.1%) and 15(10.2%) neonates with admission pulse rates <100 and 100-160 pulse per minute respectively died (Table 1).

Table 1: Socio-demographic and baseline of asphyxiated neonates admitted to Asella Teaching and referral hospital South East Ethiopia from January 2023 - June 2024

Variable	Category	Frequency	Percent
Sex	Male	156	71.9
	Female	61	28.1
Gestational ages	< 37	15	6.9
	37-40	181	83.4
	>40	21	9.7
Residence	Urban	64	29.5
	Rural	153	70.5
Age of neonate at admission	< 1 day	202	93.1
	2 - 4 days	13	6.0
	> 5 days	2	.9
Birth weight in gram	< 1500g	2	.9
	1500 - 2499g	31	14.3
	2500-3999g	180	82.9
	>4000g	4	1.8

Maternal Medical Diseases During the Index Pregnancy

Only one mother was found to have chronic medical illness which is Type 1 DM and the baby survived and discharged.

Obstetric and Gynaecologic Conditions

It was identified that 129(59.4%) of mothers of study participants had one to three times antenatal care visits, and 75(34.6%) of a place of delivery was at other health facilities. In addition, 4(80%) of neonates whose mothers had no ANC visit and 9(10%) of those whose mothers had ANC visits of four and above times had died. Moreover, 14(22.9%) of those born by cesarean section and 8(24%) of neonates born by instrumental delivery had died (Table 2,3).

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Table 2: Obstetric and Gynaecologic conditions of mothers of asphyxiated neonates admitted to Asella Teaching and referral hospital SE Ethiopia, from January 2023 - June 2024

Variable	Category	Frequency	Percent
Number of parity	Primiparous	82	37.8
	Multiparous	121	55.8
	Grand multiparous	14	6.5
Total number of ANC visit	no visit	5	2.3
	1-3x	129	59.4
	>4x	83	38.2
Place of delivery	This Hospital	138	63.6
	Health Center	49	22.6
	Home	4	1.8
	Other Hospital	26	12.0
Mode of delivery	C/D	61	28.1
	SVD	146	67.3
	Instrumental delivery	10	4.6
Duration of labor	no labor	2	.9
	< 24 hours	187	86.2
	> 24 hours	28	12.9
Time of rupture of membrane	< 18 hours	196	90.3
	> 18 hours	21	9.7

Table 3: Specific Type of Obstetric Complications

	Frequency	Percent	Valid Percent	Cumulative Percent
Preeclampsia	12	5.5	26.1	26.1
APH	12	5.5	26.1	52.2
prolonged PROM	10	4.6	21.7	73.9
Intramniotic infection	3	1.4	6.5	80.4
cord prolapse	1	0.5	2.2	82.6
post term	2	0.9	4.3	87
Obstructed Labor	2	0.9	4.3	91.3
Severe Oligohydramnious	3	1.4	6.5	97.8
Cord bleeding	1	0.5	2.2	100

Clinical Condition of the Neonates

This study found that 63(29%) neonates had early-onset neonatal sepsis, and 89(41%) had meconium aspiration syndrome (MAS). In addition, 74(34.1%), 27(12.4%), and 20(9.2%) had acute kidney injury, stage III HIE, and subgaleal hemorrhage respectively. In addition, 21(28%) of those who had and 7(4.9%) of those who do not have acute kidney injury died, and 13(8.7%) of stage II and 15(55.5%) of stage III HIE have died (Table 4).

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Table 4: Clinical conditions of asphyxiated neonates admitted to Asella Teaching and referral hospital south east Ethiopia, from January 2023 - June 2024

Variable	Category	Frequency	Percent
Neonatal sepsis	Yes	63	29.0
	No	154	71.0
Meconium aspiration syndrome	Yes	90	41.5
	No	127	58.5
Acute kidney injury	Yes	75	34.6
	No	142	65.4
Convulsion	yes	63	29.0
	No	154	71.0
Hypoglycemia	Yes	4	1.8
	No	213	98.2
Respiratory distress syndrome	Yes	5	2.3
	No	212	97.7
Hypothermia	Yes	19	8.8
	No	198	91.2
Stage of HIE	stage I	41	18.9
	Stage II	149	68.7
	stage III	27	12.4

Treatments Provided for Neonates

This study found that about 195(89.8%) and 213(98%) were resuscitated and received antimicrobial therapy respectively. In addition, 28.1% received anticonvulsants and 35.9% of them were treated with CPAP (Table 5).

Table 5: Treatments provided for asphyiated neonates admitted to Asella Teaching and referral hospital south east Ethiopia, from January 2023 - June 2024

Variable	Category	Frequency	Percent
Resuscitation	Yes	213	98.1
	No	4	1.8
CPAP	Yes	79	36.4
	No	138	63.6
Oxygen therapy	Yes	183	84.3
	No	34	15.7
Antibiotics	yes	216	99.5
	No	1	.5
Anticonvulsants	Yes	61	28.1
	No	156	71.9

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Survival Status of the Neonates

In this study, a total of 29(13.3%) neonates have died and 25(86.2%) of the death of neonates occurred during the first 7 days. the minimum and maximum survival times were 1 and 15 days respectively, The survival probability was 86%, 82 %, and 73% at the first, second, and third weeks of life, respectively. Furthermore, the neonates' median survival time was 4 days.

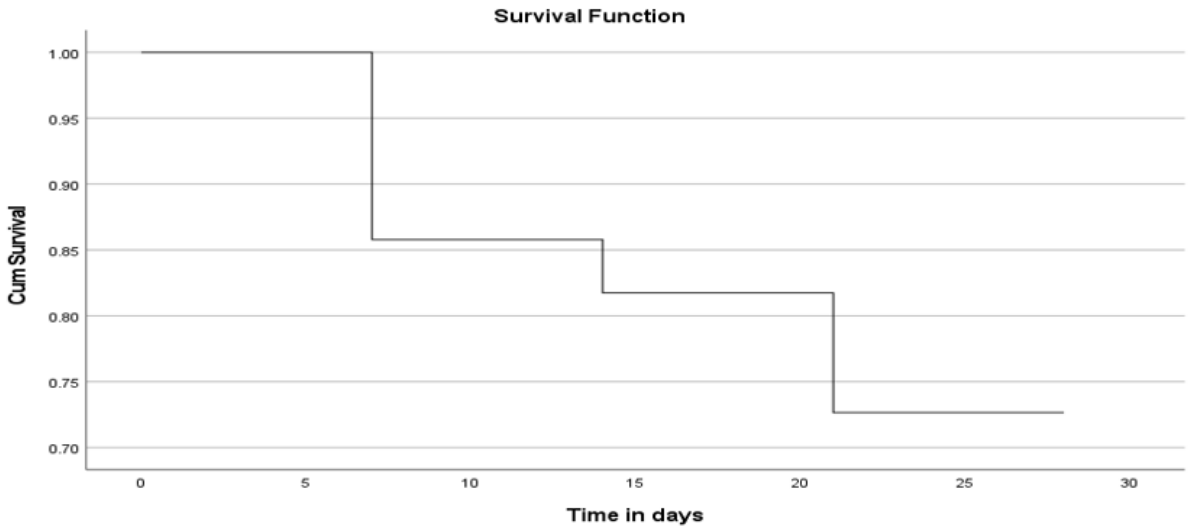

Figure 3: Survival plot of neonates admitted with perinatal asphyxia at Asella teaching and referral hospital, from January 2023 - June 2024 Asella Southeast Ethiopia.

Predictors of death among asphyxiated neonates

At a p-value <0.25 in bivariable Cox regression, 16 variables were selected for the final model: Sex of neonate, Birth weight, Gestational ages, Residence, Place of delivery, Mode of delivery, Neonatal sepsis, Meconium aspiration syndrome, Respiratory distress syndrome, Hypothermia, Hypoglycemia, Convulsion, Acute kidney injury, stage of HIE, CPAP and Anticonvulsants.

However, in multivariable Cox regression by considering 95%CI of the adjusted hazard ratio, and a corresponding P-value of ≤0.05, Sex of neonate, Gestational Age, convulsion, use of Anticonvulsants and Stages of HIE were independent predictors of mortality. Being male was significantly associated with increased mortality by 4.8 times as compared to females. Neonates with convulsion have 93% (HR: 0.07, 95 CI, 0 .009 - 0.567) significantly higher chance to die of perinatal asphyxia and neonates who took anticonvulsants have 14 times significantly increased risk of mortality. Neonates with stage III HIE have 4 times significantly increased risk of death. This study also revealed that preterm neonates have 5 times higher chance of dying compared to term neonates and also the result is statistically significant. (Table 6 below).

Table 6: Multivariable Cox regression analysis of asphyxiated neonates admitted to Asella Teaching and referral hospital south east Ethiopia, from January 2023 - June 2024.

	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp (B)	
							Lower	Upper
Sex of neonate	1.589	.704	5.091	1	.024	4.899	1.232	19.479
Birth weight in gram	-.505	.916	.304	1	.582	.604	.100	3.633
Gestational ages at birth(in weeks)	1.612	.797	4.087	1	.043	5.011	1.050	23.905
Residence	-.201	.867	.054	1	.816	.818	.149	4.476

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Place of delivery	.622	1.429	.189	1	.664	1.862	.113	30.665
Mode of delivery			5.337	2	.069			
Mode of delivery(1)	2.183	1.386	2.481	1	.115	8.873	.587	134.185
Mode of delivery(2)	.819	1.472	.310	1	.578	2.269	.127	40.599
Neonatal sepsis	-1.251	.712	3.093	1	.079	.286	.071	1.154
Meconium aspiration syndrome	-.578	.628	.847	1	.358	.561	.164	1.921
Respiratory distress syndrome	1.264	1.792	.497	1	.481	3.539	.106	118.663
Hypothermia	-1.097	1.144	.920	1	.338	.334	.035	3.143
Hypoglycemia	1.123	1.027	1.195	1	.274	3.073	.410	23.005
Convulsion	-2.664	1.070	6.199	1	.013	.070	.009	.567
Acute kidney injury	.657	.598	1.205	1	.272	1.929	.597	6.233
What was the neonates' stage of HIE?	1.409	.592	5.668	1	.017	4.093	1.283	13.057
CPAP	12.879	61.439	.044	1	.834	3.91	.094	7.76
Anticonvulsants	2.663	1.138	5.479	1	.019	14.335	1.542	133.265

DISCUSSION

This retrospective cohort study aimed to assess magnitude of death, and its predictors among asphyxiated neonates admitted to Asella Teaching and Referral hospital from January 2023 - June 2024. From the total of 217 asphyxiated neonates enrolled in this study 29(13.3%) of neonates were died.

This finding is comparable with a study conducted in South Africa which was 13.3% [25]. On the other hand the finding of this study is lower than a study in Addis Ababa Ethiopia (24.09%)[26], Nigeria (23.9%)[27], and Tanzania (23%)[28]. This finding is higher than studies conducted in Southern Ethiopia (7.85%) [11]. Which may be because the study participants' clinical conditions differed; a study in southern Ethiopia was carried out at general and district hospitals, while the current study was carried out at a referral hospital, where neonates need critical care that were referred from various health institutions are treated, lowering their chance of survival.

In this study 86.2% of the death of neonates occurred during the first 7 days of life. Which is comparable to the study done in jimma University [22]. This might be because the immediate period after birth is the most critical for oxygen delivery to the brain, and severe oxygen deprivation during this time can rapidly lead to irreversible brain damage and multi-organ failure, causing death if not promptly addressed.

Neonates with convulsion have 93% (HR: 0.07, 95 CI, 0 .009 - 0.567) significantly higher chance to die of perinatal asphyxia and neonates who took anticonvulsants have 14 times significantly increased risk of mortality. This might be due to the fact that convulsion causes the newborn to cease breathing, and if this interruption in breathing persists, it can lead to a drop in oxygen. other studies conducted in Ethiopia [11,26], and India [29] also showed similar finding.

Compared to Term neonates, preterm neonates have 5 times higher chance of dying. This is explained scientifically and clinically by the fact that preterm infants typically have feeding difficulties, undeveloped respiratory and thermoregulatory systems, and weak immune systems, which may lead to increased mortality.

When compared to neonates admitted with stage I HIE asphyxia, newborns with stage III HIE asphyxia had 4 times

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higher risk of mortality. Various scientific evidences also support this finding. The majority of deaths in neonates with asphyxia occur in severe and moderate cases due to brain damage, inadequate feeding, seizure, depressed myocardial function, and multi-organ dysfunction [30-32]. this finding is supported by studies done in India (AOR=1.60(1.04-2.46)) [18], Nigeria (AHR=4.3 (1.8–10.4)) [19] and Congo [33]. The probability that stage III HIE increases the hazard of mortality might be because of being usually lethargic, having an absent sucking reflex, and having persistent feeding difficulty. Furthermore, irregularities in heart rate and blood pressure are common during perfusion injury, the primary cause of death is mainly cardiorespiratory failure. This implies that they need close follow-up as compared to other neonates.

Primiparity, place of delivery, multiparity, mode of delivery, preeclampsia and premature rupture of the membrane were not statistically significant predictors of mortality regardless of the study carried out at Southern Nepal, and Dilla University Referral Hospital [11,34,35]. Although neonatal sepsis was prevalent, its potential influence on mortality was not significant, which might be due to the early initiation of antibiotics in the majority of neonates with perinatal asphyxia.

STRENGTH AND LIMITATIONS OF THE STUDY

Strength

Although the estimated sample size was 140, this study included all eligible 217 asphyxiated neonates available at the Asella teaching and referral hospital during the study period. However, this does not imply that always taking the entire population yields more accurate estimates than sampling; thus, we took all eligible populations because it was manageable.

Limitations of The Study

Since this study was conducted retrospectively and relied on a medical record of the neonates, recorded data on some demographic characteristics (maternal and paternal educational and occupational status) and behavioral characteristic (drug, alcohol usage) could not be available in the charts of asphyxiated babies and these variables were not integrated in the study. This may lead to missing of important predictors.

The study focuses on single hospital (ATRH), which limits the generalizability of the findings to other regions of Ethiopia or similar settings.

Lost and incomplete records were excluded and might have caused the study finding to be under or over-estimated.

CONCLUSION AND RECOMMENDATION

Conclusion

The survival status of newborns admitted with perinatal asphyxia was low. In addition, being male; stage III HIE, newborn history of convulsion and use of Anticonvulsants were the independent predictors of mortality. Therefore, special attention should be given to asphyxiated neonate with male sex and those who have seizure.

Recommendation

In addition to the care provided to asphyxiated neonates in the ATRH NICU unit, we recommend that the care of neonates with stage III HIE, convulsion and male neonate should be improved.

In addition, clinical death audits are very crucial to identify and take measures for preventable cause of death like perinatal asphyxia.

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SUPPLEMENTARY INFORMATION

Annexes

Annex -1 Data extraction checklist

Neonate's medical record number: _____

Part I: Socio-demographic and admission baseline data

S/N	Question (variable)	Response
101	Sex of neonate	1) Male 2) Female 3) not recorded
102	Age of neonate at admission	_____ days
103	Birth weight in gram	_____ gram
104	Gestational ages at birth	_____ weeks
105	Residence	_____
106	Admission pulse rate	_____bpm
107	Admission respiratory rate	_____ bpm

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108 Admission body temperature _____degree Celsius

Part II: maternal medical diseases during the index pregnancy

201 Does the mother have medical health problems during the current pregnancy?

1) Yes 2) No

202 If yes, identify the diagnosis

1) Hypertension

2) Iron deficiency anemia

3) Others (specify) ----------

Part III: Maternal obstetric and Gynaecologic conditions

301 Number of parity _____

302 Total number of ANC visit 1) no visit 2) 1-3times 3) ≥4 times

303 Was there a history of Obstetric complications?

1) Yes 2) No

304 If yes for 303, specify it 1) Preeclampsia 2) APH 3) Others (specify) --------

305 Place of delivery 1. 1) In this hospital 2) Referred_____ 3) NR

306 Duration of labor _____ hour

307 Time of rupture of membrane _____hours

308 Mode of delivery 1) C/S 2) SVD 3) instrumental 4) NR

309 Was there a history of Cord prolapse? 1) Yes 2) No

Part IV: neonatal comorbid disease and treatment provided:

A: neonatal comorbid disease (clinical condition)

401 Neonatal sepsis 1) yes 2) no

402 Meconium aspiration syndrome 1) yes 2)no

403 Respiratory distress syndrome 1) yes 2)no

404 Hypothermia 1) yes 2)no

405 Hypoglycemia 1) yes 2)no

406 Convulsion 1) yes 2)no

407 Acute kidney injury 1) yes 2)no

408 What was the neonates' stage of HIE? 1) Stage I 2) Stage II 3) Stage III

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409 Any other comorbidities _____

B: Treatments provided for the neonates

409 Resuscitation 1) Yes 2) no

410 CPAP 1)Yes 2) no

411 Oxygen therapy 1) Yes 2) no

412 Antibiotics 1) Yes 2) no

413 Anticonvulsant 1) Yes 2) no

Part V: Discharge condition

501 Date of admission(DD/MM/YY)_____

502 Date of discharge (DD/MM/YY)_____

503 Length of hospital stay in days_____

504 Discharge status: 1) Died 2) Survived

505 If died, what was the cause of death?

1) Cardiorespiratory failure 2) Multi-organ failure

3) Other_____ 4) NR

Name and signature of data collector: _____

Annex -2 Declaration

Declaration of Investigator

I, the undersigned Pediatrics and Child Health Resident, declare that this Thesis is my original work in partial fulfillment of the requirement for the Specialty certificate in Pediatrics and Child Health to my best knowledge.

Name of investigator: Abdela Abeto

Signature: _____ Date_____

Declaration of examiners

As member of the board of examiners, we examined this research thesis entitled "MAGNITUDE AND PREDICTORS OF MORTALITY AMONG NEONATES ADMITTED WITH PERINATAL ASPHYXIA AT ASELLA TEACHING AND REFERRAL HOSPITAL ASELLA, ETHIOPIA by Dr Abdela Abeto". We certify that the Research thesis is accepted for fulfilling the requirements for the specialty certificate in pediatrics and child health.

Date of Submission: _____

Name of Advisors: Signatures Date:

1. Dr. Tejitu Urgesa

2. Mr. Abdurhaman Kalu

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