COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

DEPARTMENT OF NURSING

SURVIVAL AND PREDICTORS OF ASPHYXIA AMONG NEONATES ADMITTED IN NEONATAL INTENSIVE CARE UNITS OF PUBLIC HOSPITALS OF ADDIS ABABA, ETHIOPIA, 2021.

BY: FEKADESELASSIE BELEGE (BSC)

A THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF NURSING AND MIDWIFERY FOR THE PARTIAL FULFILLMENT OF THE MASTER'S DEGREE IN NEONATAL NURSING.

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Total cost	**27,976 ETB**

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STATEMENT OF DECLARATION

By my signature below, I declare and affirm that this thesis is my own work. I have followed all ethical principles of scholarship in the preparation, data collection, data analysis and completion of this thesis. All scholarly matter that is included in the thesis has been given recognition through citation. I affirm that I have cited and referenced all sources used in this document. Every effort has been made to avoid plagiarism in the preparation of this thesis entitle on:

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ABBREVIATIONS AND ACRONYMS

AAU	Addis Ababa University
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
ANC	Antenatal Care
AOR	Adjusted Odds Ratio
APGAR	Appearance, Pulse Rate, Grimace, Activity, Respiration Rate
APH	Ante-partum Hemorrhage
AST	Aspartate Aminotransferase
BMV	Bag Mask Ventilation
CPAP	Continuous Positive Airway Pressure
CPR	Cardio Pulmonary Resuscitation
DM	Diabetes Mellitus
GMH	Gandhi Memorial Hospital
HIE	Hypoxic Ischemic Encephalopathy
HMIS	Health Management Information System
NICU	Neonatal Intensive Care Unit
PIH	Pregnancy Induced Hypertension
PNA	Perinatal Asphyxia
PROM	Prolonged Rupture of Membrane
RBS	Random Blood Sugar
SpO_2	Oxygen Saturation
SVD	Spontaneous Vaginal Delivery
TASH	Tikur Anbesa Specialized Hospital
TSB	Total Serum Bilirubin

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ABSTRACT

Background: Perinatal Asphyxia is an injury that occurs during the perinatal period due to lack of oxygen flow to the fetus or infant, which may lead to ischemia of the brain or other organs. Gathering current evidence on recovery time and survival predictors of perinatal asphyxia is crucial to fill scarcity of information.

Objective: To assess survival and predictors of asphyxia among neonates admitted in Neonatal Intensive Care Units of public hospitals, Addis Ababa, Ethiopia, 2021.

Methods: Hospital-based retrospective cohort study was conducted in four selected public hospitals of Addis Ababa, Ethiopia. Data were collected from February 15 to 15 March, 2021 by reviewing medical charts of asphyxiated neonates who were registered from January 1, 2016, to December 31, 2020. Epi data version 4.6 was used for data coding, entering and used STATA version 16 statistical software for further analysis. Cox-proportional hazards regression analysis with 95% confidence interval and P-value $\leq$ 0.05 level of significance was used to verify predictors of survival of Perinatal Asphyxia.

Result: In this study, out of 411(94.5%) participants, 305(74.2%) of them survived during the entire cohort. Overall incidence density rate of survival was found to be 10 (95% CI: 0.08-0.11) per 100 neonate-days of observation with an overall median recovery time of 8 days. Neonates those who have low birth weight (AHR: 0.67, 95% CI: 0.47- 0.96), stage II HIE (AHR: 0.70, 95% CI: 0.51 - 0.97), stage III HIE (AHR: 0.44, 95% CI: 0.27 - 0.71), occurrence of seizure (AHR: 0.61, 95% CI: 0.38 - 0.97), thrombocytopenia (AHR: 0.44, 95% CI: 0.24 - 0.80) and not supplied calcium gluconate within first days of life after birth (AHR: 0.75, 95% CI: 0.58 - 0.99) were independent predictors of time to recovery of asphyxiated neonates.

Conclusion: In this study, recovery time was prolonged in any stages of HIE compared to Saranat's staging of HIE. This implies early prevention, strict monitoring and taking appropriate measures timely is mandatory before babies transferred into highest stage of HIE for satisfactory outcomes and reduce mortality.

Keywords: Perinatal asphyxia, Predictors, Survival status, Neonatal intensive care unit.

1. INTRODUCTION

1.1 Background

Perinatal asphyxia is an interruption of gas exchange to the fetus during the perinatal period (1). After birth, the infant takes a breath which brings air into the lungs where gas exchange takes place in the alveoli through diffusion, and this is vital from the start of life out of uterus. If a baby lacks this first breath of air, this can also lead to hypoxia, hypercarbia and potential serious hypoxic ischemic damage organs. Perinatal hypoxic ischemia is the largest avoidable cause of brain insults in newborn (2,3).

Perinatal asphyxia can also be defined by using clinical parameters (bag-and-mask ventilation (BMV) at birth or APGAR score $\leq$ 6) and biochemical parameters (hypercarbia, hypoxemia and metabolic acidosis (base deficit >12 mmol/L) due to diminished gas exchange) and end organ damage (4).

As stated in different literatures, birth asphyxia is caused by antenatal, intra-natal, and fetal factors. The intra-natal factors take the largest proportional risk factor (70%) for birth asphyxia, followed by antenatal (20%) and fetal factors (10%) (5). Anemia during pregnancy, chronic hypertension, Antepartum hemorrhage, prolonged labor, low birth weight, preterm birth, caesarean section delivery, instrumental delivery, fetal distress and meconium-stained amniotic fluid are common associated factors of perinatal asphyxia (6–8).

Cardiovascular response following hypoxia includes redistribution of cardiac output to support oxygen delivery to major organs. Neonates with prolonged hypoxia and ischemia have multi-organ system injury and may manifest a combination of symptoms, such as elevated creatinine levels, oliguria, electrolyte derangements, elevated liver enzymes, spontaneous intestinal perforation, respiratory distress, pulmonary hemorrhage, thrombocytopenia, disseminated intravascular coagulopathy, intracranial hemorrhage and seizures (1). Hypoxic ischemic encephalopathy (HIE) is one of the major consequences of asphyxia and diagnosis requires abnormal neurological findings after birth. Clinicians use the Sarnat score to rate an infant’s neurologic exam after a suspected hypoxic ischemic event. Depending on Sarnat HIE stage the baby’s clinical presentation may be described as mild, moderate or severe. newborns may develop mild to moderate and/or severe encephalopathy during the 72 hours following the hypoxic-ischemic insult (9).

In some countries, trials have been carried out to determine survival status, median survival and recovery time of neonates with HIE and factors which predict the survival of asphyxiated newborns. There is variation of survival status and recovery time from place to place. For example the survival of asphyxiated babies range from 23% in developing countries (10), 63.9% in Nigeria (11), (74.3%) in Dire Dawa public hospital (12), 78.2% in Ghana (13) to 81.1% in Cameroon (14). Average length of hospital stay for surviving asphyxiated neonates was 4.84 days In Dahaka medical college (15), 7 Days in Dire Dawa public hospital and 8 days in the NICU of an Indian tertiary care center (16).

Birthplace, degree of asphyxia, basic resuscitation provided, fetal heart rate, gestational age, multiple births, birth weight, readiness to treat breathing difficulties, diagnosis of meconium aspiration syndrome or persistent pulmonary hypertension, need for advanced care (chest compression & adrenaline), occurrence of infection or seizures within 24 h from admission, maternal infections, electrolyte disturbance and parental education were identified predictor of survival of asphyxiated newborns (7,17–20).

Survival analysis is a useful method for analyzing the length of time until the occurrence of a well-defined event of interest. A unique feature of survival data is that typically not all patients experience the event by the end of the observation period, so the actual survival times for some patients are unknown. It also is useful to analyze the survival probabilities of study participants at different follow-up time points (21). Since data on asphyxiated babies include censored information, it is not compatible with standard statistical models. For this reason; the proportional hazards model are more appropriate to identify predictors that have an influence on the survival status of the asphyxiated babies.

1.2 Problem Statement

Globally, birth asphyxia is a major cause of morbidity and mortality among newborns. Approximately four million neonates become seriously deprived of oxygen during birth each year (18) and nearly 20 per 1000 deliveries will require significant resuscitation, with biochemical and clinical evidence of perinatal asphyxia (22). This transient but potentially catastrophic deprivation of oxygen in the intrapartum period is thought to be directly responsible for 691,000 deaths and 1.02 million stillbirths each year, making it the third and fifth most common cause of neonatal and childhood deaths under 5 years globally (2,3).

The proportion of asphyxiation at birth is ten times greater in developing countries than in developed countries (23). About 3.6 million (3%) of all infants have moderate to severe asphyxiation at birth, 23% dying and about the same number having severe sequelae in developing countries according to WHO estimates (24).

There is higher probability of survival of asphyxiated neonates in the western world due to advanced perinatal care, continuous fetal monitoring during intrapartum, early presentation of neonates in NICUs and treatment modalities. However, the same was not true in developing countries where the mortality rate is high and the recovery time or average hospital stay was prolonged due to many predictor (25).

Even though, most asphyxiated babies recovered, infants who are exposed to prolonged perinatal hypoxia-ischemia may have organ injury (24). Additional to organ damage babies with prolonged hypoxia may develop a short term complications (Hypoxic ischemic encephalopathy (HIE), Seizures and Death) and long-term complications (Cerebral palsy, Hearing loss, Visual impairment, Increased support requirements, Irritability, and Psychological symptoms) (22) with financial and emotional burdens on the families and communities concerned (8).

Like other parts of the world in Ethiopia, there have been important advances in knowledge of fetal and neonatal diseases and monitoring technology. But even today perinatal asphyxia remains the most frequent cause of hospitalization of a newborn, a serious condition causing significant mortality and long-term morbidity (22). The severity of neurological sequelae and the chance of survival depend upon the extent of the insult, the metabolic imbalance during the re-oxygenation period, and the developmental state of the affected organs.

Significant advancements in understanding the pathophysiology of perinatal asphyxia, management, and predictors of survival may reduce this problem (29).

Even though trials have been carried out in some countries to identify predictors of asphyxia, they are not being well investigated in my study area as well as in Ethiopia. In developing countries, such information is very crucial since the burden is very high. Therefore, this study aimed to determine the survival status of asphyxiated neonates and to investigate potential predictors that have influence their survival status and recovery time during the treatment period in public hospitals of Addis Ababa, Ethiopia.

1.3 Significance of the Study

The aim of the study will be determining the survival and predictors of asphyxia among neonates admitted in neonatal intensive care units of Addis Ababa public hospitals. Perinatal asphyxia has been recognized as the leading preventable and manageable cause of neonatal mortality in Ethiopia, Identifying predictors that contribute to the survival status of asphyxiated newborns at birth could significantly reduce the duration of hospitalization and mortality associated with this condition and contribute to the development of preventive strategies as well as treatment protocols to minimize the impact of its complications. This study also provides an opportunity to help achieve the third sustainable development goal, which is targeted to end preventable newborn deaths and work to reduce newborn mortality to 12 per 1,000 live births or fewer by 2030.

Knowing about predictors of survival for asphyxiated babies is very crucial for every health professional. This knowledge can help guide appropriate management and prevention of future problems related to PNA. The findings of this study will increase the existing knowledge and skills of health professionals about how to fasten the recovery time and increase survival probabilities of asphyxiated babies. In addition, it can provide a picture on; the socio-demographic, obstetrics, neonatal, clinico-laboratory and treatment related predictors of survival among asphyxiated newborns which will generate evidence which could be utilized for improved asphyxia management and outcomes.

The final outcome of this study will be useful for parents or care givers by providing knowledge about predictors of survival in asphyxiated babies, which could help them to plan preventive strategies and actively engage in the management of the baby. Lastly, it will be used as baseline data for further prospective studies or interventional projects.

2. LITERATURE REVIEW

2.1 Introduction

The objective of this literature review is to summarize the existing knowledge base on surviving perinatal asphyxia in developing and developed countries, to speak about the impact of these research findings to clinical practice, and to identify gaps in knowledge surrounding perinatal asphyxia survival and its predictors in Ethiopia. As a baseline, literature was examined and gathered on socio-demographic, obstetrics, neonatal and clinical, treatment related factors that impact the survival outcome of babies with perinatal asphyxia.

2.2 Survival status and recovery time of babies with perinatal asphyxia

Globally newborn mortality has shown a steady decline over the last two decades, but this decline has been sluggish in Sub-Saharan Africa. Perinatal asphyxia is a major cause of new-born deaths in the Sub-Saharan Africa region and now contributes a disproportionately large percentage to global perinatal asphyxia related deaths (25). In developing countries 23% of asphyxiated babies have a chance of survival, and 31% of surviving infants with clinical birth asphyxia have an abnormal neurologic examination (neurodevelopmental sequelae including problems with sensory-motor, auditory and language processing) at early follow-up (10).

A descriptive study conducted at a tertiary Care Hospital in Pakistan strived to assess the outcomes of 142 asphyxiated term newborns. According to this study, more than half of cases were discharged in satisfactory condition and the remaining 40.8% died (26). The outcome of death after birth asphyxia was declining from 22% previously to 7.5% more recently in Denmark ($p < 0.05$) (27). Similarly, according to a study done in Brazil, perinatal asphyxia accounted for 10% to 12% of early neonatal death. Nearly three-fourth death occurred within first days of life (28). On the other hand, a Population-based cohort study conducted by Mandira Daripa, in Brazil revealed, 22% of early neonatal deaths were accounted for by perinatal asphyxia. The survival time of those newborns was significantly poor: more than half of them (61.3%) died within the first 24 hours of postnatal age (29).

Moreover, a study done in Iran to evaluate the outcomes of infants with perinatal asphyxia found that approximately 25% of infants died from asphyxia and more experienced developmental delays during a 2-year follow-up (30).

A study conducted in a hospital of South-east Nigeria, revealed that 61.3% of neonates survived and discharged from the newborn unit (20). Similarly, 63.9% of the newborns were discharged and 25.5% of newborns died in another retrospective study done in Nigeria (11). A prospective case-control study done in Cameroon showed that 81.1% of asphyxiated babies had satisfactory outcomes, 12.2% discharged with complications and 6.7% died during the study period out of the total 90 cases with asphyxia (14). A study which was conducted in Ghana, showed that 78.2% of asphyxiated babies survived and the rest died out of the total 289 asphyxiated babies admitted at Korle-Bu Teaching Hospital NICU during the study period (13).

A study carried out in Ethiopia for the assessment of emergency obstetric and Neonatal Care in 3804 facilities providing childbirth services a 1025 chart reviews of babies born with difficulties breathing, and found that 71% were discharged alive from hospitals and health centers (19). However, a registry based cohort study in Northern Tanzania reported perinatal asphyxia was a leading cause of death (n = 245, 45.7%) with a case fatality rate of 23.8% (31). In Nigeria in one study, perinatal asphyxia accounted for 42.1% of the total neonatal mortality (32).

Among the total 35 newborns admitted in neonatal intensive care units of Dire Dawa public hospital for the management of perinatal asphyxia, majority (74.3%) of the neonates were successfully treated or discharged and the overall median recovery time of neonates admitted in NICUs was 7 Days with 95% CI (6.525-7.475) (12). The average length of hospital stay for surviving asphyxiated neonates was different from institution to institution. It was 4.84 days in Dahaka medical college (15), 3.8 ± 4.12 days in Specialist Hospital in Gusau, Nigeria (11), 8 days the in NICU of an Indian tertiary care center (16) and 9.07±4.85 days for a governmental referral hospital in central India (33).

2.3 Predictors of birth asphyxia Survival

Various studies done on perinatal asphyxia survival have addressed different factors which affect survival, such as birth outside the hospital, mode of delivery, prolonged labor, prolonged rupture of membranes, prematurity, low birth weight, low Apgar score, severity of asphyxia, depressed clinical state at admission, bradypnea, major electrolyte disturbance, bag-mask ventilation at birth and co-morbid illnesses. Differences in survival time among asphyxiated babies have been reported in different countries and in different studies (7,19,32–34). Some of the literature regarding survival time and predictors of survival among asphyxiated babies are reviewed below.

2.3.1 Factors related to Sociodemographic and Obstetrics predictors

Some evidence showed the association between socio-demographic and obstetric variables towards survival of birth asphyxia. For instance, a prospective cohort study was done in Nigeria to determine the association between socio-demographic variables and survival of birth asphyxia. According to the report, the chance of surviving was significantly lower in infants who had teenage mothers and less educated mothers. Other variables like maternal employment and place of residence did not differ significantly between the groups (35).

A study done in southern Nepal revealed paternal education was the most significant risk factor, associated with a 41% lower birth asphyxia mortality risk (7). Additionally, a longitudinal study done in Nigeria, reported that semi-skilled maternal occupation was a significant predictor of mortality in asphyxiated newborns (RR: 8.85; 95% CI: 1.10-71.47) (36). However, another study done in India and south Africa found no risk- effect relationship between socio-demographic variables and mortality in asphyxiated neonates (18,33,34).

A lot of antepartum and intrapartum factors play a major role in neonatal morbidity and mortality due to perinatal asphyxia. A study done in India found that newborns whose mothers had inadequate pre-natal care had a significantly higher mortality rate than infants of mothers with access to care (p =0.01) and maternal anemia had a significant influence on outcome (OR 3.07 CI 1.12-8.41 p=0.02). Other risk factors, such as hypertension, eclampsia, maternal diabetes, , intrapartum fever and antepartum hemorrhage did not significantly increase death from asphyxiation at birth (33).

Findings of a study in Nepal stated that maternal fever and signs of pre-eclampsia contributed a higher risk for birth asphyxia mortality. History of a prior child death (7), history of eclampsia, maternal history of hypertension, mode of delivery and antenatal care attendance, did not significantly predict birth asphyxia mortality (18,35,36).

A prospective study done in Nigeria, South Africa and Nepal revealed that birth outside the hospital, mode of delivery (18,37), prolonged labor, prolonged rupture of membranes and multiple births (twin or triplet) all were significantly associated with neonatal deaths from asphyxia (7). Moreover, A study done in India showed that premature rupture of membranes, meconium stained fluid, parity and place of delivery were statistically significant risk factors of mortality, but modes of delivery was not (34).

According to the 2016 Ethiopia Emergency Obstetric and Newborn Care Assessment, cesarean or assisted vaginal delivery increased the odds of surviving birth asphyxia by twofold compared to vaginal delivery (38). A study done in Tanzania reported birth outside of health institutions increase mortality by 4.6 fold compared to inborn babies (AOR = 4.63 95% CI: 1.17 – 19.62), but there was no association between mode of delivery and risk of mortality (17). Similarly, a study in Nigeria found that babies born in facility (AOR = 1.22; 95% CI: 1.06-1.78) were more likely to survive than out-born babies (20).

2.3.2 Factors related to Neonatal predictors

A study done in Ethiopia compare the odds of surviving among term asphyxiated babies and babies that have normal birth weight with that of preterm and low birth weight newborns. According to this study, term babies had 1.5 times greater chance of survival and those who have normal birth weight had 2.4 times greater chance of survival compared to preterm and low-birth weight babies(19). Furthermore, in northern Nigeria, one study revealed for each additional kilogram a participant had at admission the chance of survival of that asphyxiated baby increased by 89%. Other neonatal factors such as sex of the baby, age at clinical presentation, gestational age and delayed crying after birth were not significantly associated with mortality (35). Another study done in South Africa revealed gestational age, birth weight and gender did not differ significantly between the two groups(survival & non survival) (39).

A four-year prospective Study done in Enugu (Nigeria) noted that female infants had significantly higher likelihood of death from asphyxia. Other factors like age at presentation, gestational age and birth weight did not have a significant association with mortality (37).

However, a study done in southern Nepal showed gestational age, birth weight and sex all had significant association with mortality. The risk of mortality from birth asphyxia among premature infants was 2.28-fold higher, among very low birth weight infants was 11.88 fold higher, and for males was about 29% higher (7). Similarly, premature infants were had five times more risk of death with birth asphyxia but birth weight, age at presentation and gender had no association with mortality according to findings of a southeast Nigerian study (36). In Nepal, a descriptive observational study was carried out on death of neonates from birth asphyxia versus presentation time. According to this study, from the total death more than half of the neonatal deaths were recorded within 6 hours and 42.9% were die after 6 hours (24).

Another prospective cohort study done in Nigeria showed that about one-third of deaths occurred within 24 hours of presentation, while about two-thirds died within 72 hours of admission and the least number of deaths occurred after 7days (10.7%) (35).

A study conducted in Pakistan revealed that late arrival to the hospital when in labor was significantly adversely affecting outcomes. Comparing the severity of HIE with the time of arrival at the hospital, Stage I HIE was predominant in referral time less than 24 hours followed by stage II HIE cases whereas Stage II was more common in referral time 24- 48 hours, followed by Stage III HIE (26).

2.3.3 Factors related to Clinical and laboratory predictors

A retrospective observational study was done in a low-resource setting to determine factors associated with mortality among asphyxiated neonates. According to this study depressed clinical status (inability to suck, lethargic, and hypotonic/flaccid tone at admission) , low 5^{th} minute Apgar score, occurrence of seizures or infection within first day from admission, were the major factors associated with mortality (17). Another study conducted in south Africa showed relation of Apgar score and outcomes of asphyxiated babies. 9 times and 19 times higher mortality was recorded if the baby had low Apgar score (<5) at 5^{th} and 10 minutes respectively, and no spontaneous respiration at 20 minutes also was a predictor of poor outcome (OR 27.2; 95% CI 6.9 - 117.4) (4).

Similarly, a retrospective cross-sectional study conducted in Asmara, Eritrea revealed that Apgar score and neonatal mortality had significant inverse association (OR= 2.28 95% CI 1.09–4.76) and (OR= 2.07 95% CI 1.02-4.22) in 1st and 5th minute respectively (40).

A study of Uchenna et al. examined vital signs of a neonate at presentation as a predictor of neonatal mortality from perinatal asphyxia. They found that hypoxia (SpO_2 = < 60% on room air), bradypnea (RR= < 30b/min) and Heart rate ≤120 b/min were predictors of neonatal mortality from asphyxia. However, they did not find a significant difference in newborn mortality among infants who had hypothermia and hyperthermia (37). A study conducted in Katihar Medical College Hospital, India showed that the different clinico-laboratory factors significantly associated with mortality during the first 72 hours after birth included hypotension, hypothermia, hypoglycemia, hypoxemia and birth injury (34).

According to a study done in Nepal neonates with HIE stage I had good prognosis with survival rate of 95%, and poor outcomes were recorded in HIE stage III with survival rate of 25% (41). Parallel to this, several studies recognized the relation of mortality due to perinatal asphyxia with severity of asphyxia. Majority of stage I HIE neonates had recovered and had satisfactory outcome while Severely asphyxiated babies (stage III HIE) were more likely to die than mild and moderately asphyxiated babies (34,37,42,43).

A study done in southern Nigeria showed that most of the asphyxiated babies had multi-systemic adverse features. Among them babies with cyanosis, respiratory distress, apnea, abdominal distension, feeding intolerance, oliguria/anuria, bleeding disorders, abnormal muscle tone, seizures, bulging fontanel, and coma had significant association with mortality (p = ≤0.01) (32).

Another prospective observational study conducted in India indicated that neonates who presented with cyanosis, convulsions, anemia and extended capillary refill time were significantly associated with increased mortality but lethargy, hypothermia, hyperthermia and apnea were no significantly associated with mortality (33). Presence of respiratory distress at admission increased the risk of mortality by 3.7 fold. Otherwise presence of altered consciousness, poor suck, and hypoxic ischemic encephalopathy staging were not associated with in-patient mortality on multivariable analysis discussed in a study done in Nigeria (35).

Regarding laboratory findings between babies who survived and those who died from perinatal asphyxia, the mean hematocrit, plasma potassium and urea were high among babies who died compared to those who survived asphyxia in the first 24 hours of life while plasma sodium and glucose were significantly lower (32). A study by Thakur et al. found the severity of electrolyte imbalance mostly correlated with the severity of birth asphyxia. Among this hyponatremia, hyperkalemia and hypocalcemia predict birth asphyxia mortality (44). According to a study conducted in Nepal high blood glucose in the first 12 hours is associated with poor prognosis in asphyxiated term infants (P = 0.017) (45). Additionally, a study done in India revealed that there were blood glucose and serum calcium level discrepancies between survival and non-survival, but these did not predict survival (33).

An observational prospective study from India indicates Apgar score combined with hepatic dysfunction can be used as a prediction marker for neonatal mortality. The severity of hepatic dysfunction correlates well with increasing severity of asphyxia. The mean aspartate aminotransferase (AST) value were 76.3 ± 37.4 U/L Vs 23.5 ± 8.5 U/L, the mean of alanine aminotransferase (ALT) were 82.2 ± 48.08 U/L Vs 26.5 ± 7.8 U/L, the mean of alkaline phosphatase (ALP) were 369.6 ± 123.05 U/L Vs 208.2 ± 46.9 U/L, the mean of serum albumin were 32.6 ± 5.5 g/L Vs 40.9 ± 6.5 g/L and the mean of total serum bilirubin level were 5.5 ± 2.01 mg/dL Vs 4.5 ± 1.2 mg/dL in asphyxiated babies versus normal babies, respectively and these differences were statistically significant (P , 0.001) (46).

2.3.4 Factors related to Treatment related factors

A study done in south Africa found that bag-mask ventilation at birth was one of the notable determinants of survival of neonates with perinatal asphyxia (39). Another prospective observational study which was done in India confirmed that bag and mask resuscitation of the neonate was significantly associated with mortality from perinatal asphyxia (p=0.004) (33).

According to a study done in Ethiopia, administration of oxygen was not significantly associated with survival of asphyxiated babies in multi variant analysis. However, newborns who have been provided with any form of resuscitation (bag mask ventilation , intubation or stimulation) were eight times more likely to survive than those who did not receive resuscitation (19).

A retrospective study was conducted in South Africa to determine the odds of developing severe hypoxic ischemic encephalopathy and/or chance death those newborns that needed chest compression and Adrenaline administration. According to this study, those neonates were very sick and who had chest compression were at 4.5 times and those who took adrenaline administration 81 times greater risk of developing severe HIE and/or death (4). Similarly, a study performed in Tanzania showed that those babies who received aminophylline were 9 times more likely to die than those who did not receive aminophylline, but there was no significant difference in babies who were given diazepam and furosemide (17). A randomized control trial done for assessing the efficacy of prophylactic intravenous calcium admiration in high risk neonates within first five days of life, showed there is a difference in experiencing the symptoms of hypocalcemia ($p=0.007$) and requirement of hypocalcemia treatment ($p=0.0004$) in newborns those who got intravenous calcium infusion compared to control group (47).

2.4 Conceptual framework

This conceptual framework shows the association between dependent variables and independent variables which is adapted from different literature. For example, survival of babies was significantly lower in mothers who were teenage mothers, had longer duration of labor (35). Inborn delivery and cesarean section or assisted mode of delivery increased survival (20,48). Being premature and very low birth weight had a higher birth asphyxia mortality risk (7). Electrolyte disturbance within the first 24 hours predicted birth asphyxia survival (44). Newborns who got any form of CPR (bag mask ventilation or intubation) had an increased survival rate compared to those who did not receive resuscitation (19). Contrary, the chance of developing complication and/or dying after chest compression and Adrenaline administration was high in babies who were very sick (4).

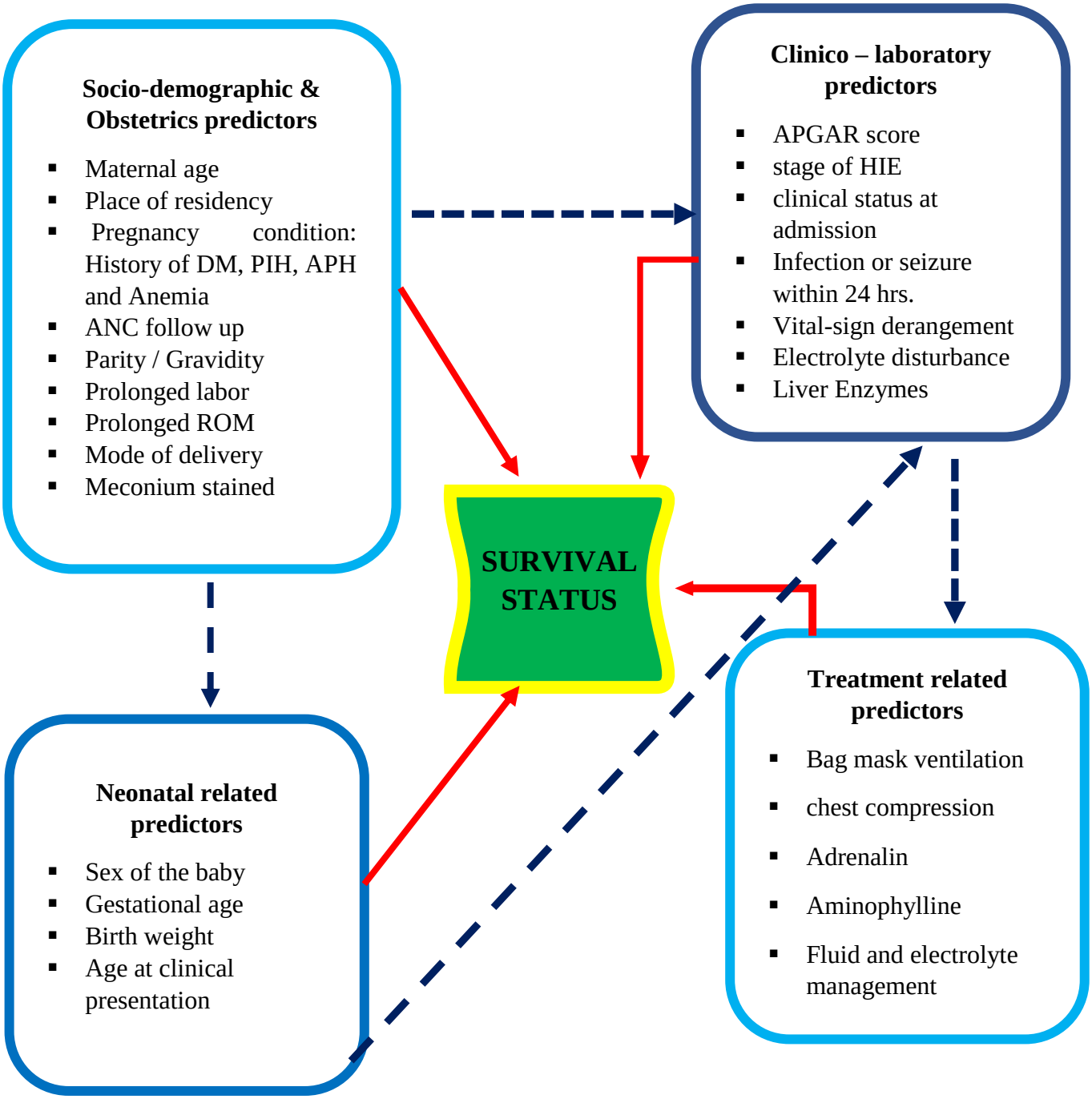

Figure 1: Conceptual frame that shows survival status of perinatal asphyxia and predictors of survival at neonatal intensive care units of Addis Ababa public hospitals, Ethiopia, 2021**.**

3. OBJECTIVES

3.1 General objective

To assess survival and predictors of asphyxia among neonates admitted in neonatal intensive care units of public hospitals from January 1st, 2016 to December 31st , 2020 Addis Ababa, Ethiopia.

3.2 Specific objectives

1) To determine incidence density rate of survival among asphyxiated neonates admitted in NICUs of Addis Ababa public hospitals.
2) To determine median recovery time of asphyxiated neonates admitted in NICUs of Addis Ababa public hospitals.
3) To identify predictors of survival from perinatal asphyxia among neonates admitted in NICUs of Addis Ababa public hospitals.

4. METHODS AND MATERIALS

4.1 Study area and Study period

The study was carried out at four randomly selected public hospitals of Addis Ababa, Ethiopia, from February 15 to 15 March 2021 using records of admitted asphyxiated babies in NICUs from 1st January 2016 to December 31st, 2020. Addis Ababa is Ethiopia's capital city with a wide variety of ethnic groups almost home of all ethnicity found in the country. Addis Ababa city is divided in to 11 sub-cities containing 118 woreda at an altitude of 7,700 feet (2,355metres). Based on the projected population value for 2019, the city has an estimated total population of 4, 592,000 (48). The town has twelve government hospitals. Five hospitals belong to Addis Ababa Health Authority, four to Federal Ministry of Health, one to the ministry of Education (AAU), and two to the defense force. Of those eleven have a neonatal unit. The study was conducted in Tikur Anbesa Specialized hospital, Yekatit 12 hospital medical college, St. Peter Specialized Hospital and Gandhi memorial hospital which were selected by lottery method.

4.2 Study Design

Institution based retrospective cohort study was conducted in Addis Ababa selected public hospitals.

4.3 Population

4.3.1 Source Population

All asphyxiated neonates admitted in the neonatal intensive care units of public hospitals of Addis Ababa during the study period.

4.3.2 Study Population

All randomly selected records of asphyxiated neonates admitted in the neonatal intensive care units of selected public hospitals of Addis Ababa from January 1, 2016 to December 31, 2020.

4.4 Inclusion and Exclusion Criteria

4.4.1 Inclusion criteria

All records of asphyxiated newborns who were admitted in NICUs of selected public hospitals of Addis Ababa during the study period.

4.4.2 Exclusion criteria

Asphyxiated neonates who had incomplete medical records and asphyxiated babies those who had major congenital anomalies were excluded from this study.

4.5 Sample Size and Sampling Procedure

4.5.1 Sample Size Determination

The single population proportion formula was used to calculate the sample size for the first objective, taking into account the following statistical assumptions.

P = the proportion of survival in newborns who have undergone perinatal asphyxia = 50 % (Because there was no study in my study area or in another area where the population is similar).

Z α/2 = the corresponding Z score of 95% CI

d= Margin of error (5%)

N= Sample size

$$N= \frac{Z(a/2)^2 P(1-P)}{d^2} = \frac{(1.96)2*0.5*0.5)}{0.0025} = 384.16 \sim \mathbf{384.2}$$ = 10% missing data=38.42.

Therefore, the sample size calculated with adding of 10% for missed data is **423**.

For the second objective, the sample size was determined using a double population proportion formula by considering gestational age, degree of asphyxia, birth weight and place of birth, as all of these factors predict survival in newborns who are asphyxiated at birth (20). Among those predictors, birth weight was found to be an independent predictor that gave a maximum of 395 sample size having an assumptions of (P1= 76.9%, P2= 26.1%), by adding 10% for missing data gives a total sample size of **435.** It was calculated by taking two-sided significant level (α) of 5 %, power (ZB) 80 % and 1:1 ratio of non-exposed to expose and OR= 2.23. Finally, maximum sample size (N= 435) was a final sample size for this study.

4.5.2 Sampling technique and procedure

Four public hospitals (Tikur Anbesa, Yekatit 12, Gandhi and St Paul hospitals) were selected by lottery method from eleven public hospitals in Addis Ababa that have NICU clinics. Proportional allocation formula was used to select the study participants from each hospital and each year based on the five years total of the study time period.

After that, medical records numbers of babies diagnosed with perinatal asphyxia were isolated from the registration log book. Then, from the isolated medical record numbers in each hospital, computer generated simple random sampling technique was applied to select the study participants. Finally, the selected medical charts were reviewed from February 15 to March 15, 2021.

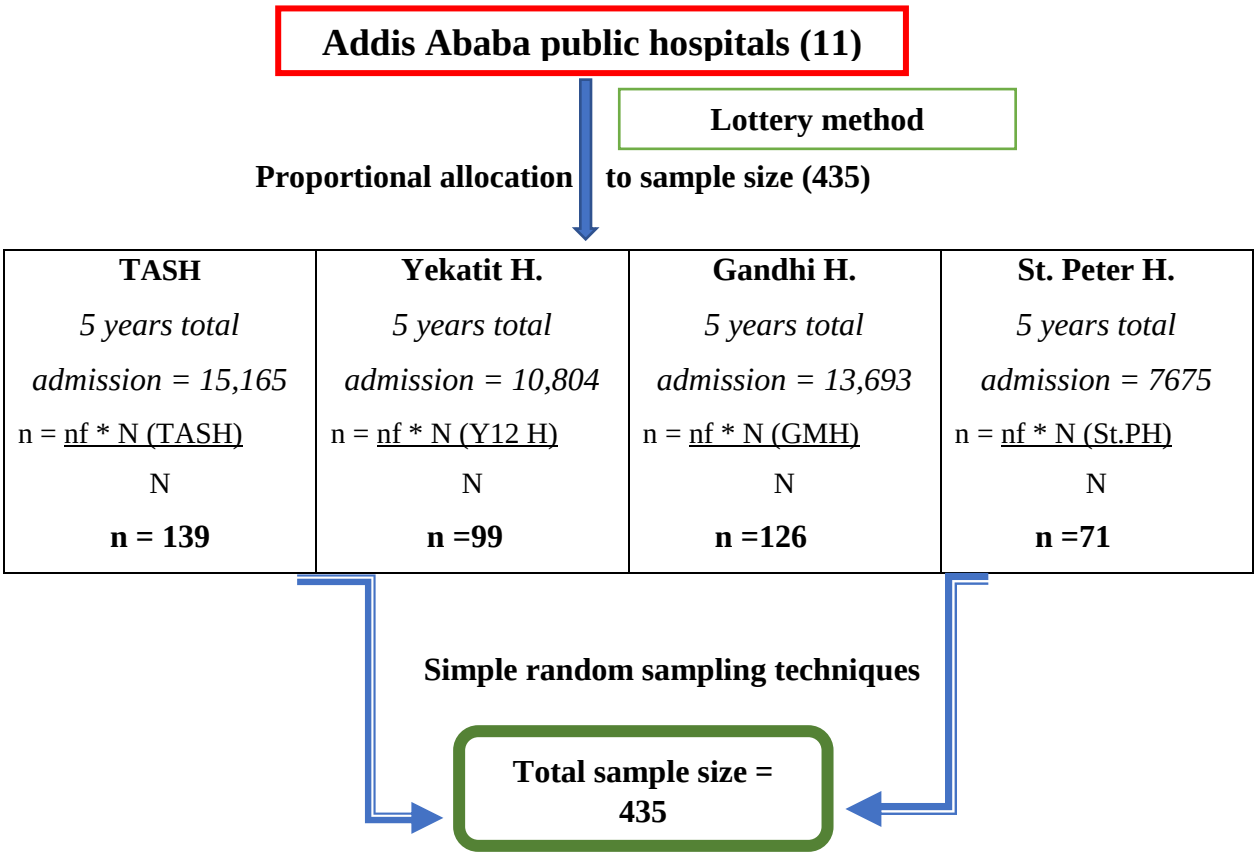

Figure 2: Schematic presentation of sampling procedure on survival status and predictors of survival in asphyxiated newborns admitted to NICUs of public hospitals, A.A, Ethiopia, 2021.

4.6 Variables of the Study

4.6.1 Dependent Variable

Time to Recovery

4.6.2 Independent Variables

- **Socio-demographic and Obstetrics factors: -** maternal age, place of residency, gestational hypertension, antepartum hemorrhage, ANC follow up, parity, prolonged labor, prolonged rupture of membrane, mode of delivery and meconium stained.

- **Neonatal related predictors: -** Sex of the baby, gestational age, birth weight and age at clinical presentation.
- **Clinico–laboratory predictors:** - Apgar score, crying, stage of HIE, clinical status at admission, infection or seizure occurrence within 24 hours, vital-sign derangement, electrolyte disturbance and liver enzyme derangement.
- **Treatment related predictors: -** Bag mask ventilation, chest compression, Adrenalin, Aminophylline, fluid and electrolyte management.

4.7 Operational Definitions of Variables

Perinatal asphyxia - will be considered on the basis of the clinical diagnosis made by a health care provider and recorded on the charts.

Stages of HIE - it will be determined on the basis Saranat's classifications of the clinical diagnosis made by a health care provider (stage 1, stage 2 and stage 3).

Major congenital anomalies – a wide range of abnormalities of body structure and function that present at birth, like heart defect, neural tube defect and Down's syndrome.

Incidence density rate of survival – It will be computed by dividing number of events to total follow up time in person-days.

Survival time – number of days it takes from admission until a baby is recovered from PNA (that can be measured by using Incidence density rate and median recovery time).

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

Censored - are those newborns who had death summary sheet, against medical advice (caregivers sign on behalf of their baby to leave the treatment before recovery), or referred to other health facilities.

Died - are those newborns who passed away and whose death report is recorded on the chart.

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

Event - newborns who recovered from PNA.

4.8 Data Collection Procedure

4.8.1 Data collection tool

A data abstraction format was adapted from the standardized HMIS registration book, PNA follow up chart and other peer reviewed articles (20,32,34,35,39). Data abstraction was designed based on study objectives, and contains four parts; checklists related to socio-demographic and obstetric related factors, neonatal related factors, clinical and laboratory factors, and treatment related factors which were collected from medical records.

4.8.2 Data collection procedure

Four BSC Nurses for data collection and two BSC Nurses recruited for supervision and coordination of the whole data collection processes. One day training was given to data collectors and supervisors regarding significance of the study and truthful completion of the checklist and ethical considerations to standardize the data collection. Then the records of all study participants were selected according to the eligibility criteria and all available information on patient records was checked. Then, they extracted all relevant variables that meet the study objectives from patients' charts by using a structured data extraction format. The starting point for retrospective follow-up was the time of diagnosed PNA and the end point was date of discharge or 28 days of age after birth. In the case of two or more laboratory results were recorded on the chart within 24 hours, the average values were used and the recovery was confirmed by the discharge note completed by registration.

4.9 Data quality Assurance

To ensure quality of the data, Pretest was carried out on 5% (22 charts) of the study samples at the Tikur- Anbesa specialized hospital and errors found during the verification process was corrected and modified to ensure the agreement of the data abstraction format with the study objectives. Completeness of the collected data was checked onsite on a daily basis during data collection and prompt feedback was given by the supervisor and the principal investigator.

All completed data collection forms examined for completeness and consistency during data management, storage, cleaning and analysis. Consistency were also assessed by random selection of medical records by the principal investigator and cross-checking them for similarity.

4.10 Data processing and analysis

The collected data were coded, entered and cleaned in Epi data version 4.6 and then exported to STATA Version 16.0 statistical software for further analysis. The necessary assumption of Cox-proportional hazard regression model was checked by using the Schoenfeld's residual test and the Log-rank test. Descriptive and inferential statistics was used to present the data. Descriptive statistics like frequency and percentage were used to summarize the socio-demographic characteristic and the clinical characteristics of the study participants.

The outcomes of neonates were dichotomized into recovered or censored categories. Kaplan Meier survival curve was used to estimate survival time, and log rank test was used to compare the survival curves among categorical predictors. Bi-variable Cox proportional hazards regression model was fitted for each explanatory variable. Then, those variables having an association in bivariate analysis (P-value < 0.2) were entered in the final Cox-regression analysis to identify independent predictors of survival of asphyxiated neonates. Hazard ratio with 95% confidence interval and p-values used to measure the strength of association and to identify statistically significant predictors. In the multivariable Cox-regression analysis, variables having P-value < 0.05 was considered as significant predictors of survival of asphyxiated neonates. Finally, the results were summarized and presented in texts, tables and graphs.

4.11 Ethical considerations

Ethical clearance was obtained from the Institutional Review Board (IRB) of the University of Addis Ababa, school of nursing and midwifery, Addis Ababa city health bureau and St. Peter Specialized Hospital. All information collected from patients' chart kept under strict confidentiality and not disclosed to any person other than principal investigator.

4.12 Dissemination of results

The results of the study will be submitted to Addis Ababa University, School of Medicine and allied Health Science College. The finding and recommendations will be distributed to all public hospitals in Addis Ababa those who have NICU clinic, Addis Ababa city health bureau, minister of health and other organizations working on related area to be used as a baseline for intervention. Attempts will be made for publication of the research in a reputable Journal.

5. RESULT

Four hundred thirty five charts of asphyxiated neonates were reviewed; 411(94.48%) were eligible for this study; 24 charts were excluded (9 had major congenital malformation and 15 charts were not available during data collection time).

5.1 Socio-demographic & Obstetric characteristics of mothers of study participants

Most of the mothers 351(85.4%) were between the age of 20 to 34 years. The age of the mother ranged from 16 to 40 years with the median age being 26 years. Among all, 411 mothers 334(81.3%) were from Addis Ababa. More than half of 239(58.15%) mothers gave birth for the first time and almost all 401(97.6%) had attended antenatal care during their pregnancy. The mode of delivery was spontaneous vertex delivery in 235(57.18%) of cases, with 115(28%) of being cesarean delivery (C-section).

Among the pregnant woman who had Obstetrics &medical complication recorded, 25(6%) of the pregnant woman had Hypertension during their pregnancy, among that 22(88%) were pregnancy induced hypertension (Preeclampsia/Eclampsia). Likewise, 15(3.65%) mothers had antepartum hemorrhage and 27(6.5%) had history abortion. More than one third of (37.7%) newborns were born from mothers who had meconium stained amniotic fluid and 63(15%) of them had fetal distress during intrapartum period. Out of the total 411 newborns admitted in four Addis Ababa public hospitals, around half (46.7%) of the babies were born from outside of admitting institution (Table 1).

5.2 Neonatal characteristics of the study participants

Out of the cohort 411 (60.58%) were males, while comparing the mean age of neonates at presentation on NICUs was prolonged in Out-born babies (9.6 + 24.7) and censored (5.2 $\pm$ 16 hours) compared to 0.9 + 2.2 hours for Inborn babies and 4.9 $\pm$ 18 hours for survived neonates from asphyxia. Around one sixth (17%) of babies cried at the time of birth and nearly 6% of neonates had normal APGAR score ($\geq$ 7) at first minutes of life in both survivors and censored cases (Table 2).

Table 1: Socio demographic and Obstetrics characteristics of pregnant mother who had admitted asphyxiated baby at NICUs of Addis Ababa public hospitals, Ethiopia 2021(n=411).

Covariates	Category	**Total** Number (%)	**Status**	
			Survived Number (%)	Censored Number (%)
Maternal Age	<20 years	22(5.35)	18 (5.90)	4(3.77)
	20-34 years	351(85.40)	255(83.61)	96(90.57)
	>34 years	38(9.25)	32(10.49)	6(5.66)
Place of residency	Addis Ababa	334(81.27)	247(80.98)	87(82.08)
	Out of Addis Ababa	77(18.73)	58(19.02)	19(17.92)
Parity	Primiparous	239(58.15)	182(59.67)	57(53.77)
	Multiparous	172(41.85)	123(40.33)	49(46.23)
ANC follow up	No	10(2.43)	7(2.30)	3(2.83)
	Yes	401(97.57)	298(97.70)	103(97.17)
Time of delivery	Day-time	209(50.85)	151(49.51)	58(54.72)
	Night-time	202(49.15)	154(50.49)	48(45.28)
Place of delivery	Inborn	219(53.28)	153(50.16)	66(62.26)
	Out born	192(46.72)	152(49.84)	40(37.74)
Mode of delivery	SVD *	235(57.18)	172(56.39)	63(59.43)
	Assisted delivery	61(14.84)	46(15.08)	15(14.15)
	C/S delivery	115(27.98)	87(28.52)	28(26.42)
Duration of labor	Normal	354(86.13)	260(85.25)	94(88.68)
	Prolonged	57(13.87)	45(14.75)	12(11.32)
Duration of rupture of membrane	< 18 hours	386(93.92)	286(93.77)	100(94.34)
	>18 hours	25(6.08)	19(6.23)	6(5.66)
Obstetrics & medical conditions	Cord problems	12(2.92)	8(2.62)	4(3.77)
	Hypertension	25(6.08)	15(4.92)	10(9.43)
	Pre/Eclampsia	22(88)	14(93.33)	8(80)
	APH**	15(3.65)	10(3.28)	5(4.72)
	Oligohydramnios	10(2.43)	6(1.97)	4(3.77)
	fetal distress	63(15.33)	55(18.03)	8(7.55)
	Multiple pregnancy	11(2.68)	7(2.30)	4(3.77)
	MSAF ***	155(37.71)	122(40)	33(31.13)
	Abortion History	27(6.57)	16(5.25)	11(10.38)

*- Spontaneous vaginal delivery, **-Antepartum hemorrhage, ***- Meconium stained amniotic fluid

Regarding the 5th minutes APGAR score, two third (66%) of survivors and three fourths (75%) of censored cases had low APGAR score (<7) at fifth minutes of life. Most of the newborns (70%) had normal birth weight and 25.6% had low birth weight. Nearly (15.3%) were preterm and 37(9%) were post term (Table 2).

Table 2: Neonatal characteristics of Asphyxiated baby who were admitted at NICUs of Addis Ababa public hospitals, Ethiopia 2021(n=411).

Covariates		Category	Total	Status	
			Number (%)	**Survived** Number (%)	**Censored** Number (%)
Sex of baby		Male	249(60.58)	182(59.67)	67(63.21)
		Female	162(39.42)	123(40.33)	39(36.79)
Birth weight		Normal	287(69.83)	220(72.13)	67(63.21)
		Big baby	19(4.62)	17(5.57)	2(1.89)
		Low birth weight	105(25.55)	68(22.30)	37(34.91)
		Mean BW in Kg.	2.82±0.65	2.88±0.62	2.64±0.69
Gestational Age		Term	311(75.67)	237(77.70)	74(69.81)
		Post term	37(9.00)	29(9.51)	8(7.55)
		Preterm	63(15.33)	39(12.79)	24(22.64)
Postnatal Age at presentation		<24 hours	378(91.97)	282(92.46)	96(90.57)
		24 – 72 hours	23(5.6)	15(4.92)	8(7.55)
		>72 hours	10(2.43)	8(2.62)	2(1.89)
		Mean age in Hours	5±17.5	4.9±18	5.2±16
Cried immediately at birth		Yes	70(17.03)	49(16.07)	21(19.81)
		No	341(82.97)	256(83.93)	85(80.19)
APGAR score	1^{st} min.	≥7	24(5.84)	18(5.9)	6(5.66)
		<7	387(94.16)	287(94.1)	100(94.34)
	5^{th} min.	≥7	128(31.14)	101(33.11)	27(25.47)
		<7	283(68.86)	204(66.89)	79(74.53)

5.3 Clinical and Laboratory characteristics of the study participants

The most frequent identified additional medical complications at admission among asphyxiated newborns and during their hospital stays were hypothermia (86.13%), and respiratory distress (51.82%), MAS (64.96%), and hypoglycemia (4.62%). From the total nighty-nine (24.09%) of the newborns presented with Stage III HIE, only one out of eight could be survived and discharged alive. Among censored neonates, 57.6% and 35.9% were admitted with Stage III and Stage II HIE, respectively. More than half of survived neonates presented in NICUs with altered consciousness and depressed Moro reflex. Among medical complications that confirmed after admission and treated during their hospital stays, Sepsis (HAI), neonatal seizure and hyperbilirubinemia were the leading diagnosis 36.9%, 23.1%, and 6.81%, respectively. 23(5.6%) babies manifested signs of acute kidney injury and 3.65% had signs of necrotizing enterocolitis (Table 3).

Table 3: Clinical and Laboratory characteristics of Asphyxiated baby who were admitted at NICUs of Addis Ababa public hospitals, Ethiopia 2021 [n=411].

Covariates	Category	Total	Status	
		Number (%)	Survived Number (%)	Censored Number (%)
Altered consciousness at admission		264(64.23)	172(56.39)	92(86.79)
Depressed Moro reflex at admission		270(65.69)	173(56.72)	97(91.51)
HIE stage at admission	Stage 1	127(30.9)	120(39.34)	7(6.60)
	Stage 2	185(45.01)	148(48.2)	38(35.85)
	Stage 3	99(24.09)	38(12.46)	61(57.55)
Additional medical conditions (diagnosis) at admission	Respiratory distress	213(51.82)	156(51.15)	57(53.77)
	hypothermia	354(86.13)	255(83.61)	99(93.40)
	Hypoglycemia	19(4.62)	13(4.26)	6(5.66)
	MAS *	267(64.96)	195(63.93)	72(67.92)
Medical complication developed during their hospital stay	Hyperbilirubinemia	28(6.81)	26(8.52)	2(1.89)
	Necrotizing enterocolitis	15(3.65)	9(2.95)	6(5.66)
	Acute kidney injury	23(5.6)	14(4.59)	9(8.49)
	Thrombocytopenia	20(4.87)	15(4.92)	5(4.72)
	Seizure	95(23.11)	71(23.28)	24(22.64)
	Sepsis (HAI)	152(36.98)	112(36.72)	40(37.74)
	Others**	19(4.62)	15(4.92)	4(3.77)
Laboratory investigation within 24 hours of age (Mean ± SD)	WBC (cell/mm^3) [n=310]	19.81±0.57	19.37±0.58	21.74±1.7
	HCT (%) [n=310]	53.99± 0.57	53.74±0.6	55±1.4
	Platelet (10^3) [n=310]	191.96±4.63	196.76± 4.9	171.62±12
	Sodium (mEq/L) [n=123]	136.5±6.4	136.7±6.3	135.2±7
	Potassium(mEq/L) [116]	5.8±1.4	5.8±1.3	5.96±1.7
	Calcium(mEq/L) [n=60]	8.6±2.1	8.8±1.8	7.9±3.1
	RBS (g/dl) [n=241]	61.6±67.8	61.4±64.9	62.2±75.5
	AST (U/L) [n=57]	225.71±41.4	214.2±42.4	321.2±165.5
	ALT (U/L) [n=57]	73.82±13.4	70.6±12.8	100.5±70.9
	Cr (mg/dl) [n=186]	1.15±0.06	1.12±0.07	1.44±0.12

*- meconium aspiration syndrome, **-others (anemia, polycythemia, DIC and malnutrition)

At admission 46(11.2%) had gasping type breathing or respiratory rate less than 30 breathe per minute, 20(4.9%) had bradycardia, 356(86.62%) were hypothermic and 103(32.80%) had low oxygen saturation (SpO2 less than 85%). Out of the total 305 survived neonates 184(65.25%) had normal respiratory rate, 252(89.36%) had normal heart rate, 90(31.91%) were normo-thermic and 90(46.15%) had normal oxygen saturation level with in their 24 hours of postnatal age (Figure 3).

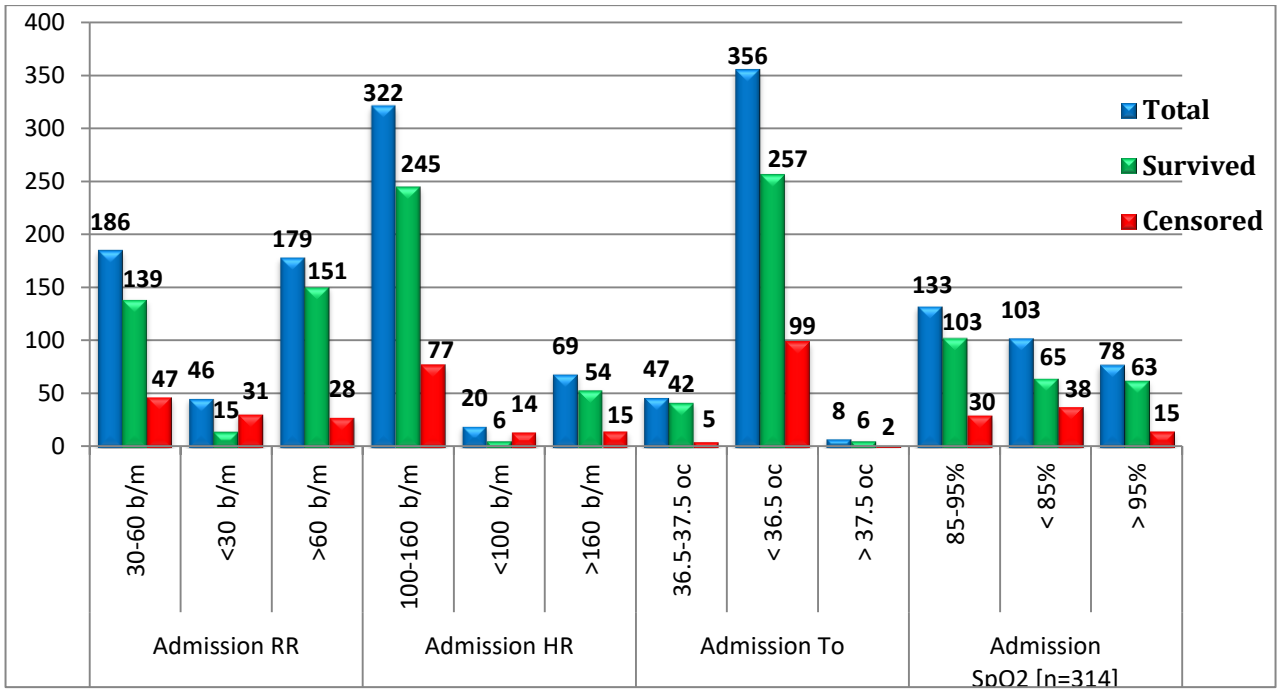

Figure 3: Admission Vital-signs of asphyxiated neonates admitted at four selected hospitals from January 1, 2016 to December 31, 2020 [n=411].

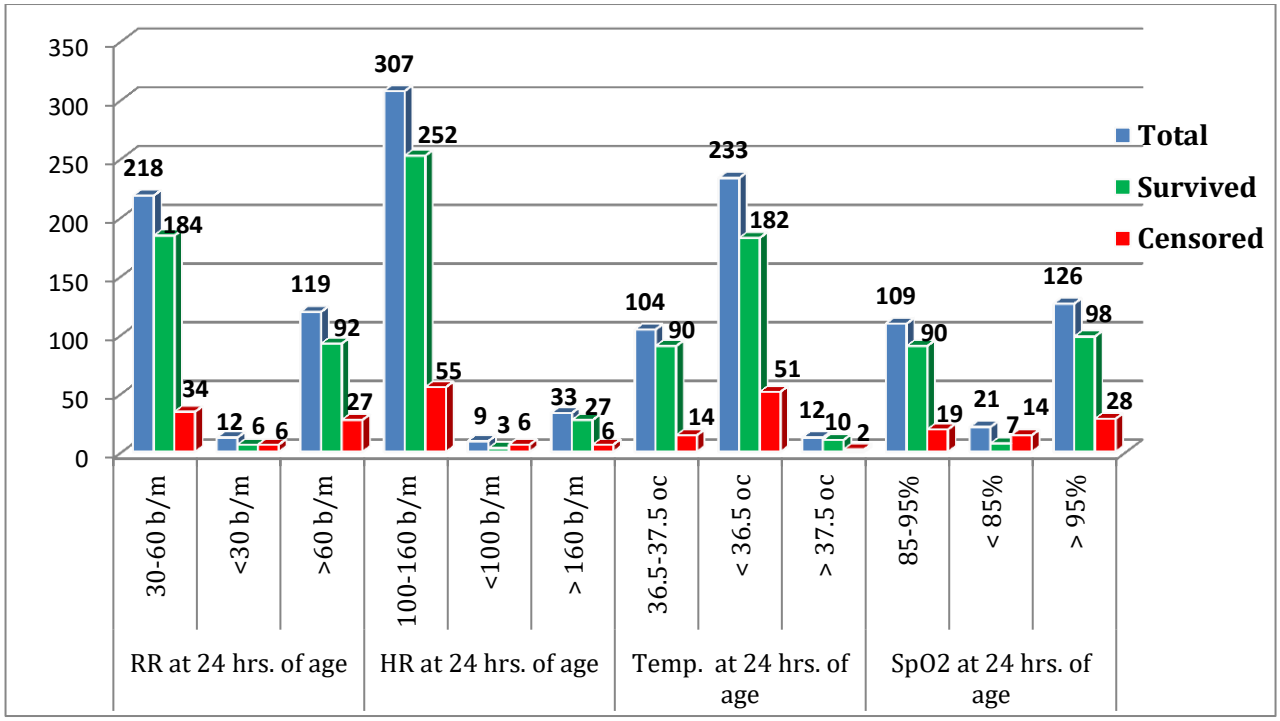

Figure 4: Vital-signs at the age of 24 hours of postnatal age among asphyxiated neonates admitted at four selected hospitals from January 1, 2016 to December 31, 2020 [n=349].

The mean white blood cell count and hematocrit level were high in censored babies than survived (21.74+1.7 Vs 19.37+0.58) and (55+1.4 vs 53.74+0.6), respectively. On the contrary mean platelet count was lower in censored babies (171.62±12 vs 196.76± 4.9) than survived babies. The mean serum sodium and calcium level in censored babies were lower than survived but higher in Potassium, random sugar, AST, ALT and creatinine level with in first day of postnatal age (Table 3).

5.4 Treatment characteristics of the study participants

Majority of the newborns (88.32%) were resuscitated at birth and 59.12% put on Oxygen after resuscitation and at NICUs care. About 112(27.25%) neonates were took anticonvulsant and 36(8.76%) were took aminophylline during their hospital stay. Two third of the total fluid were prepared and administered for 65.7% of babies treated with intravenous fluid (Figure 5).

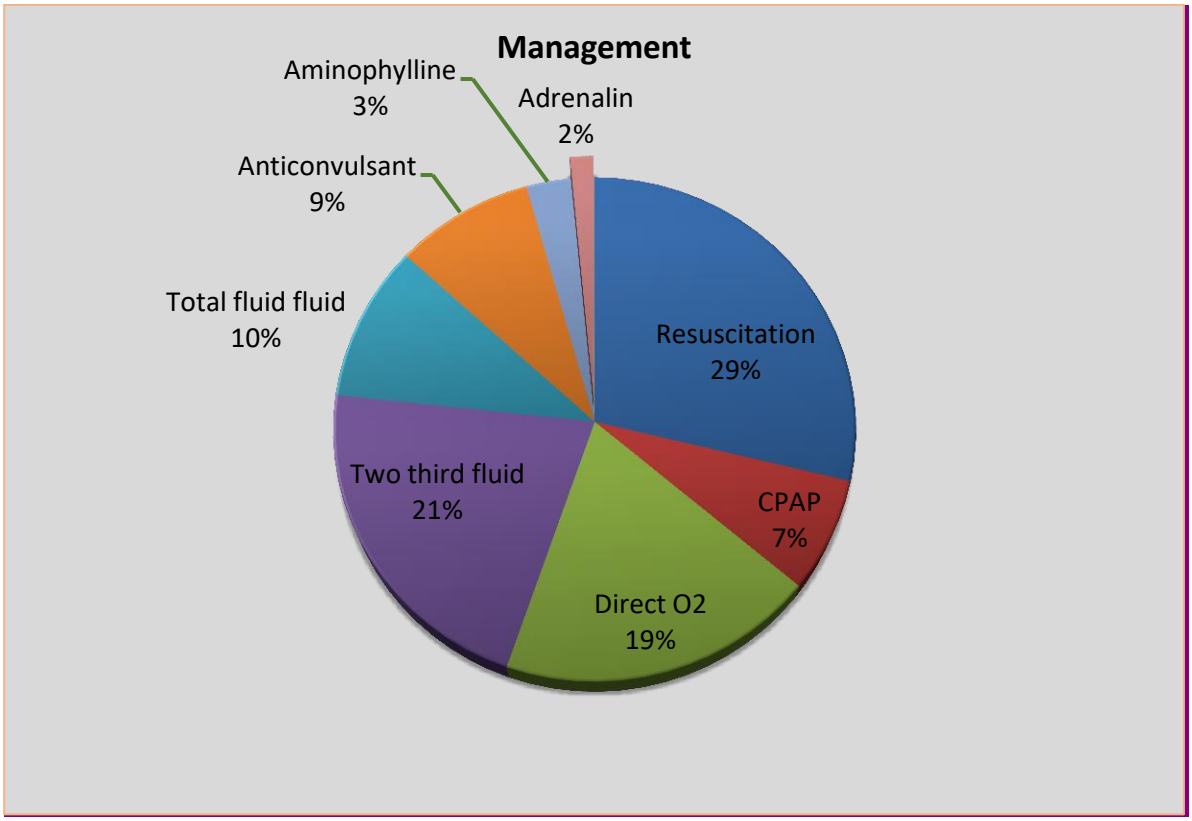

Figure 5: Treatment characteristics of Asphyxiated baby who were admitted at NICUs of Addis Ababa public hospitals, Ethiopia 2021.

5.5 Survival status of asphyxiated neonates

Four hundred eleven admitted asphyxiated babies were followed a total of 3058 neonate-days with a minimum of 1 hour to a maximum of 28 days, with a median survival time of 8 days (95% CI: 7.527- 8.473). Overall, during the entire cohort 305(74.2%) of asphyxiated neonates were survived and 106(25.8%) were censored. Among those 99(24.09%) died, 6(1.5%) left against and 1(0.24%) lost follow-up. And also, most (65%) of the censored babies were recorded with in seventy-two hours of postnatal age. The overall survival rate (incidence density) of this study was found to be 10 per 100 neonatal-days of observation (95% CI: 0.09 – 0.11) and estimated cumulative survival was 0.99, 0.96, 0.63, 0.20, 0.06 and 0.04 at 1,3,7,14,21 and 28 days, respectively.

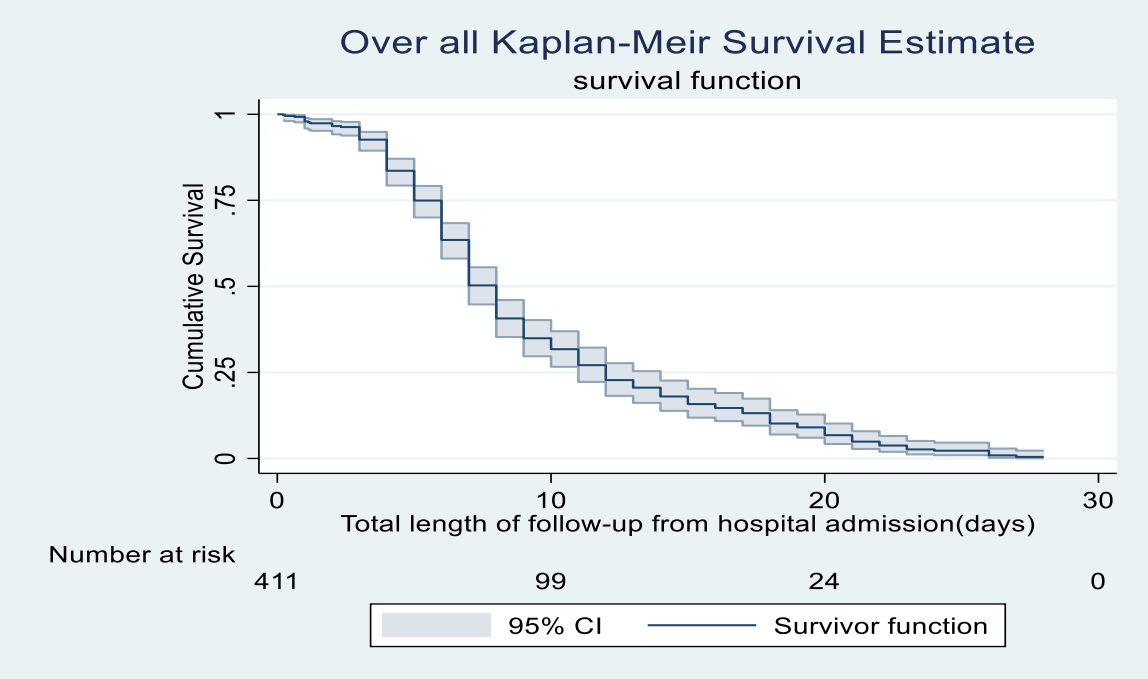

Figure 6: Overall Kaplan-Meier survival estimate of Asphyxiated neonates admitted in Addis Ababa public hospitals from 2016-2020, Addis Ababa, Ethiopia, 2021.

5.6 Time to recovery among different groups of asphyxiated neonates

Log-rank test (Mantel-Cox) was conducted to assess the existence of any significant difference in survival time among different categories of explanatory variables. According to this study, the median recovery time for newborns diagnosed with stage 1 HIE were (6 days with 95% CI: 5.45 – 6.54) much faster than stage 2 and 3 HIE, (8 days 95% CI: 6.92 – 9.07) and (14

days 95% CI: 10.71 – 17.29), respectively. The median recovery time for low birth weight had longer than those of big and normal birth weight newborns (9 days Vs 6 and 7 days).

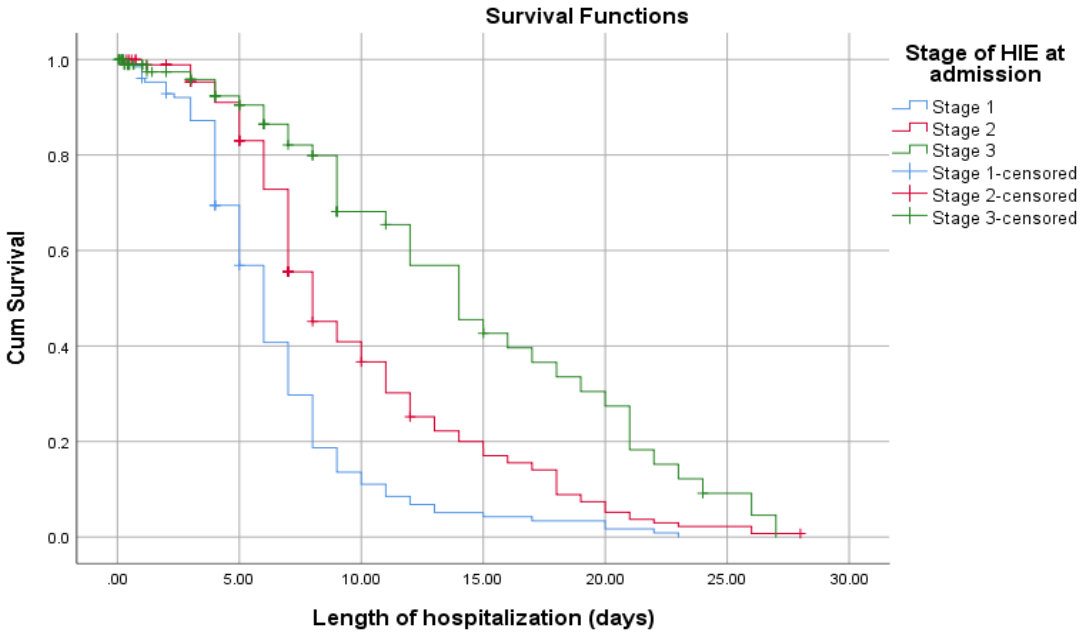

Figure 7:- The KM survival curves compare recovery time with different HIE stages among Asphyxiated baby who were admitted at NICUs of Addis Ababa public hospitals, Ethiopia, from 2016-2020.

Figure 8 shows those babies who got calcium gluconate within 24 hours together with intravenous fluid slightly faster median recover time than counterparts (7 days 95% CI: 6.21 – 7.78) and (8 days 95% CI: 7.44 – 8.55), respectively. Furthermore, the median recovery time was nearly double in Thrombocytopenic newborns than those who had normal platelet count during their hospital stays (13 days Vs 7 days). This difference was statistically significant with p-value < 0.0001. Furthermore, A baby who experienced neonatal seizure within 24 hours had prolonged median recovery time (11 days 95% CI: 9.48 – 12.52) compared to than those who had not seizure or had after 24 hours of post-natal age (7 days 95% CI: 6.5 – 7.49) and (9 days 95% CI: 7.15 – 10.85), respectively. The difference was significant statistically.

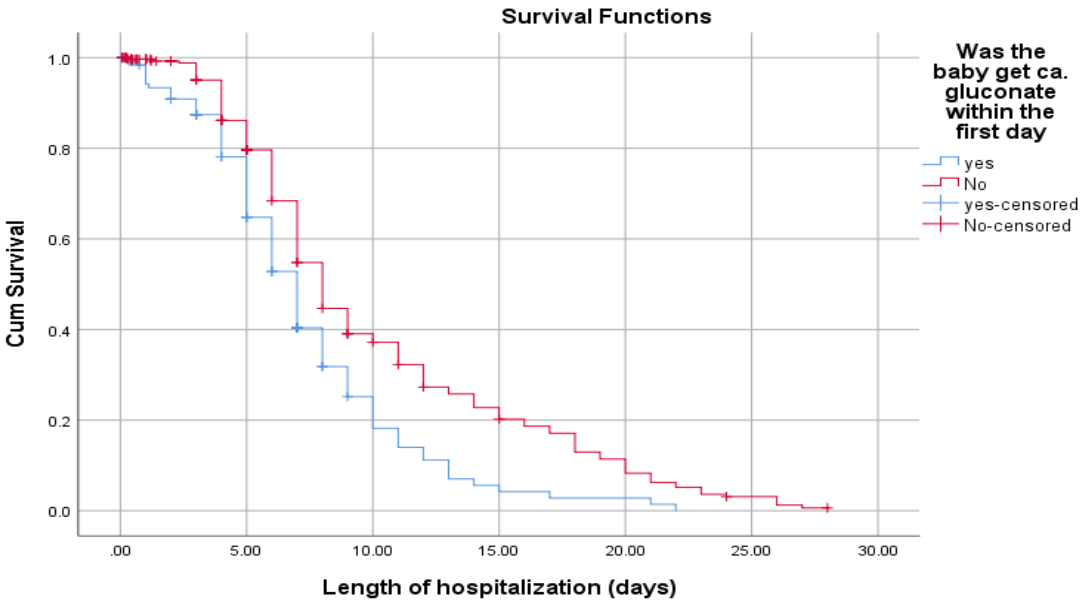

Figure 8:- The KM survival curves compare recovery time with different groups of Asphyxiated baby who were took ca^{++} gluconate and did not admitted at NICUs of Addis Ababa public hospitals, Ethiopia, from 2016-2020.

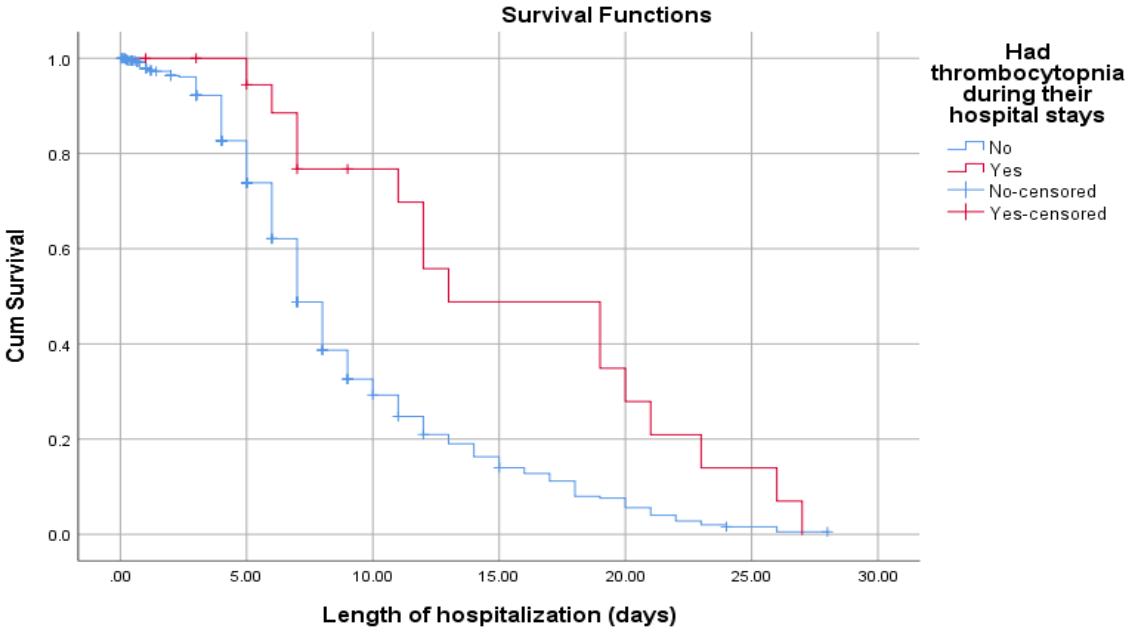

Figure 9:- The KM survival curves compare recovery time with different platelet count among Asphyxiated baby who were admitted at NICUs of Addis Ababa public hospitals, Ethiopia, from 2016-2020.

Based on this log-rank statistical test procedure place of delivery, mode of delivery, 5th minutes APGAR score, sepsis, hyperbilirubinemia, acute kidney injury and resuscitation were not statistically significant (P-Value <0.05). This means that, the KM curves are not statistically different with respect to categories of significant covariates or we have no enough evidence to say that there has difference on survival curve.

Table 4:- Median survival time and log-rank test survivors of Asphyxiated baby who were admitted at NICUs of Addis Ababa public hospitals, Ethiopia 2021.

Variable	Category	Median survival time in days (95% CI)	Log rank test	P- value
Birth weight	Normal	7(6.48 – 7.52)	10.31	0.0058
	Big baby	6(3.37 – 8.62)		
	Low birth weight	9(7.41 – 10.58)		
Gestational Age	Term	7(6.49 – 7.51)	10.05	0.0066
	Post term	8(5.94 – 10.06)		
	Preterm	9(7.02 – 10.97)		
Age at presentation	<24 hours	7(6.53 – 7.46)	8.66	0.0131
	24 – 72 hours	20(0.00 – 41.38)		
	>72 hours	21(16.87 – 25.13)		
HIE stage	Stage 1	6(5.45 – 6.54 0	67.29	0.0000
	Stage 2	8(6.92 – 9.07)		
	Stage 3	14(10.71 – 17.29)		
Altered Consciousness	No	7(6.45 – 7.53)	24.1	0.0000
	Yes	9(8.11 – 9.89)		
Depressed Moro reflex	No	6(5.41 – 6.59)	42.92	0.0000
	Yes	9(7.68 – 10.32)		
Seizure	No	7(6.5 – 7.49)	14.42	0.0007
	Yes, before 24 hours	11(9.48 – 12.52)		
	Yes, after 24 hours	9(7.15 – 10.85)		
NEC	No	7(6.51 – 7.49)	6.18	0.0129
	Yes	12(6.58 – 17.42)		
thrombocytopenia	No	7(6.52 -7.48)	11.18	0.0008
	Yes	13(4.55 – 21.45)		
Aminophylline	No	7(6.51 – 7.48)	6.69	0.0097
	Yes	16(8.33 – 23.67)		
oxygenation	No	6(5.21 – 6.79)	26.12	0.0000
	Yes	8(7.48 – 8.52)		
Ca^{++} gluconate	Yes	7 (6.21 -7.78)	18.16	0.0000
	No	8(7.44 – 8.55)		
Over all		**8 (7.527- 8.473)**		

5.7 Predictors of Survival status of asphyxiated neonates

Cox proportional hazard regression model was used to analyze the association between the recovery time from perinatal asphyxia and covariates. The independent variables were analyzed separately with the outcome variable and those variables fitted at P-value less than 0.2 and non-collinear independent variables were included in the multivariate Cox regression model. Forty-one independent variables analyzed in bivariate cox regression analysis. Among that, parity, ANC follow up, time of delivery, place of delivery, duration of rupture of membrane, cord problems, hypertension, antepartum hemorrhage, oligohydramnios, fetal distress, multiple pregnancy, abortion history, sex of baby, cried immediately at birth, 1st minutes APGAR score, respiratory distress, hypothermia, hypoglycemia, types of fluid management, electrolyte derangement and use of anticonvulsant were not association with survival of asphyxiated babies ($P \geq 0.2$). The remaining 22 variables (those which had P-value < 0.2) transferred in to multivariate cox regression analysis for further analysis. In multivariate cox regression analysis, only five independent variables had significant association with survival of asphyxiated neonates (Table 5).

The result of multivariate cox regression analysis shown that being low birth weight was found 33% less likely to recover faster from asphyxia compared to those with normal birth weight (AHR: 0.67, 95% CI: 0.47- 0.96). The time of recovery were slower or prolonged when the stage of HIE stages increase. Neonates diagnosed with HIE stage II had 30% and HIE stage III had 56% decrement in survival compared to Stage I HIE diagnosed babies (AHR: 0.70, 95% CI: 0.51 - 0.97) and (AHR: 0.44, 95% CI: 0.27 - 0.71), respectively. Regarding comorbidities, neonates who developed thrombocytopenia were 56% less likely to recover earlier than those of who had normal platelet count (AHR: 0.44, 95% CI: 0.24 - 0.80) and neonatal seizure appear within 24 hours of postnatal age were 39% and after 24 hours of postnatal age were 31% lower probability to recover faster compared to neonates who had not experienced seizure (AHR: 0.61, 95% CI: 0.38 - 0.97) and (AHR: 0.69, 95% CI: 0.49 - 0.97), respectively. Neonates who received calcium gluconate through intravenous fluid with in 1st days of life were hastened the recovery time by 25% (AHR: 0.75, 95% CI: 0.58 - 0.99) (Table 5).

Table 5: Bivariate and Multivariate Cox regression analysis results of Asphyxiated baby who were admitted at NICUs of Addis Ababa public hospitals, Ethiopia, 2021 [n=411].

Covariates	CHR (95% CI)	P-value	AHR (95% CI)	P- value
Maternal Age				
20 – 34 years	1		1	
<20 years	0.94(0.58 – 1.52)	0.812	1.22(0.73 - 2.04)	0.455
>34 years	1.34(0.92 – 1.94)	0.120	1.28(0.85 - 1.95)	0.241
Place of residency				
Addis Ababa	1		1	
Out of Addis Ababa	0.78(0.58 – 1.05)	0.105	0.89(0.64- 1.23)	0.479
Mode of delivery				
SVD	1		1	
Assisted delivery	0.92(0.66 – 1.27)	0.621	0.89(0.62 - 1.26)	0.506
C/S delivery	0.81(0.62 – 1.04)	0.107	0.89(0.66 - 1.19)	0.418
Prolonged labor				
No	1		1	
Yes	1.26(0.92 – 0.74)	0.142	1.21(0.85 -1.71)	0.292
Birth weight				
Normal	1		1	
Big baby	1.16(0.71 – 1.91)	0.554	1.24(0.70 - 2.19)	0.454
Low birth weight	0.63(0.48 - 0.83)	0.001	**0.67(0.47 - 0.96)**	**0.029 ***
Gestational Age				
Term	1		1	
Post term	0.60(0.42 – 0.85)	0.004	0.96(0.61 - 1.50)	0.841
Preterm	0.87(0.59 -1.29)	0.494	0.93(0.59 - 1.46)	0.753
Age at presentation				
<24 hours	1		1	
24 – 72 hours	0.82(0.49 – 1.38)	0.470	0.45(0.16 - 1.23)	0.121
>72 hours	0.45(0.22 - 0.92)	0.031	0.64(0.28 - 1.43)	0.275
Fifth minutes APGAR				
≥7	1		1	
<7	0.81(0.64 - 1.03)	0.091	1.03(0.78 - 1.35)	0.838
HIE stage				
Stage 1	1		1	
Stage 2	0.51(0.40 -0.66)	0.000	**0.70(0.51 - 0.97)**	**0.033 ***
Stage 3	0.27(0.19 - 0.40)	0.000	**0.44(0.27 - 0.71)**	**0.001 ***
Altered Consciousness				
No	1		1	
Yes	0.59(0.47 - 0.74)	0.000	0.97(0.72 - 1.30)	0.837

Depressed Moro reflex				
No	1		1	
Yes	0.49(0.39 - 0.62)	0.000	0.79(0.57 - 1.10)	0.164
Sepsis				
No	1		1	
Yes	0.85(0.67 - 1.07)	0.164	0.83(0.64 - 1.07)	0.143
Seizure				
No	1		1	
Yes, before 24hours	0.55(0.36 - 0.85)	0.006	**0.61(0.38 - 0.97)**	**0.036 ***
Yes, after 24 hours	0.67(0.49 - 0.92)	0.013	**0.69(0.49 - 0.97)**	**0.034 ***
Meconium aspiration syndrome				
No	1		1	
Yes	0.83(0.65 - 1.05)	0.121	0.89(0.68 - 1.16)	0.386
Hyperbilirubinemia				
No	1		1	
Yes	0.76(0.51 - 1.14)	0.191	1.28(0.81 - 2.01)	0.285
Necrotizing enterocolitis				
No	1		1	
Yes	0.46(0.24 - 0.91)	0.025	0.64(0.30 - 1.36)	0.245
Acute kidney injury				
No	1		1	
Yes	0.69(0.40 - 1.18)	0.171	0.90 (0.49 - 1.64)	0.726
Thrombocytopenia				
No	1		1	
Yes	0.45(0.26 -0.75)	0.003	**0.44(0.24 - 0.80)**	**0.007 ****
Aminophylline				
No	1		1	
Yes	0.48(0.26 -0.89)	0.019	0.80(0.40 - 1.58)	0.515
Oxygenation				
No	1		1	
Yes	0.57(0.40 - 0.82)	0.002	0.69(0.45 - 1.07)	0.095
Resuscitation at delivery				
No	1		1	
Yes	0.80(0.60 - 1.07	0.134	1.00(0.71 - 1.41)	0.994
Ca^{++} gluconate				
Yes	1		1	
No	0.61(0.48 - 0.79)	0.000	**0.75(0.58 - 0.99)**	**0.039 ***

NB: - *Significant (P-value < 0.05), **significant (p-value<0.01) and HR=1 is reference variable.

5.8 Test of proportional hazard assumption by Schoenfeld's residuals

Testing the proportional hazard assumption is vital for interpretation and use of fitted proportional hazard models. Therefore, in this study goodness-of-fit (GOF) particularly the Schoenfeld's residuals proportional hazard assumption test for the individual covariates and global tests was used. The findings indicated that all individual variable included in the model were satisfy PH assumptions (p-value>0.05) and (Global for Cox proportional hazard P-Value=0.393 > 0.05) (Table 6).

Table 6: Results of Test of proportional hazard assumption in Asphyxiated baby who were admitted at NICUs of Addis Ababa public hospitals, Ethiopia 2021.

Variables	rho	chi2	df	P-value
Maternal age	0.02694	0.24	1	0.6249
Place of residency	-0.08385	2.2	1	0.1381
Mode of delivery	-0.08408	2.35	1	0.1252
Duration of labor	0.00861	0.02	1	0.8752
Birth Weight	-0.06928	1.76	1	0.1849
Gestational Age	-0.01242	0.05	1	0.8190
Age at presentation	0.05026	0.86	1	0.3525
Fifth APGAR	0.03719	0.47	1	0.4908
HIE stages	0.08139	1.96	1	0.1619
Altered Consciousness	-0.00631	0.01	1	0.9098
Moro	-0.01935	0.12	1	0.7277
Sepsis	-0.0138	0.06	1	0.8084
Meconium aspiration syndrome	-0.03578	0.45	1	0.5031
Seizure	0.0655	1.38	1	0.2399
Hyperbilirubinemia	0.06493	1.35	1	0.2454
Necrotizing enterocolitis	-0.01955	0.13	1	0.7183
Acute kidney injury	0.04277	0.6	1	0.4401
Thrombocytopenia	0.06727	1.49	1	0.2227
Aminophylline	0.04956	0.8	1	0.3718
Use of oxygen	-0.02069	0.15	1	0.6953
Resuscitation at delivery	-0.01437	0.07	1	0.7844
Ca^{++} gluconate	0.02164	0.15	1	0.6969
global test		**23.15**	**22**	**0.3934**

6. DISCUSSION

Estimation of the median recovery time and identification of predictors of survival for asphyxiated newborns is crucial for the management and caring of asphyxiated neonates in resource limited environment. The primary objective of this study was to estimate the incidence density rate of recovery and assess predictors of survival among asphyxiated newborns admitted in NICUs. From the total of 411 asphyxiated babies enrolled in this study 305(74.2%) of neonates were survived and discharged from the NICUs. This finding is comparable with a cohort study conducted in Dire-Dawa public hospitals which was 74.3% (12). On the other hand the finding of this study is lower than a study was conducted in Cameron (14) and Ghana (13) where 81.1% and 78.2 % of neonates recovered, respectively. The discrepancy between the results may be explained by scope of the study settings and study period. Both of studies were conducted in a single health facility and a single year. In addition, the study conducted in Cameron was case-control and it used only APGAR score for diagnosing or identifying the cases. Current findings of this study is higher than a study conducted in Nigeria (61.3%) (20). This may be due to difference in study participant's characteristics and study design. Moreover, recovery rate in the present study is higher from the study conducted in Pakistan which was 59.2% (26). Difference in study design, sampling method and study participant's difference might a possible explanation for the discrepancy.

The overall median recovery time of NICUs admitted asphyxiated newborns in the cohort was found to be 8 days (95% CI: 7.527- 8.473). This finding was consistence with a study done in Dire-Dawa (7 days) and India (8 days), (12,16). On the opposite it is lengthen than a study conducted in Nigeria (3.8 days) (11) and in Bangladesh (4.84 days) (15). This gab might be associated with difference in health care facilities setting and majority of their study participants were inborn babies and present in NICUs earlier than 12 hours of life. Along with this, the overall incidence density rate of survival of asphyxiated babies in this study was found 10 (95% CI: 0.09 – 0.11) per 100 neonates – day's observation.

Several studies have been confirmed low birth weight and preterm birth contributed to poor prognosis of asphyxiated newborns (49–51). This study also revealed that low birth weight and preterm neonates have less chance of surviving compared to their counter parts and also the result is statistically significant.

The scientific and clinical explanation behind this is low birth weight babies and /or preterm babies mostly have feeding difficulties, immature thermoregulatory and respiratory center, poor immune systems and not delivering adequate (standardize) NICUs care may lead poor prognosis and prolonged hospital stay. This result is lower than a study conducted in Nigeria which was 2.2 times more likely to die (20). This might be due to difference in sample size, study design and place of delivery. On the other hand, preterm babies have prolonged recovery time and lower chance of surviving than term and post term babies in our study but it has no statistically significant. This might be explained due to difference in sample size, variable categorization and study area and also they have frequency percentage difference in prematurity (15.34% Vs 34.7%).

Along with BW and GA, recovery time and survival status of asphyxiated newborns was differing in age of the neonates at the time of presentation. According to this study, neonates present in the NICU within 24 hours nearly three times faster recovered compared from those who present after 24 hours of their post-natal age and the result has significance association in bivariate analysis but not in multivariate cox proportional hazard model analysis. This finding supported by a study conducted in Nigeria (35,52), Nepal (24). Unlike to this findings a study done in Pakistan showed that delayed presentation in NICUs were significantly associated with asphyxia morbidity and mortality (26). This discrepancy might be due to difference in frequency of babies present within 24hours and study population was only term babies.

Amongst the clinical and laboratory predictors, Stage of HIE, occurrence of seizure and thrombocytopenia were factors that had influence in survivals and recovery time of asphyxiated babies. According to the findings of this study recovery time and survival status of asphyxiated newborns was differ in each stages of HIE. The incidence density rate of survival from stage I, stage II and stage III HIE were 14, 9 and 5.5 per 100 neonates- days' observation, respectively. The chance of survival and recovered faster from asphyxia is higher in those neonates diagnosed stage I HIE compared to stage II and stage III HIE. This result was supported by other findings (15,33,35,42,43). This might be different reasons. Primarily, In fact, central nervous system is one of the systems affected highly next to renal system followed asphyxia. When the stage of HIE increases the primary and secondary energy failure commonly appeared this leads to development of different neurologic sequel and decrease the prognosis of the asphyxiated babies (53).

Secondly, the management mostly is not effective in most cases once exposed for prolonged hypoxia and multiple organ damage occurs. Lastly, neonates having advanced stage of HIE mostly kept NPO (nothing per mouth) due to fear of necrotizing enterocolitis this exacerbate malnutrition and thrombocytopenia. This may overcomplicate the existing problem with requiring additional time and resource to manage the complications related to this.

Other clinical related predictors that have significant association with survival and recovery time from perinatal asphyxia are seizure occurrence. Occurrence of seizure in asphyxiated neonates usually associated poor outcomes or indicates that the severity of encephalopathy is moderate or severe. This supported with different literatures (17,27,54). In this study**,** approximately 8.1 % of asphyxiated newborns had seizure features with in the first days of life and nearly 15.1% developed after 24 hours of admission with decrement of survival by 39% and 31%, respectively. However, a study conducted in Tanzania revealed that 28 percent of the newborn babies developed seizure within 24 hours of age and 12.6 % were beyond 24 hours with the odd's ratio of 3.48 and 0.26 times more likely to die compered to babies without seizure (17). Despite the difference in study design, the difference may be explained difference in prevention mechanisms, like immediate and effective resuscitation in labor ward, earlier management of metabolic derangement and appropriate usage of anticonvulsant.

Even though, there is no statistical association in multivariate analysis there is a mean discrepancy in common liver enzyme (AST & ALT), electrolyte (Na^+, K^+ and Ca^{++}), random blood sugar (RBS), and hematocrit (HCT) between survivors and non-survivors. The mean of non-survivor asphyxiated babies were higher in all laboratory parameters mentioned above except sodium and calcium. This finding is consistent with a study done India and Nigeria (32,46,55). This might be due to birth asphyxia can induce an enzyme pattern in serum compatible to hypoxic hepatitis and causes disruption of ATP-dependent sodium-potassium pump and cause excessive depolarization.

Occurrence of thrombocytopenia was the contributing factors for low survival of asphyxiated newborns in this study. But, it is not clear whether it can contribute directly to the outcome or a clinical sign of severity of precipitating complications, like perinatal asphyxia which have a poor prognosis by itself.

According to the result of this study, thrombocytopenic-asphyxiated babies had poor chance of survival than non-thrombocytopenic neonates. This may be due to by increase the bleeding tendencies form major organ, like pulmonary, brain, and intestine. This is due to asphyxia impaired megakaryocytopoiesis and platelet production, increased platelet consumption and sequestration. This finding is supported by the clinical practice that most asphyxiated babies have moderate to severe thrombocytopenia and this cannot be easily manageable with one or two platelet transfusion. And also, there is a scarcity of packs of platelets at any time when needed.

Lastly, the current study found that administration of Ca^{++} gluconate in 1^{st} days of life together with in intravenous fluid therapy has potentially beneficial effects for the baby and enhance chance of survival than those who do not took prophylactic calcium gluconate. Hypocalcemia in newborns with asphyxia is mostly common in one of the following scientific reasons, low calcium intake, hyperphosphatemia, excess bicarbonate and functional hypoparathyroidism (1). A randomized control trial conducted to check efficacy of prophylactic intravenous calcium administration in first 5 days of life conclude symptoms of hypocalcemia and requirement of hypocalcemia management was decreased in those newborns who took intravenous calcium infusion (47).

7. STRENGTH AND LIMITATIONS OF THE STUDY

Strength

Data were collected over the period of five years (from 2016 – 2020) by well-trained data collectors. This can give a chance to see current situation and give the opportunity to take any corrective measures to enhance the survival of asphyxiated newborns. In addition, it incorporates more than forty independent covariant which may have influence on recovery time or survival of asphyxiated babies. This gives an intuition for the researchers especially those who need go through prospective cohort.

Limitations

Despite the above potential strength, this study has some limitations. It was conducted retrospectively and relied on a medical record of the neonates in each health facility. Hence, recorded data on some demographic characteristics (maternal and paternal educational and occupational status), behavioral characteristic (drug, alcohol usage) and health facilities readiness (availability of well-trained health professional and necessary equipment to manage breathing difficulties) could not be available in the charts of asphyxiated babies and these variables were not integrated in the study. This may leads to missing of important predictors. Furthermore, Time of discharge was considered as a recovery time unless they recorded cured or treated in the chart and stages of perinatal asphyxia was considered as HIE stages unless they recorded clearly this leads to over or underestimated of findings. Lastly, excluding of the incomplete medical records may also contribute to selection bias.

8. CONCLUSION AND RECOMMENDATIONS

8.1 Conclusion

In the current findings, nearly three-fourths of asphyxiated babies had satisfactory outcome during the entire cohort. Besides, the overall incidence rate of survival was 10 per 100 neonates-day observations. Low birth weight, stages of HIE, occurrence seizure, thrombocytopenia and taking of calcium gluconate in the first day of life were identified as a predictors for the survival time of asphyxiated newborns.

8.2 Recommendations

As showed in the result of this study, mortality of newborns was high and had prolonged hospital stay as compared to other studies. it needs more emphasis and corrective measures if needs achieving the Ethiopian Health Sector Transformation plan of reducing neonatal mortality to 10 per 1000 livebirths at the end of 2020. So the following recommendations are forwarded to the respective organs based on the findings of this study.

1. **To federal minister of health and other stake holders**

Comprehensive effort should be undertaken to improve quality health service provided in health facilities, enhance the competency of health workers and ensure availability of necessary equipment and setup to manage neonatal complications. Along with this, better to revise the current national guideline to include fluid, nutritional, oxygenation and electrolyte derangement management of asphyxiated babies. Furthermore, should be give emphasis on quality care at ANC follow up time to promote maternal health conditions and anticipate obstetric related complications.

2. **Health facilities**

Health facilities should focuses on procurement or fulfil intrapartum monitoring equipment (continuous fetal monitoring) and better to establish advance life support team in the labor ward or strengthen linkage of NICU teams with labor ward team (attending in every high risk delivery). In addition, Clinical death audits are very crucial to identify and take measures for preventable cause of death like perinatal asphyxia.

3. To health care providers working

Even though, there needs further study, health workers should be cautious and encouraged to take appropriate measures when a baby has electrolyte derangement, seizure occurrence within 24 hours and thrombocytopenia. And also, better to ensure early investigation for all asphyxiated babies and improve documentation process, proper use of PNA follow up chart.

Lastly, by taking current findings as an input, researchers are encouraged to conduct further prospective studies to have strong evidences on survival and predictors of perinatal asphyxia. Health facility readiness to manage breathing difficulties, qualities of nursing care, and Socio economic factors also suggested to be addressed on.

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10. APPENDIX

Annex 1: Data extraction form (Checklist)

This tool is prepared for the collection of socio-demographic, obstetric, neonatal, clinical, laboratory, treatment and outcome related information that are important for the assessment of survival status and predictors of survival among asphyxiated neonates admitted in neonatal intensive care units of public hospitals, Addis Ababa, Ethiopia, 2020. All this information was retrieved from individual patient record without including the names of the clients. This information was collected by health care providers (BSc Nurses) who are working at the hospital NICU clinic.

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Data collection date ____ /___/2013 E.c

Name of the Hospital ----------

Name of data collector ---------- signature----------

Name of supervisor ----------signature----------

Code no ----------

Is baby asphyxiated **Yes** ☐ **No** ☐ **(If no stop filling the questioner)**

If yes, stage of PNA at initial diagnosis = _____

Date of admission _____/____/_____ **E.c**

Admission diagnosis = _____

Part I: Socio demographic characteristic

No	**Socio demographic information**	**Possible answers**	**Remark**
101	Age of the mother	_____ years	
102	Place of residency	1. Rural 2. Urban (regional, zonal / district town)	
	PART-II Obstetric characteristics		
201	Parity	_____	
202	Gravida	_____	
203	Previous history of abortion	1. Yes 2. No	
204	ANC visit	_____	
205	Place of delivery	1. Inborn 2. Out born	
206	Modes of delivery	1. Spontaneous Vertex delivery 2. Assisted vacuum delivery 3. Assisted forceps delivery 4. Caesarian section	
207	Time of delivery	1. Day time 2. Night time	
208	Duration of labor	_____ hours _____ minutes	
209	Duration of ROM	1. ≤ 18 hours 2. > 18 hours	
210	Amniotic fluid	1. Clear 2. Meconium stained _____ (grade)	
211	Type of pregnancy	1. Singleton 2. Twin 3. Other (specify) _____	

212	Pregnancy related conditions	Anemia	1. Yes 2. No	
		Ante-partum hemorrhage	1. Yes 2. No	
		Gestational DM	1. Yes 2. No	
		Preeclampsia/ Eclampsia	1. Yes 2. No	
		Oligohydramnios	1. Yes 2. No	
		Fetal distress	1. Yes 2. No	
		Cord problems	1. Yes 2. No	
		If others, specify	_____	
	Part III: Neonatal characteristics			
301	Sex of baby	1. Male 2. Female		
302	Gestational age	_____ weeks _____ days		
303	Birth weight	_____ grams		
304	Did the baby cry	1. Yes 2. No		
306	Age at presentation	_____ hours		
	Part IV: Clinical and Laboratory characteristics			
401	APGAR score	1. 1^{st} min = _____ 2. 5^{th} min = _____ 3. 10^{th} min= _____ 4. 20^{th} min =_____		
402	Depressed clinical status at admission	Level of consciousness	1. Normal 2. Lethargic 3. Hyperalert	
		Tone	1. Normal 2. Hypotonic 3. Hypertonic	
		Reflexes	1. Normal 2. Depressed 3. Exaggerated	
403	Vital sign, SpO_2 and RBS at admission, 6hr, 12hrs. and 24 hrs. after admission	1. Respiratory Rate	___, ___, ___, ___ b/min	
		2. Pulse rate	___, ___, ___, ___ b/min	

		3. Temperature rate	___, ___, ___, ___ ^{O}C	
		4. Oxygen saturation	___, ___, ___, ___ %	
		5. Random blood sugar	___, ___, ___, ___ mg/dl	
404	Serum electrolyte within 24 hours	Sodium	_____ mmol/L	If get 2 result take the repeat one
		Potassium	_____ mmol/L	
		Chloride	_____ mmol/L	
		Calcium (Ionized)	_____ mmol/L	
405	Complete blood count within 24 hours	White blood cell count	_____ k	
		Hematocrit	_____ %	
		Platelet	_____ k	
406	Liver function test	Aspartate Aminotransferase (AST)	_____ u/L	
		Alanine aminotransferase (ALT)	_____ u/L	
		Total bilirubin	_____ mg/dl	
407	Medical complications developed during their hospital stay	1. Hypoglycemia 2. Hyperbilirubinemia 3. Necrotizing enterocolitis 4. Acute kidney injury 5. Thrombocytopenia 6. Seizure 7. Sepsis (Hospital Acquired Infections) 8. Others _____		

Part V: Treatment related factors				
501	How managed the baby	Resuscitation	1. Bag mask ventilation 2. Chest compression 3. Intubation 4. Adrenalin	
		Antibiotics	1. Yes 2. No	
		Aminophylline	1. Yes 2. No	
		Oxygen	1. Direct O_2 2. CPAP	
		Fluid management	1. Two third 2. Total fluid	
		Calcium gluconate with in first day of life	1. Yes 2. No	
Part VI: Outcomes of the neonates and length of hospitalization				
601	Final outcome	Recovered ☐ Censored ☐		
602	Date of discharge	____/_____/_____ E.c		
603	Length of hospitalization	_____ hours / days		