ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCE

DEPARTMENT OF ANESTHESIA

Survival Status and Predictors of Mortality among Neonatal Surgical Patients in Selected Addis Ababa Public Hospitals, Ethiopia 2023/24: Multicenter Retrospective Cohort Study.

By

Wasihun Aragie (BSc in Anesthesia)

A RESEARCH THESIS SUMMITED TO ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCE DEPARTMENT OF ANESTHESIA FOR PARTIAL FULFILLMENT OF DEGREE OF MASTER SCIENCE IN ADVANCED CLINICAL ANESTHESIA

JUNE, 2024

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Full Title of Research	Survival Status and Predictors of Mortality among Neonatal Surgical Patients in Selected Addis Ababa Public Hospitals, Ethiopia 2023/24: Multicenter Retrospective Cohort Study
Duration of Research	From January 1/2021-December 31/2023
Study Area	Tikur Anbessa Hospital, Zewuditu Memorial Hospital and St. Paul Hospital Millennium Medical College
Total Cost of Research	**24,000 Birr**
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Declaration

I consequently swear that the thesis I am submitting is entirely original work of mine, and that I conducted my study adhering to the strictest ethical guidelines. Every source I utilized to create this work has been correctly attributed and referenced. It is my whole obligation to make sure the work is accurate and honest.

This thesis is being turned in to partially complete the requirements of Addis Ababa University's Master of Anesthesia program. When it's finished, it will be archived in the university library and available for checkout by users in accordance with library policies. I hereby certify that I have not previously submitted my thesis to any other university in order to be considered for a certificate, degree, or other credential.

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Acknowledgment

I'd like to extend my heartfelt thanks to Addis Ababa University College of Health Science School of Medicine and Department of Anesthesia for providing me with this opportunity to develop my thesis. I also appreciate the support of Wollo University, which sponsored my Master's education. I would like to express my sincere gratitude to my advisors, Eyayalem Melese and Lidya Haddis, for their unwavering support, valuable feedback, and guidance throughout the research process.

I would like to express my gratitude to the staff of ZMH, TAH, and SPMMC, particularly the Data clerk personnel. I would like to offer special thanks to the data collectors who contributed to the study. Additionally, I would like to extend my heartfelt thanks to my friends Dr. Mengstie Mulugeta, Habtu Tsehayu and Fassil Mihretu, for their valuable technical support throughout my proposal and thesis development process.

Abstract

Introduction: *Neonatal surgery is one of the most challenging procedures globally, although many neonatal surgical procedures are done, the mortality and morbidity remain high particularly in low and middle-income countries. There is limited data in Ethiopia about neonatal surgical mortality, so this study aimed to investigate the survival status and predictors of mortality among neonatal surgical patients in Addis Ababa Public Hospitals.*

Objective: *To assess the survival status and predictors of mortality among neonatal surgical patients in selected Addis Ababa public hospitals from 2021-2023.*

Methods: *A multi-center retrospective cohort study was done on 290 neonatal surgical patents in three governmental hospitals in Addis Ababa selected using systematic random sampling from January 2021- December 2023. The data were entered to Epi-data version 4.6 and transferred to STATA version 15 for analysis. Bi-variant and Multi-variant Cox regression model was used to analysis and determine the predictor variables. Hazard ratio with 95% confidence interval was computed and p-value < 0.05 was considered statistically significant.*

Result: *From a sample of 313 patients, 290 were included for final analysis and followed for median follow-up of 21 days. The overall mortality among neonatal surgical patients was 21.72% with an incidence rate of 0.21 cases per 100 person-day observation. Pre term (AHR=6.36(95% CI,1.77 - 22.81), Underweight (AHR=5.47, 95% CI:1.55-19.24), Apgar score 0-3 (AHR=25.52, 95% CI:1.91-332.6), Preoperative NICU Admission (AHR=2.70, 95% CI:1.38- 5.73), ASA class III patients (AHR=4.95, 95% CI:1.01-24.27), and Postop NICU admission (AHR=0.19, 95% CI:0.05-0.71) were found to be significantly associated with mortality of neonatal surgical patients.*

Conclusion: *The mortality of neonatal surgical patients was high. The predictors of mortality were pre term, underweight, preoperative and postoperative NICU admission, ASA class III and Apgar score ≤3. Neonates that need to be given more consideration are those who have Apgar score ≤3, and those who are pre term and underweight.*

Keywords: *mortality, neonatal surgery, predictors, survival*

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Table1: Acronym and Abbreviation

AHR	Adjusted Hazard Ratio
AKI	Acute Kidney Injury
ANC	Antenatal care
ARM	Anorectal Malformation
ASA	American Society of Anesthesiology
Apgar	Appearance, Pulse, Grimace, Activity and Respiration
BLS	Black Lion Specialized Hospital
BW	Birth Weight
CD	Compact Disk
CDH	Congenital Diaphragmatic Hernia
CHD	Congenital Heart Disease
CHR	Crude Hazard Ratio
CI	Confidence Interval
CVS	Cardio Vascular System
DRG	Diagnosis Related Group
EA	Esophageal Atresia
ECMO	Extracorporeal Membrane Oxygenation
FBA	Foreign Body Aspiration
GA	Gestational Age
GDP	Gross Domestic Product
HC	High Care
HMIS	Health Management Information System
HSD	Hirchisprung Disease
IHPS	Infantile hypertrophic pyloric stenosis
IRB	Institutional Review Board
ISS	Infection Severity Score
LBW	Low Birth Weight
LMICs	Low and Middle Income Countries
MDG	Millennium Development Goal
NICU	Neonatal Intensive Care Unit
NSM	Neonatal Surgical Mortality
OR	Operation Room
SDG	Sustainable Development Goals
SPMMC	St. Paul's Hospital Millennium Medical College
STATA	Statistical Software for data Science
STS-CHS	Society of Thoracic Surgeons Congenital Heart Surgery
TEF	Tracheo Esophageal Fistula
TPN	Total Parenteral Nutrition
TTH	Tamale Teaching Hospital
UK	United Kingdom
US	United State
USA	United States of America
USD	United State Dollar
VACTERL	Vertebral Anorectal Cardiac Tracheoesophageal Renal and Limb anomalies.
WHO	World Health Organization
ZMH	Zewuditu Memorial Hospital

CHAPTER ONE: INTRODUCTION

1.1. Back ground information

The neonatal period is the first 28 days of a child's life after birth. It is a period of extremely rapid change, and many important things can happen during this time. The World Health Organization (WHO) indicates that between 17 and 43% of infant mortality can be due to congenital anomalies(1). For congenital malformations, many cost-effective, life-saving procedures that can enhance long-term results. Surgery is an essential but frequently overlooked aspect of congenital anomaly treatment options, especially in low- and middle-income nations(2). Neonatal surgical mortality means that neonates die in the hospital or die in 30 days of the operation(3).

One of the disciplines of pediatric surgery that has seen tremendous progress in the last 50 years is neonatal surgery(4). Neonatal mortality was higher in neonates with gastroschisis than in neonates with non-gastroschisis surgical conditions. Failure to initiate enteral feeding and sepsis were variables related to death in infants with gastroschisis. Other factors which increase surgical mortality the length of surgery 2 hours, need for mechanical ventilation, need for large dose of vasopressor and reoperation(5,6).

Even though abdominal wall abnormalities, gastrointestinal perforation, and Congenital Diaphragmatic hernia (CDH) continue to pose a significant mortality risk in developed countries such as Japan, the overall mortality rate of new-born surgical patients has fallen dramatically decreased to 10%. A high rate of chromosomal abnormalities outcomes in a poor prognosis for abdominal wall deformities(7). Numerous other reasons could be responsible for an increase in survival including the development of advanced respiratory support machines, use of volume-adjustable pumps, central venous catheters, broad-spectrum antibiotics, hospital infection control teams, and monitoring equipment in neonatal intensive care units (NICU)(8,9).

When we compared neonatal surgical mortality in developed countries, the mortality rate is extremely high in low-income countries. The main contributing factors to this mortality were sepsis and neonates with congenital abnormalities. The highest mortality primary surgical diagnosis was esophageal atresia(10).

Africa's newborn surgical outcomes have improved in 20 years through cost-effective care modifications, increased healthcare financing, regional coordination, and foreign partnerships. These are examples of potential initiatives that might assist in addressing the problems and improving outcomes(11).

Surgical mortality remains a significant concern in pediatrics surgery, with multiple factors contributing to this outcome. Further research is needed to identify the most effective strategies for reducing neonatal surgical mortality and improve outcomes for these vulnerable patients.

1.2. Statement of the Problems

The World Health Organization (WHO) estimates that 6700 neonatal fatalities occurred per day in 2020, or 2.4 million newborns die in the first month of life. The probability that the infant will survive is significantly influenced by the place of birth. With 27 deaths per 1000 live births in 2020, Sub-Saharan Africa had the highest newborn mortality rate, followed by Central and South Asia with 23 deaths per 1000 live births Compared to neonates born in high-income countries a newborn in Sub-Saharan Africa has a 10 fold higher risk of dying in the first month. The leading causes of newborn death include preterm delivery, infection, and birth abnormalities(12).

According to a research conducted in United States of America, 3.1% of newborns required extensive surgery or were diagnosed with a significant congenital abnormality(13). Congenital abnormalities account for a major component of the global health burden that can be surgically addressed(14). The mean cost of the congenital malformations per hospital admission expressed in Diagnosis Related Group (DRG) points was significantly higher compared to the other hospitalizations. Surgical conditions requiring timely postnatal surgery place a significant financial burden on the healthcare system (20).

One study in the United Kingdom shows that there is a national requirement for one neonatal surgical bed per 5,000 births. Intensive care, high care (HC), and special care accounted for 37%, 46%, and 17% of bed days, respectively. This equates to an annual service cost of £2 million, or about £250,000 per 5,000 births(15). Similarly South Asia as a region invests around 12,913 USD to attain sustainable development goals in 2030 to decrease neonatal mortality, but currently it is not on track to achieve this goal which has one of the highest rates of newborn mortality in the world, which is around 25 per 1000 live births(16).

The majority of operative resources for pediatric surgery groups in low and middle-income countries are used for emergency and urgent operations, which results in an accumulation of complex congenital procedures (17). Here in Ethiopia, the infant mortality rate was 47 deaths per 1,000 live births, and the under-5 mortality rate was 59 deaths per 1,000 live births. This means that 1 in 17 children in Ethiopia die before reaching age 5. There has been a slight increase in neonatal mortality since 2016, from 29 to 33 deaths per 1,000 live births(18).

1.3. Research questions

What is the survival rate of neonates after surgical intervention for 28 days?

What are the primary causes of death in neonatal surgical cases?

1.4. Justification of the study

The study of mortality in neonatal surgical patients is a critical and timely topic that warrants investigation. Neonatal surgery is a high-risk field, and the mortality rate remains unacceptably high. By understanding the factors that contribute to mortality in this population, we can identify opportunities to improve care, reduce mortality rates, and enhance patient outcomes.

This study will use a retrospective cohort design, using Cox proportional hazard ratio to identify potential predictors of mortality and utilizing a large data set of neonatal surgical patients from multiple hospitals. The data set includes socio-demographic, preoperative, intraoperative and postoperative data including surgical procedures, and postoperative outcomes.

Here in Ethiopia, there are many studies related to neonatal mortality, but studies on the survival or time to death of neonatal patients after surgical procedures are rare. Reducing neonatal mortality is an essential part of the third Sustainable Development Goal (SDG), which is to end preventable child deaths(19). To achieve this aim, it will require an understanding, and estimation of the levels and trends in neonatal surgical mortality by using a statistical model that can be used to assess the main predictor factors for mortality and time to death in neonatal surgical patients.

1.5. Significance of the study

This study will contribute to the development of evidence-based strategies to reduce neonatal surgical mortalities and improve the outcomes of these vulnerable groups. This finding will have important implication for policy-makers, health care providers, and families affected by neonatal surgical mortalities. This study will change the clinical practice by informing policy decisions related to neonatal surgical care, such allocating resources for specialized care units or developing guidelines for perioperative care.

CHAPTER TWO: LITERATURE REVIEW

Neonatal surgical patients refer to newborns that require surgical treatment within 0-28 days of their life due to various conditions, like congenital anomalies, or surgical emergencies. Neonatal surgery is considered the most challenging and complex type of surgery, as it involves operating on newborn babies who are still adjusting to the outside world. Neonatal surgery is performed on extremely fragile and vulnerable patients, which increases the risk of complications and mortality.

2.1. Neonatal surgical mortality

The reported neonatal surgical mortality (NSM) rates vary widely around the globe, ranging from 4% to 80 %. Many retrospective and prospective studies show that neonatal mortality is high especially in middle and low income countries. In United States, surgical neonatal mortality for preterm was 4.9% and for term neonate was 2.0%(3). In Japan neonatal surgical mortality is around 7% presence of congenital anomaly like CDH, abdominal wall defect and gastrointestinal perforation accounts higher percentage even if ECMO and infant intervention have no such advantage for neonatal survival (20).

In Bangladesh neonatal surgical mortality was about 14.2%(21). In South Africa it is around 21.74%(22). Research conducted in different Egyptian hospitals shown mortality rates ranging from 11% to 30.6% (23–27). Factors contributing to this high mortality include conditions like necrotizing enterocolitis, small bowel obstruction, and various congenital anomalies, with sepsis being a common cause of death(28). In Cote d'Ivoire neonatal mortality after surgery is around 24% (29). A 7-month prospective study in Iraq reveals 31.5% of neonatal surgical mortality(30). The retrospective study, which was done in South Africa for two years, shows that 30.6% died during the hospital stay(31). In Rwanda neonatal surgical mortality was about 52.7(32). and in Nigeria it was around 62.2%(33).

Retrospective review of medical records conducted in Ethiopia at Tikur Anbessa Specialized Hospital, neonatal surgical mortality is 0.03% for HSD and 73.5% for treche-oesophageal fistula(34).

2.2. Factors affecting neonatal surgical mortality

2.2.1. Socio demographic factors

Socio demographic factors play a crucial role in neonatal surgical mortality outcomes. Factors such as race, ethnicity, gender, socioeconomic status, maternal education, economic status, and antenatal care utilization have been identified as significant predictors of neonatal mortality(21,35,36). Studies highlight disparities in health care quality across different populations, emphasizing the importance of considering these factors in models for survival and neurodevelopmental outcomes in neonates undergoing surgery(37).

In a retrospective study conducted at Tamale Teaching Hospital (TTH) in Ghana's neonatal intensive care unit (NICU) with surgical conditions, a neonate presenting with less than 7 days of life accounts for the majority of deaths, which is 85.1%, followed by neonates aged between 8 and 14 days, which accounts for 8.5%. 15.3% of newborns who presented during the first seven days of their lives passed away, compared to 8.1% of those who presented later(38). In contrast based on the Andrew H smith study in America there is no association between adjusted mortality and morbidity with neonatal gestational age(39).

According to the retrospective descriptive study on Tanzanian tertiary care hospital, among 822 patients with congenital anomalies, Male children comprised 64%(40). Male neonates have been consistently reported to have a higher neonatal mortality rate than their female counterparts(41). Study in Nepal shows that neonatal death rate was greater in boys than girls(42). Based on the study in Cuba neonates in the youngest and oldest age groups at the time of surgery faced the highest risk of death(43).

Based on Alamirew et al. study the average neonatal mortality difference in rural residences was increased by 3.99 times compared to urban mothers' residences(44). Similarly study on Nepal and China shows neonatal mortality in rural area is high (45,46). Neonates born from mother which have different co-existing disease like DM, Preeclampsia and Epilepsy have high risk of mortality(47–49).

Interval between admission and surgical intervention time also affects the survival of neonatal surgical patients based on study in Nigeria(50). Another important factors of mortality was Apgar score according to the research which is done in Sweden neonates born with lower Apgar score higher risk of mortality in all gestational age(51).

2.2.2. Types of congenital anomaly

Mortality rates for neonates with congenital anomalies vary, with factors such as gestational age and being out born significantly predicting mortality in babies operated for small intestinal anomalies(52). Congenital anomalies are the second commonest cause of infant deaths in the United Kingdom(53).

According to the European prospective multicenter observational study, the risk of critical events was increased by prior neonatal medical conditions, congenital anomalies, or both in those requiring preoperative intensive support(54). The four-year retrospective study in Bangladesh shows neonatal surgical mortality is around 14.6%, gastroschisis and esophageal atresia are the main causes of this mortality(55). A study in Ghana shows that gastroschisis, omphalocele, imperforated anus are the main causes for mortality(56).

A prospective study at Kamla Raja Hospital found the gastrointestinal system as the most common neonatal surgical condition, with tracheoesophageal fistula being the most common(57). Another retrospective study in Tunisia found esophageal atresia and bowel obstruction to be the most common diagnoses, with congenital diaphragmatic hernia being the highest-risk cause of death(58).

A review of neonatal surgery challenges in African countries found abdominal wall defects, anorectal malformations, Hirschsprung's disease, necrotizing enterocolitis, and volvulus neonatorum to be the most common cause(11,59,60).

To reduce neonatal surgical mortality related to congenital anomalies, several recommendations can be drawn from different research papers. Actively looking for associated anomalies, especially those involving the digestive system, is crucial for improving outcomes(61,62).

2.2.3. Sepsis and infection

Sepsis and infection play significant roles in neonatal surgical mortality. Studies show that sepsis is a major factor contributing to mortality in neonates following abdominal surgery, with a mortality rate of 48% within 30 days(63). Factors such as central line-associated bloodstream infections, respiratory tract infections, and surgical complications increase the risk of sepsis and mortality in neonates undergoing gastrointestinal or abdominal wall surgery(59). Furthermore, preterm babies are more susceptible to sepsis-related mortality, with approximately half of

postoperative mortality attributed to the synergistic effects of preoperative sepsis and prematurity(64,65).

Prospective cohort study in UK shows that 13.5% of neonates underwent abdominal and thoracic surgery develop infection and, this was the main cause for hospital stay and mortality(66). Similar to the above study preoperative pneumonia was strongly associated with increased incidence of postoperative mortality and complications in children after surgery in USA(67). A systematic review in the US found that abdominal surgical site infections in infants after abdominal birth defect surgery were 6%(68). Preterm neonates are more susceptible to sepsis, with half of postsurgical mortality and complications (69). Understanding and addressing these risk factors are crucial in improving outcomes and reducing neonatal surgical mortality.

2.2.4. Gestational age and birth weight of neonate

Based on the findings of the Society of Thoracic Surgeons Congenital Heart Surgery (STS-CHS) in the United States, birth during the early term period of 37 to 38 weeks' gestation is associated with worse outcomes after neonatal cardiac surgery(70). According to Nicholas J study in USA neonates who operated in preterm gestational age had higher risk of mortality(71). In another single-center audit of cardiac surgery interventions at a tertiary pediatrics center in Australia, there was an increased risk of mortality and rate of complication in low birth weight and premature infants compared with gestation and appropriate weight(72).

According to the study in China, pre term and low birth weight infants have higher mortality rate(73). Other studies also show that the overall 30-day mortality rate for preterm neonates, term neonates, and non-neonates was 4.9%, 2.0%, and 0.1%(3,41,74–76). ASA score 3 or above increases 30-day post-operative mortality of neonatal surgical patients(77).

2.2.5. Intraoperative factors

In neonatal surgical cases, various intraoperative factors play a crucial role in determining mortality outcomes. Factors such as the duration of surgery exceeding 120 minutes, loss of blood greater than 10% of total blood volume, the need for prolonged ventilation, requirement of high doses of vasopressors, and the occurrence of reoperations have been identified as significant predictors of neonatal surgical mortality(5,78). Additionally, postoperative challenges like sepsis

and respiratory issues have been linked to higher mortality rates in neonates undergoing surgery(63,79).

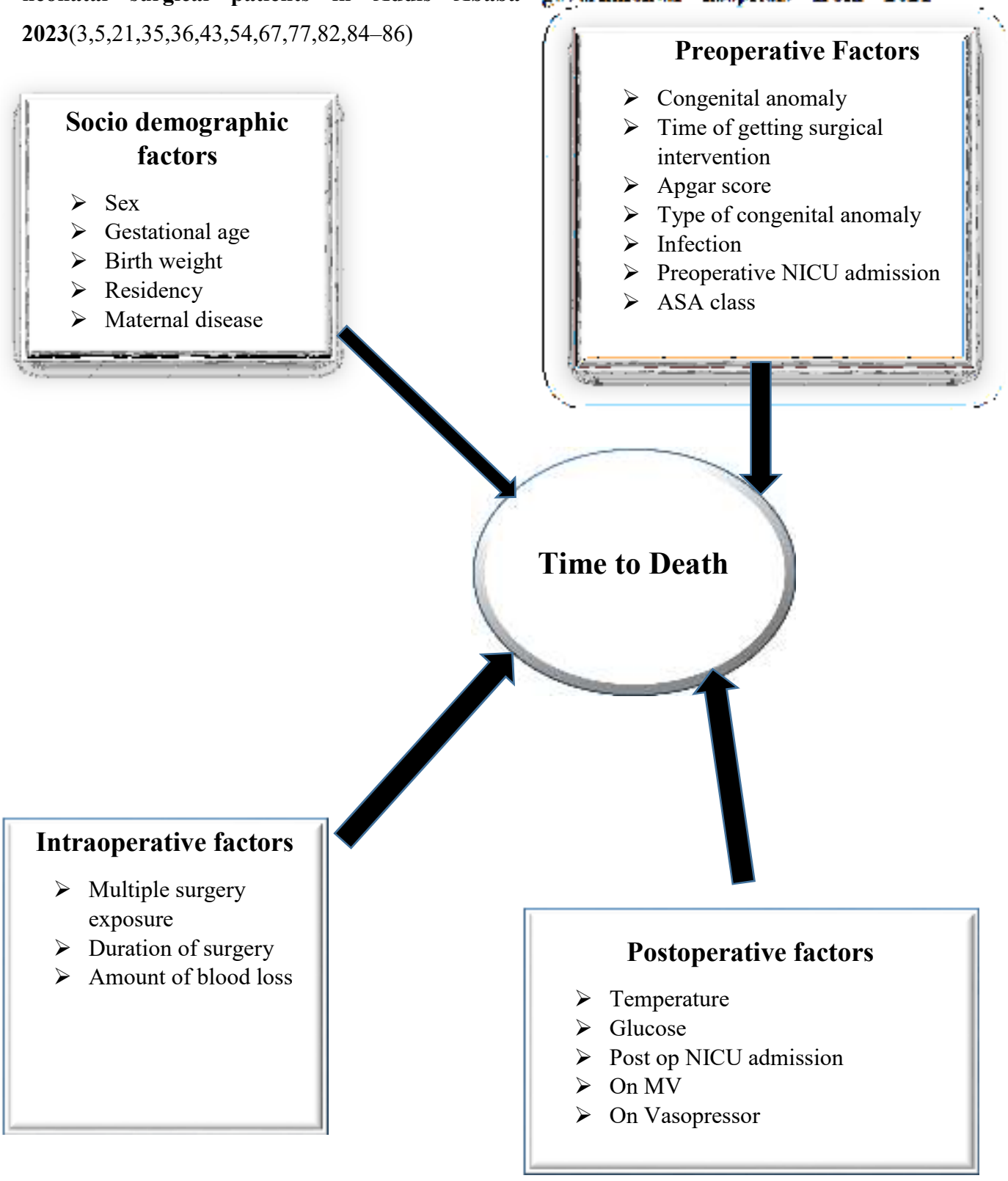
Implementing strategies to minimize the duration of surgery, optimize postoperative care, and promptly address complications during and after surgery are essential to improve outcomes and reduce neonatal surgical mortality rates. Moreover, identifying and addressing these intraoperative and postoperative risk factors early on can significantly impact the overall survival of neonates undergoing surgical procedures(80).

2.2.6. Post-operative factors

According to the study Tadesse et.al neonates having body temperature less than 35.5 degree centigrade body temperature have higher mortality rate(81). Lowest temperature at admission was associated with higher neonatal mortality based on the study which is done in Brazil(82). But in contrary to the above study in china shows that there is no direct association between intraoperative hypothermia and neonatal mortality(83). Based on the study done in India, neonates need prolonged ventilation and higher doses of vasopressors increased the odds of mortality by 5.77 and 25.65 times respectively(5,54,84).

One study in Indonesia shows that neonates admitted in ICU with abnormal glucose hypoglycemia or hyperglycemia has increased mortality by 3.05 times compared with normal glucose level. Another study which conducted in Pakistan also shows neonates with hypoglycemia also high risk of mortality(84,85). NICU admission plays a crucial role in neonatal outcomes, as evidenced by various studies. A retrospective study in Canada highlighted that NICU admission for prolonged time was significantly associated with neonatal mortality(86). In contrast to the above study Postoperative NICU admission increases survival rate according to Siddharth V, et.al study in India(87).

Figure1: Conceptual framework of survival status and predictors of mortality among neonatal surgical patients in Addis Ababa governmental hospitals from 2021-2023(3,5,21,35,36,43,54,67,77,82,84–86)



CHAPTER THREE: OBJECTIVE

3.1. General objective

- To assess the survival status and predictors of mortality among neonatal surgical patients in selected Addis Ababa public hospitals from 2021-2023.

3.2. Specific objectives

- To assess the survival status of neonatal surgical patients in selected Addis Ababa public hospitals.
- To identify the predictors of mortality in neonatal surgical patients in selected Addis Ababa public hospitals.

CHAPTER FOUR: METHODS

4.1. Study design

A multi-center retrospective cohort study design was conducted from January 1, 2021 to December 31, 2023 at selected public hospitals in Addis Ababa. Tikur Anbessa Hospital, Zewuditu Memorial Hospital, and St. Paul Hospital Millennium Medical College.

4.2. Study area

The study was conducted in purposively selected Addis Ababa public hospitals based on the higher number of neonates admitted for surgery in Addis Ababa hospitals. Addis Ababa is the capital and largest city of Ethiopia. According to the world population review for 2023, the population is now estimated at **5,460,591.**

TAH is the largest specialized hospital in Ethiopia, with over 700 beds, and serves as a training center for undergraduate and postgraduate students.

Zewuditu Memorial Hospital is located in central Addis Ababa, Ethiopia. The hospital is named after Empress Zewuditu currently the hospital is providing services to the community with 520 personnel.

St. Paul Hospital Millennium Medical College's is located in Addis Ababa, Ethiopia built by Emperor Haile Selassie I; the hospital gives service for more than 300,000 patients annually on average.

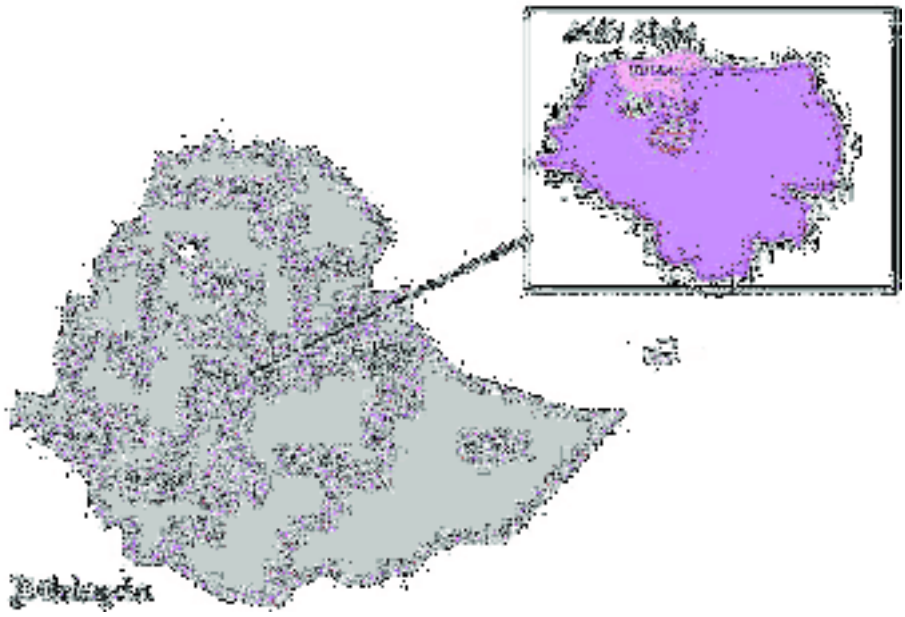


Figure 2: Map of study area (TAH, SPMMC and ZMH)

4.3. Population

4.3.1. Source population

All neonates who underwent surgery in selected public hospitals in Addis Ababa from January 1, 2021, to December 31, 2023.

4.3.2. Study population

The study populations were neonates who underwent surgery in three selected hospitals who meet the inclusion criteria and selected for sample during the study period.

4.4. Sample size and sampling technique

4.4.1. Sample size calculation

Previous studies conducted for neonatal surgical mortality have not utilized the Hazard Ratio, so we can't use power calculation with hazard ratio to identify the predictor factors. The single population proportion formula was used to calculate the sample size. Based on the previous study on black lion hospital(34). **p= 24.4** so **q= 1-p = 75.6, $Z_{a/2}$** = Z-score of the 95% confidence interval = **1.96**, and W = margin of error = **5%**

$n = (z_{\alpha/2})^2 p\,(1-p)$

$n = (z\alpha/2)2p\,(1-p)/w2$

n= $(1.96)^2$*0.244(1-0.244)/ $(0.05)^2$

N=3.84*0.184/0.0025= 284

The total sample size was 284. With a 10% non-respondent rate, the final sample size was n = **313**.

4.4.2. Sampling procedure

The study participants for each hospital were selected using proportion allocation technique by dividing the number of admission in each hospital multiplied by sample size (n=313) by total number of admission of neonatal surgical patients in three hospitals (N=1169). Study participants from each hospitals using simple random sampling technique using the card number of patients from the logbook registry as a sampling frame who were admitted during the study period.

K =**1,169/313**=Approximately **4.**

N_T (1169) = Total number of neonatal surgical patients from 2021-2023.

n (313) = Total sample size

N_{ZMH} (354) =Total number of neonates who underwent surgery in Zewuditu Memorial Hospital.

N_{TAH} (511) = Total number of neonates who underwent surgery in Tikur Anbessa Hospital.

N_{Paul} (305) = Total number of neonates who underwent surgery in St. Paul Hospital Millennium Medical College.

N in each hospital = Total sample size **(n)** ×the average number of neonatal surgical patients in a given hospital from 2021-2023.

N in Zewuditu Memorial Hospital will be= $n \times N_{ZMH}/N_T = 312 \times 354/1169 =$ **94**

N in Tikur Anbessa Hospital will be $= n \times N_{TAH}/N_T = 312 \times 510/1169 =$ **137**

N in St. Paul hospital will be $= n \times N_{St.\ Paul}/N_T = 312 \times 305/1169 =$ **81**

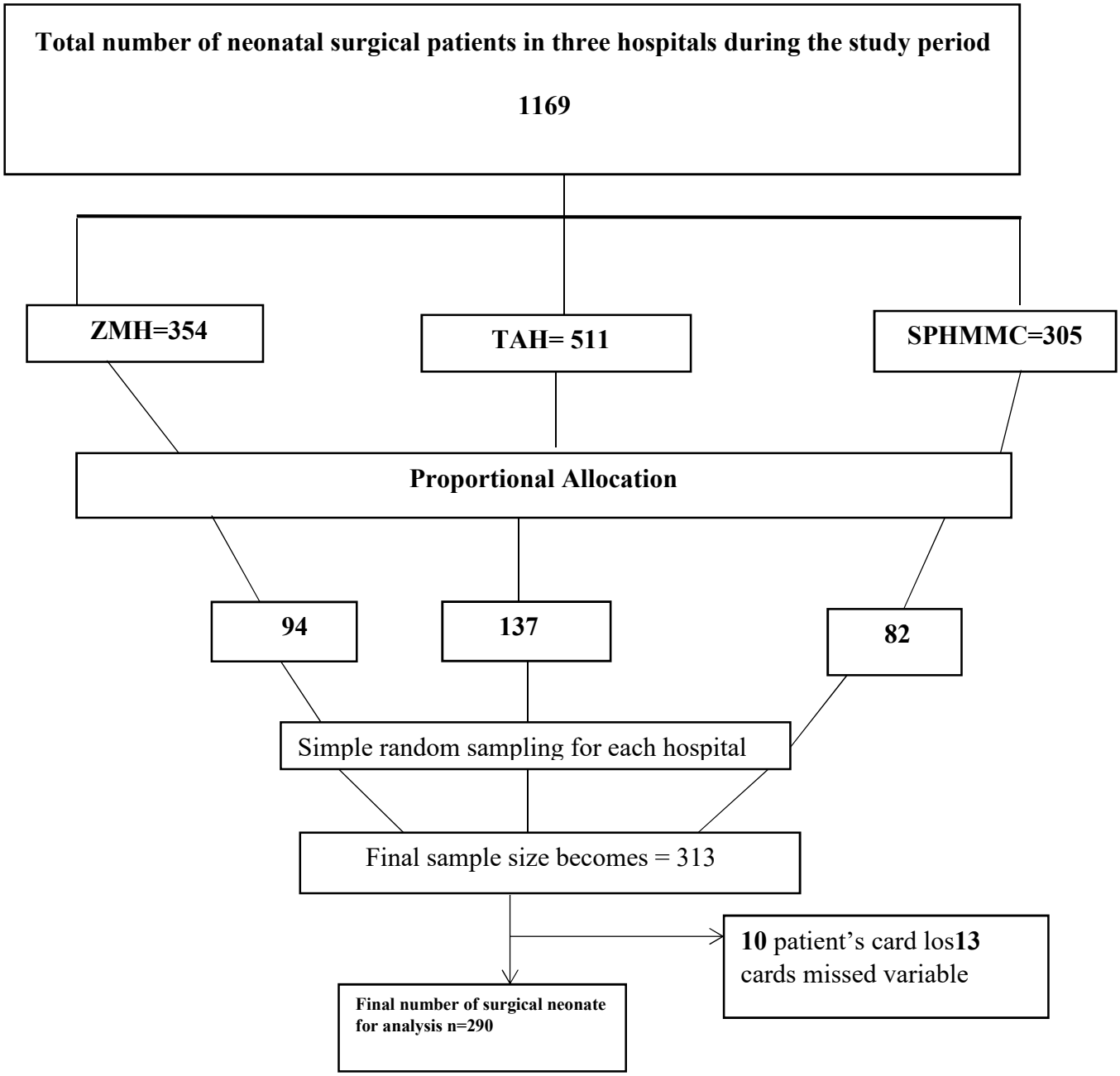


Figure3: Flow diagram of proportional allocation and sampling of study participant

4.5. Inclusion and Exclusion criteria

4.5.1. Inclusion criteria

All neonates who underwent surgery at major OR in selected Addis Ababa public hospitals from January 1, 2021 to December 31, 2023.

4.5.2. Exclusion criteria

- Patients who had missing key variables were excluded from the study during the study periods (birth weight, gestational age, ASA class).
- Records were not available.
- Procedures done in minor OR.

4.6. Variables of the study

4.6.1. Dependent variable

Time to death

4.6.2. Independent variable

Socio demographic factors

Sex, gestational age, birth weight, residency, maternal disease

Preoperative factors

Presence of congenital anomaly, time of getting surgical intervention, Apgar score at 5 minute of delivery, type of congenital anomaly, infection , preoperative NICU admission, ASA class

Intraoperative factors

Multiple surgery exposure, duration of surgery, amount of blood loss

Postoperative factors

Temperature, glucose, post op NICU admission, need of mechanical ventilation, need of vasopressor

4.7. Data collection Analysis and quality control

4.7.1. Data collection procedure

After training two anesthesia professionals about how to extract data from patient card, data collection was performed from the card registration room under the guidance of one MSc anesthetist at Black Lion Specialized Hospital, Zewuditu Memorial Hospital and St. Paul Hospital. The data extraction tool was adopted from different literatures.

4.7.2. Data quality control

To guarantee the accuracy of the data, 32 patients, or 10% of the estimated sample size, was undergo pre-assessment of patient's chart at Yekatit 12 hospital to identify questions that don't make sense for participants or problems with the questionnaire that might lead to biased answers. One day before data collection, the supervisor and data collectors received training on the study goal and how to evaluate documents in line with the format for data extraction. The primary investigator and another supervisor oversaw the entire procedure. The supervisor and lead investigator checked the completed forms daily for accuracy.

4.7.3. Data processing and analysis

Missing values and outliers were checked using explorative data analysis. Nonlinearity between log hazard and covariant was checked using martingale residual. The probability of death among neonatal surgical patients was described using the Kaplan-Meier curve and log rank test for categorical variable. Before fitting the cox regression model, the data fitness and proportional hazard assumption were tested with log-log plot (log survival probability vs. log survival time).

A bivariate Cox regression analysis was conducted to measure the effect of each independent variable on the dependent variable. In the multivariate Cox regression analysis variables with a p-value less than 0.2 in the bivariate Cox regression analysis were used to find the independent predictor of mortality. The adjusted hazard ratio with 95% confidence interval was used for potential risk factors in the multivariate model. A p-value of 0.05 is considered statistically significant association. The goodness of fit test was checked with the Cox Snell residual.

4.7.4. Operational definitions

Censored

Surgical neonates are those who underwent surgery but were discharged or transferred to another institution without knowing their outcome.

Survival status

The outcome of neonatal surgical patients in the operating room (OR), intensive care unit (ICU), or ward

Event

Mortality of neonatal surgical patients in the operating room (OR), intensive care unit (ICU), or ward during perioperative period.

Incomplete records

If the patient's record is misleading during admission, the discharge date and outcomes may be inaccurate.

Survival time

The time from a neonatal operation to the death of neonates after the operation

Follow up time

It is a time when neonate's health will be followed after surgical intervention.

Length of stay

It is the length of time elapsed between a neonate's hospital admittance and discharge.

Blood Loss Classification

Minor: blood loss ≤15% of total blood volume.

Moderate: blood loss 15-25% of total blood volume.

Sever: blood loss ≥25% of total blood volume.

Apgar score

Normal Apgar= 7-10

Moderate Apgar= 4-6

Sever Apgar= 0-3

Prolonged NICU admission > 7 days stay

Prolonged period on Mechanical ventilation and vasopressor >7 days stay

Maternal co-existing= if the mother has Diabetes, seizure, hypertension disorder

Hypoglycemia < 40mg/dl

Duration of surgery: The time elapsed between induction of anesthesia and recovery from anesthesia.

Infection= Presence of gram Negative bacteria in blood culture.

4.7.5. Ethical Consideration

Ethical clearance was obtained from Addis Ababa University College of health science department of anesthesia with protocol number of **Anes/11/2023/2024**. Since this is secondary data, informed consent was not required from each client; instead, it was sent to the head of the respective hospital's management.

4.7.6. Dissemination of results

The research's findings will be distributed to Addis Ababa Public Health and Emergency Management Directorate, the College of Health Science, the Department of Anesthesia, and Addis Ababa University. The study results will be delivered to the local health bureau, TAH, ZMH and SPHMMC. The outcomes will be released for a peer-reviewed academic publication.

CHAPTER FIVE: RESULT

5.1. Socio-demographic characteristics of neonatal surgical patients

From the sample of 313 neonatal surgical patients who were randomly selected as study participants, 290 patients were included in the final analysis the remaining 10 patient cards is lost and 13 patient card were missed essential variables. The majority of neonatal surgical patients were males, they accounted for 163 (56.21%) of the total neonatal surgical patients. About 216(74.48%) were from urban. Most neonatal surgical patients ages are less than 10 day they account for 128(44.14%). Neonates got surgical intervention within 24 hours are113 (38.97%). Most of neonatal surgical patients were term at birth which accounted for 192(66.21%) of the total neonates who underwent surgery.

Table2: Socio-demographic factors of neonatal surgical patients from January 1 2021 to December 31 2023 in selected Addis Ababa public hospitals, Ethiopia.

Variable	**All Episodes (%) n=290(100)**	**Censored, n (%) n= 227 (78.28)**	**Event, n (%) n= 63 (21.72)**
Residency			
Rural	74(25.52)	56(24.67)	18(28.57)
Urban	216(74.48)	171(75.33)	45(71.43)
Sex			
Male	163(56.21)	130 (57.27)	33 (52.38)
Female	127 (43.79)	97(42.73)	30(47.62)
Weight			
Under weight	47 (16.21)	40(17.62)	7(11.11)
Normal weight	187(64.48)	179(78.85)	8(12.70)
Over weight	56(19.31)	8(3.52)	48(76.19)
Age			
≤ 10 day	128(44.14)	76(33.48)	52(82.54)
between10-20	120 (41.38)	111(48.90)	9(14.29)
≥ 10 day	42(14.48)	40(17.62)	2(3.17)
Gestational Age			
Pre term	60(20.6)	6(2.64)	54(85.71)
Term	192(66.21)	186(81.94)	6(9.52)
Post term	38(13.10)	35(15.42)	3(4.76)

5.2. Clinical characteristics of neonatal surgical patients

From the total of neonates who underwent surgery 209(72.07%) neonates had 1 or more congenital anomaly. Out of these congenital anomalies neural tube defect covers the highest

number which is 82(28.28%) followed by ARM 39(13.45%), TEF with or without EA 25(8.62%) and CHD 21(7.24%).

Out of the total neonates who underwent surgery 52(17.99%) become hypothermic and 81(28.03%) become hyperthermia. 65(22.41%) neonates developed hypoglycemia.

After operations, 220(75.86%) were admitted in NICU out of this 68(23.45%) were on mechanical ventilators and 42(14.48%) on vasopressor.

Table3: Clinical data of neonatal surgical patients *from January 1 2021 to December 31 2023 in selected Addis Ababa public hospitals, Ethiopia.*

Variable	All Episodes (%) n=290(100)	Censored, n=227(78.28%)	Event, n=63(21.72%)
Presence of congenital anomaly			
Yes	209(72.07)	152(66.96)	57(90.48)
No	81(27.93)	75(33.04)	6(9.52)
APGAR Score			
7-10	171(58.97)	126(55.51)	45(71.43)
4-6	111(38.28)	94(41.41)	17(26.98)
0-3	8(2.76)	7(3.08)	1(1.59)
Presence of infection			
Yes	79(27.24)	35(15.42)	44(69.84)
No	211(72.76)	192(84.58)	19(30.16)
Preoperative NICU admission for a prolonged time			
Yes	127(43.79)	81(35.68)	46(73.02)
No	163(56.21)	146(64.32)	17(26.98)
Urgency of Surgery			
Emergency	72(24.83)	43(18.94)	29(46.03)
Elective	218(75.17)	184(81.06)	34(53.97)
American Society of Anesthesiologist Class			
ASA 2	168(57.93)	165(72.69)	3(4.76)
ASA 3	103(35.52)	62(27.31)	41(65.08)
ASA 4	19(6.55)	0(0.00)	19(30.16)
Postoperative NICU admission for a prolonged time			
Yes	220(75.86)	162(71.37)	58(92.06)
No	70(24.14)	65(28.63)	5(7.94)
Neonates on Mechanical Ventilation for a prolonged time			
Yes	68(23.45)	20(8.81)	48(76.19)
No	222(76.55)	207(91.19)	15(23.81)
Neonates on vasopressor for a prolonged time			
Yes	42(14.48)	9(3.96)	33(52.38)
No	248(85.52)	218(96.04)	30(47.62)

5.3. Survival status of neonatal surgical patients

In this study, neonates were followed for a minimum of 12 hours to maximum of 28 days, with median survival time of 21 days. Based on this the total person observation-time was 2,999.1 person days. In this study 63(21.72%) of neonates died out of neonatal surgical patients. About

227 (78.28%) of neonatal surgical patients were censored. 212(73.10%) are alive, 8(2.76 %) were discharged alive, 2(0.69%) were discharged against medical care, and 5(1.72%) were referred to other hospitals.

The incidence of death among neonatal surgical patients was found to be 2.1 cases per 100 person-day observation. The cumulative probability of failure on the first day and at the end of the follow up period was 1.04% and 65.08% respectively.

Figure4: pie chart of proportion survival status of neonatal surgical patients from January 1 2021 to December 31 2023 in Addis Ababa public hospitals.

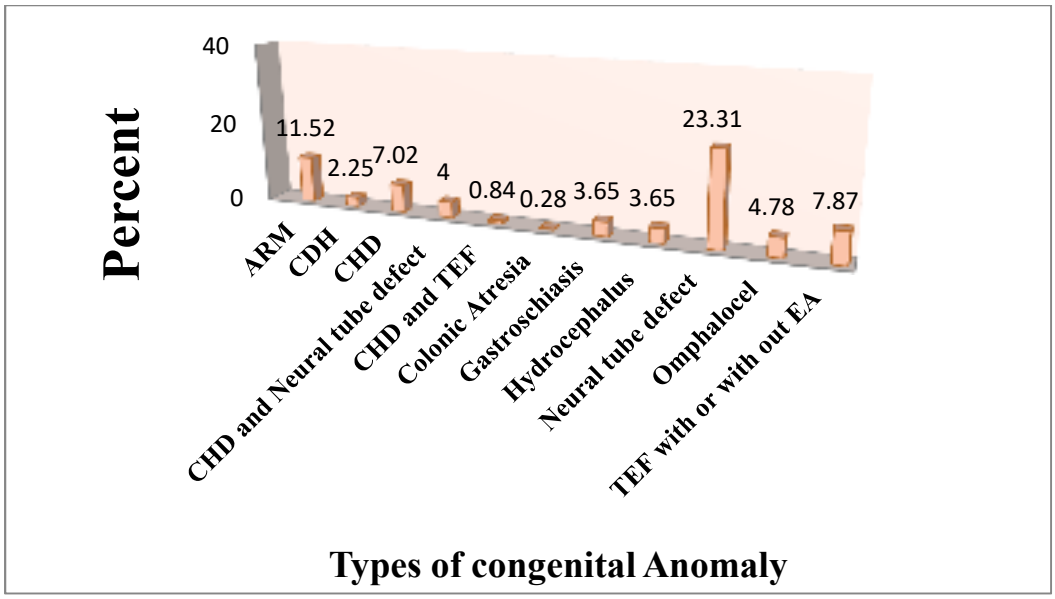


Figure5: bar chart of proportion of neonatal congenital anomaly that underwent surgery from January 1 2021 to December 31 2023 in selected Addis Ababa public hospitals.

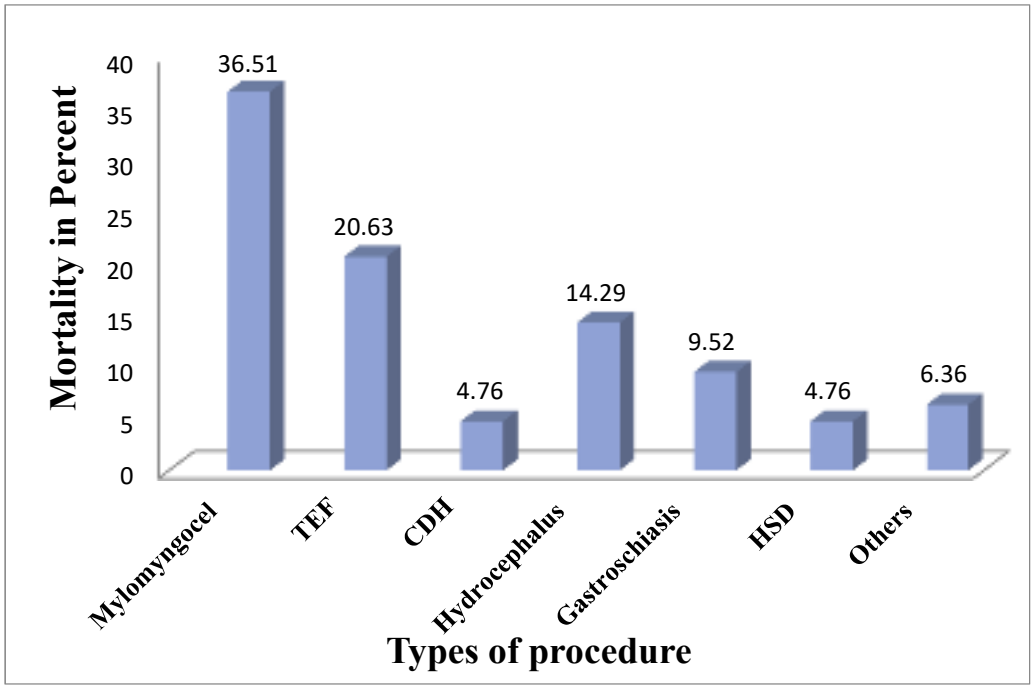


Figure6: bar chart of proportion of type of procedure and mortality from January 1 2021 to December 31 2023 in selected Addis Ababa public hospitals.

Mylomyngocel accounts the highest percent of death 24(36.51%) followed by TEF with or without EA (20.63%) and hydrocephalus (14.29%) respectively.

5.3.1. Predictors of mortality among neonatal surgical patients

The failure estimate graph of neonatal surgical patients is described with the Kaplan-Meier failure function as follows;

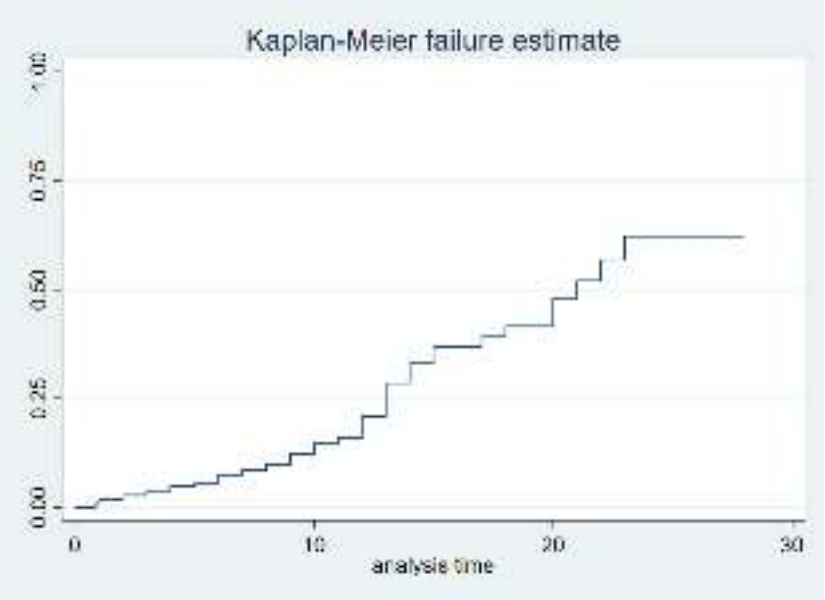


Figure7: Overall Kaplan-Meier failure estimates of neonatal surgical patients in selected Addis Ababa public hospitals from January 1 2021-December 31 2023, Ethiopia.

For each categorical variable the long rank test is used was used to determine if there is statistically significance difference between the survival function of groups. So based on the test there was a statistically significant difference in timing of getting surgical intervention, age, gestational age, weight, presence of congenital anomaly, presence of infection, prolonged preoperative NICU admission, urgency of surgery, number of previous surgical exposure, amount of blood loss, body temperature after operation, prolonged postoperative NICU admission, presence of hypoglycemia, prolonged mechanical ventilation and prolonged vasopressor usage ($p<0.05$). However, there was no significance difference among categories of residency, Apgar, sex, presence of maternal coexisting disease and ASA classification.

Table 4: median survival time and log rank test for equality of survival functions among neonatal surgical patients from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.

Variable	Category	Median Survival time (95% CI)	Log rank Test(X^2)	P-value
Residency	Rural	18(16,20)	0.41	0.5242
	Urban	20(18, 22)		
Time of getting	≤24 hr.	25(23,28)	142.95	0.0000
Surgical	24-48 hr.	22(20,24)		
Intervention	48-72 hr.	13(11,15)		
	≥72 hr.	8(5,10)		
Age of neonate	≤10 day	17(15,19)	28.19	0.0000
	10-20 day	22(19,24)		
	≥20 day	19(15,22)		
Gestational age	Pre term	10(9,12)	165.40	0.0000
	Term	27 (25, 28)		
	Post term	22(19, 24)		
Weight	Under weight	11(9,12)	134.73	0.0000
	Normal	23(22,24)		
	Over weight	18(16,20)		
Sex	Male	20(18, 23)	0.16	0.6852
	Female	18(16,20)		
Presence of	Yes	19(17,21)	6.03	0.0141
Congenital anomaly	No	17(16,18)		
APGAR	7-10	19(17,21)	2.44	0.2947
	4-6	20(18,22)		
	0-3	12(9,14)		
Presence of infection	Yes	13(11,15)	60.19	0.0000
	No	24(22,26)		
Preoperative NICU	Yes	18(16,20)	13.19	0.0003
Admission	No	20(18,22)		
Urgency of surgery	Emergency	14(12,16)	17.69	0.0000
	Elective	22(20,24)		
ASA class	ASA 2	24(23,24)	69.20	0.0000
	ASA 3	17(15,19)		
	ASA 4	13(10,15)		
Presence of maternal	Yes	18(15,21)	1.63	0.2023
Co-existing disease	No	19(17,20)		
No of	None	22(20,24)	41.86	0.0000
previous surgery	Only 1	15(13,18)		
Exposure	≥2	8(4,12)		
Duration of surgery	≤1 hr.	12(11,13)	17.52	0.0000
	1-2hr.	22(20,23)		
	2-3hr.	18(16,20)		
	≥3	16(13,19)		
Amount of blood loss	Mild	27(26,28)	120.37	0.0000
	Moderate	13(6,13)		
	Severe	9(11,14)		
Body Temperature	Hypothermia	14(12,17)	33.53	0.0000

	Normothermia	22(20,24)		
	Hyperthermia	18(16,21)		
Presence of	Yes	16(13,18)	4.35	0.0370
Hypoglycemia	No	20(19,22)		
Post op NICU	Yes	19 (17,21)	4.71	0.0300
Admission	No	17(16,18)		
On mechanical	Yes	13(11,15)	79.56	0.0000
Ventilation	No	22(20,23)		
On Vasopressor	Yes	11(9,14)	64.56	0.0000
	No	23(21,2)		

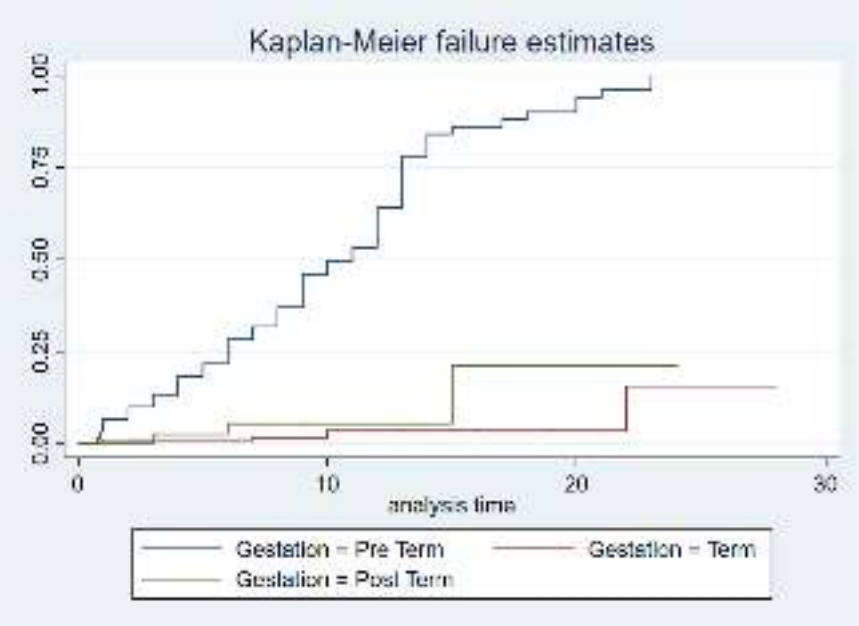


Figure 8: The Kaplan-Meier survival curves compare survival time of neonatal surgical patients with groups of gestational age from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.

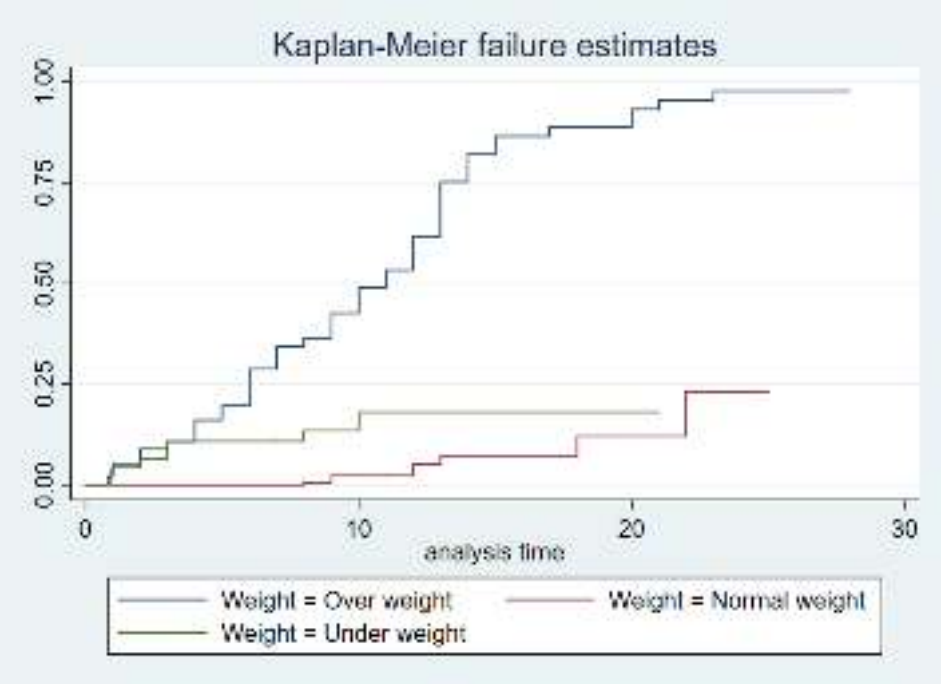


Figure9: The Kaplan-Meier survival curves compare survival time of neonatal surgical patients with groups of weight from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.

5.4. Cox proportional hazard model of neonatal surgical patients

All covariant and the whole model satisfied the proportional hazard assumption by using Schoenfeld residuals test (chi-square=21.62, global test value= 0.4215). By using Cox proportional hazard regression, the relationship between independent variable and mortality risk of neonatal surgical patients was examined. Factors gestational age, weight, time of getting surgical treatment, age of neonate, presence of congenital anomaly, Apgar score, presence of infection, preoperative NICU admission, urgency of surgery, ASA class, previous surgery exposure, amount of blood loss, Body temperature. Hypoglycemia, need of post op NICU admission, need of mechanical ventilation, and need of vasopressor had p-value of less than 0.2 on bivariate analysis.

Moreover, variables those have p-value less than 0.2 in bivariate analysis were included in multivariate Cox regression model and which had a P-value of less than 0.05 were gestational age, birth weight, need of preoperative NICU admission, Apgar score, ASA class and need of preoperative NICU admission.

Table5: multivariable cox regression analysis for predictors of mortality among neonatal surgical patients in Addis Ababa public hospitals from January 1 2021- December 312023.

Variable	Category	Survival Status		Crude HR(95% CI)	Adjusted HR(95% CI)	P-value
		Censored	Event			
Time of getting surgical treatment	≤24 hr.	144	6	**1**		
	24-48 hr.	110	8	1.98(0.64, 6.14)	1.24(0.31, 5.10)	0.765
	48-72 hr.	23	46	14.39(5.55, 37.29)	1.69(0.45, 6.32)	0.429
	≥72 hr.	2	17	42.69(14.91,121.8)	3.44(0.71, 16.68)	0.125
Age of neonate	≤10 day	79	63	6.77(1.64, 27.89)	4.41(0.59,32.52)	0.145
	10-20 day	153	12	1.51(0.33 ,7.01)	2.55(0.30, 21.60)	0.389
	≥20 day	47	2	**1**		
Gestational age	Pre term	7	68	29.01(12.45, 67.59)	6.36(1.77, 22.81)	0.004**
	Term	236	6	**1**		
	Post term	36	3	2.42(0.60, 9.69)	2.53(0.49, 13.05)	0.270
Weight	Under weight	9	60	4.63(1.67, 12.83)	5.47(1.55, 19.24)	0.008*
	Normal	226	10	**1**		
	Over weight	44	7	20.95(9.9, 44.34)	1.44(0.55, 3.74)	0.445
Presence Of Congenital anomaly	Yes	160	64	2.73(1.17, 6.39)	1.38(0.41, 4)	0.575
	No	119	13	**1**		
APGAR	7-10	147	59	**1**		
	4-6	120	17	0.65(0.37, 1.13)	0.63(0.29, 1.33)	0.208
	0-3	12		0.71(0.09,5.18)	25.5(1.91,332.6)	0.013*
Presence of infection	Yes	37	57	6.31(3.68,10.84)	2.09(0.97,4.78)	0.065
	No	242	20	**1**		
Preoperative NICU Admission	Yes	93	56	3.00(1.80, 4.99)	2.70(1.38, 5.73)	0.005*
	No	186	21	**1**		
Urgency of surgery	Emergency	52	32	2.76(1.67, 4.57)	1.37(0.59 , 2.99)	0.513
	Elective	227	45	**1**		
ASA class	ASA 2	215	3	**1**		
	ASA 3	64	54	19.37(5.98, 62.76)	4.95(1.01, 24.27)	0.049*
	ASA 4	0	20	36.92(10.84,125.6)	1.68(0.29, 9.86)	0.563
No of previous surgery	None	252	44	**1**		
	Only 1	26	24	2.97(1.72,5.81)	0.7(0.56, 1.26)	0.745
Exposure	≥2	1	9	7.60(3.45, 16.73)	0.9(.28, 2.79)	0.826
Amount of blood loss	Mild	250	6	**1**		
	Moderate	28	60	35.14(12.96, 95.31)	2.5(0.88, 7.62)	0.083
	Sever	1	11	20.52(8.75, 48.09)	3.3(0.83, 13.11)	0.088
Body Temperature	Hypotermia	22	41	5.66(2.94, 10.94)	1.8(0.57, 2.49)	0.173
	Normotermia	187	15	**1**		
	Hyperthermia	69	21	2.69(1.33, 5.41)	0.97(0.49, 2.49)	0.951
Hypoglycemia	Yes			1.77(1.02, 3.07)	0.81(0,38, 1.73)	0.601
	No			**1**		
Post op NICU Admission	Yes	190	71	2.63(1.05, 6.62)	0.19(0.05, 0.71)	0.021*
	No	89	6	**1**		
On mechanical Ventilation	Yes	20	58	9.01(5.01, 16.18)	1.15(0.71, 2.8)	0.763
	No	171	14	**1**		
On Vasopressor	Yes	9	40	5.95(3.62, 9.81)	1.6(0.68, 3.3)	0.183
	No	182	32	**1**		

Hint: *=Significant p<0.05, **Significant p<0.005

5.5 Interpretation of multivariate in terms of Adjusted Hazard Ratio

Keeping all other covariates constant pre term neonatal surgical patients had approximately 6 times likely to die (AHR=6.3, 95% CI: 1.77, 22.81) than term neonates. The risk of neonatal surgical patient was 5.47 times greater for neonates born with low birth weight than for neonates born with normal birth weight (AHR=5.47, 95% CI: 1.55, 19.24). The hazard rate of mortality among neonatal surgical patients with severe Apgar score (0-3) was more than 25 times than those neonates with normal Apgar score (7-10) (AHR=25.52, 95% CI: 1.91, 332.6).

The mortality hazard of neonates preoperatively admitted to NICU was approximately 3 times higher than neonates not admitted in NICU (AHR=2.70, 95% CI, 1.38, 5.73). The hazard rate of death for patients with ASA 3 was 4.97 times higher than ASA 2 neonatal surgical patients (AHR=4.97, 95% CI: 1.01, 24.27).

The mortality hazard of neonates postoperatively not admitted to NICU was approximately 81% greater than neonates admitted in NICU (AHR=0.19, 95% CI: 0.05, 0.71).

CHAPTER SIX: DISCUSSION

The overall incidence of mortality among neonatal surgical patients in this study from 2021-2023 was 21.72% with 95% confidence interval of (0.1732 - 0.2687). In this study we found that factors such as the gestational age and weight of neonate, Apgar score, ASA class, preoperative NICU admission, and postoperative NICU stay for prolonged period were significantly linked to mortality among neonatal surgical patients.

This result is consistent with the finding of studies done in South Africa, Egypt and Black Lion Specialized hospital(22,25,34). The possible reason might be these countries have limited access to specialized healthcare services, limited resources and infrastructure, healthcare system constraints.

However this finding is greater than the study which was done in Ghana, Bangladesh, USA and Japan(3,7,21,38). This deference might be happen due to study design, sample size, limited use of medication, parenteral nutrition. In Bangladesh they collect data from death registration, in Ghana the study was conducted in NICU, single center and used relatively large sample size compared to our study. USA the study participants were preterm neonates(88,89). Additionally USA and Japan are grouped under high income countries so they might use advanced equipment and availability of parenteral nutrition.

In contrary our study result is lower compare with, Nigeria, Rwanda(32,33). The above discrepancy might happen due to study design and sample size. In Nigeria they only use 45 neonates and select only emergency cases; in Rwanda they used large sample size around 1313(32).

In our study neonates with low birth weight were shown to have increased risk of mortality among neonatal surgical patients. This finding is similar to the study done in USA(32,90). The possible reason might be low birth weight is associated with intrauterine growth retardation, prematurity, inhibited growth and development(91).

In this study preterm neonates were strongly associated with neonatal surgical mortality. This result is consistent with the study done in USA(71). This might be due to Premature populations had higher risk of sepsis, pneumonia, bleeding requiring transfusion(71).

Our study also revealed that neonates with low Apgar score had significantly higher mortality risk than compared with neonates had higher Apgar score. This finding is similar with the study done in china(92). This may be associated with sever neurological morbidity and low Apgar score that can occur due to birth asphyxia so the neonates might develop global organ damage(93,94).

Neonatal surgical patients preoperatively admitted in NICU had high risk of mortality than neonates not admitted to NICU. This finding is similar with study done in Iraq(95).The possible explanation might be preoperative NICU admitted patients may be premature, low birth weight, have respiratory distress syndrome, may have congenital malformation(96).

Neonatal surgical patients postoperatively admitted in NICU for prolonged time had low risk of mortality than neonates not admitted to NICU. This finding is similar with the study done in India(87). The possible explanation might be neonates admitted in NICU after operation gets CVS and respiratory support, with good follow up. In contrast our study contradicted with the study in Canada, they explained that postop NICU admission increased the risk of infection and leads to mortality(86).

Our study also showed that higher ASA class would affect the survival status of neonatal surgical patients compared ASA II. Our result is consistent with Portugal(55). The possible justifications are higher the American Society of Anesthesiologists (ASA) physical status classification system assigns a score based on the patient's overall health. Higher ASA classes (ASA III-V) indicate greater surgical risk and higher mortality rates(97,98).

6.1. Limitation and Strength of the study

6.1.1. Strength of the study

- The information was collected from admissions over three consecutive years using proportional allocation, potentially boosting the number of events and reducing variability.
- Another key strength of the study was use of multicenter study.

Limitation of the study

- The study was retrospective design so important factors like type intraoperative complication, presence of preoperative dehydration, may not be appropriately documented.
- Since it was secondary data, we were not able to confirm whether the principal surgeon was a senior or a resident who operated the neonate.

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATION

7.1. Conclusion

Neonatal surgical mortality is high. This study found that the following factors are independently contributed for neonatal surgical patients to die: low birth weight, premature birth, admission to the neonatal intensive care unit (NICU), ASA class, and low Apgar score.

7.2. Recommendation

To reduce the mortality of neonates and improve the overall health outcomes of newborns after surgery, we will recommend implementing the following actions for health professional, stakeholders, and researchers.

For Health professionals and Stakeholders

- ✓ Detail preoperative Assessment and optimization of ASA 3 patients before operation.
- ✓ Give special attention for neonates admitted in NICU before and after operations.
- ✓ Develop different guideline to manage preterm and underweight neonates in perioperative period.

For researchers

In this study we identified the major predictors of mortality after neonatal surgery, so for researchers we will recommend to

- ✓ Conduct research about neonates admitted in NICU before operation and after operations.
- ✓ Conduct research on the prolonged effect of low Apgar score on neonates who needs surgery.
- ✓ Conduct a prospective cohort study to assess the impact of surgery on preterm and underweight neonates.

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Annex Ⅰ check list

English version checklist tool.

This data extraction checklist is prepared to collect socio-demographic, preoperative, intraoperative and post-operative information that is important for assessing outcomes and predictors of neonatal surgical patient mortality at Tikur Anbessa Hospital, Zewuditu Memorial Hospital, and St. Paul Hospital Millennium Medical College. All this information was retrieved from individual patient cards without mentioning the names of clients. This information was collected by health care providers (BSc anesthetist). **Contact information**

Phone: +251932359875 and **+251910029297**

Data collection date…….Month…….year
Name of Hospital……..
Name of data collector…….signature…….
Name of supervisor……signature……
Code no……

Table6: Data collection checklist for conducting of study on survival status and predictors of mortality among neonatal surgical patients in selected Addis Ababa public hospitals, Ethiopia 2023/24

No.	Factors	Possible Answers
1	Residency	1. Rural 2.Urban
2	Time of getting surgical intervention	1. ≤24 hours 2.24-48 hours 3.48-72 hours 4. ≥72 hours
3	Age in days	1. ≤ 10 Days 2. 10-20 days 3. ≥20 days
4	Gestational age	1. Preterm 2. Term 3. Post term
5	Maternal coexisting disease	1.Yes 2.No
6	Birth weight	1. Under weight 2. Normal weight 3. Over weight
7	Sex	1. Male 2. Female
8	Residency	1. Rural 2. Urban
9	Is there any presence of congenital Anomaly	1. Yes

		2. No
10	If your answer is yes for the above question types of congenital Anomaly	1.ARM 2.CDH 3.CHD 4.CHD and Neural tube defect 5.CHD and TEF 6.Colonic Atresia 7.Gastroschiasis 8.Hydrocephalus 9.Neural tube defect 10.Omphalocel 11.TEF with EA 12. Other Specify……
11	Apgar Score	1.7-10 2.4-6 3.0-3
12	Urgency of surgery	1.Elective 2. Emergency
13	Preoperative NICU admission	1.Yes 2. No
14	Presence of maternal coexisting disease	1.Yes 2.No
15	Presence of infection	1.Yes 2. No
16	Indication for Operation	Short answer…
17	ASA Classification	1. ASA Ⅰ 2. ASA Ⅱ 3. ASA Ⅲ 4. ASA Ⅳ 5.ASA Ⅴ
18	Duration of Surgery	1. ≤1 hour 2.1-2 hour 3.2-3 hour 4. ≥3 hour
19	Amount of blood loss	1.Mild blood loss 2.Moderate blood loss 3. Sever blood loss
20	Number of surgery	1. None 2. 1 previous exposure 3. 2 and above previous exposure
21	Preoperative NICU admission	1. Yes 2. No

22	Body temperature	1. Hypothermic 2. Normothermic 3. Hyperthermic
23	Presence of low blood sugar(RBS) after operation	1. Yes 2. No
24	Admission to NICU	1.Yes 2.No
25	On mechanical ventilation	1.Yes 2.No
26	On inotropic	1.Yes 2.No
27	Last status of the neonate after operation	1. Alive 2. Died 3. Referred to other hospital 4.Discharged 5.Against medical treatment
28	Survival time after operation	In day (…)

Annex Ⅱ: Information sheet

Title of research project: Survival Status and predictors of mortality among neonatal surgical patients from January 2021-December 2023 in selected Addis Ababa public hospitals, Ethiopia. Multicenter, Retrospective Cohort Study.

Name of Investigator: Wasihun Aragie (BSC Anesthetist)

Name of Organization: Addis Ababa University, College of Health Science, School of Medicine, Department of Anesthesia**.**

Name of Sponsor: Addis Ababa University

Introduction: This information sheet is designed for administrative and coordinator staff at Black Lion Specialized Hospital, Zewuditu Memorial Hospital, and St. Paul Hospital Millennium Medical College. The purpose of this document is to inform the relevant offices of the research objectives, data collection methods, and to obtain their permission to conduct the research.

Purpose of the Research Project: The purpose of this study is to determine the survival rates and identify factors that contribute to mortality among neonates that undergo surgical procedures in selected public hospitals in Addis Ababa, Ethiopia, from January 1, 2021 to December31, 2023.

Procedure: To achieve this goal, relevant data was obtained from the medical records of neonates, specifically focusing on information related to the study.

Risk and /or Discomfort: The collection of data from medical records posed no risk to the patients, as no identifying information such as names or addresses was recorded. The information was kept confidential and stored in a secure location. The data was only used for the purpose of this study and was not shared or used for any other purpose.

Benefits: While the study does not directly benefit individuals whose medical records are involved, there is a clear indirect benefit for program participants. By informing the development of a predictive strategy, the study contributes to better care and treatment for survivors and future

newborns. Ultimately, the primary direct benefit of the study is to healthcare organizers and administrators, who can use the findings to improve their services and programs.

Confidentiality: To ensure the confidentiality of the information, the study collected data from medical charts without including patient names. The gathered data was kept private and stored in a secure file cabinet. Additionally, the information was only accessible to the investigator, and it was protected by a locked system with a password-protected computer. This ensures that the data remains confidential and secure.

Person to contact: This study was revised and approved by Addis Ababa University, College of Health Science, School of Medicine, and Department of Anesthesia. If you have any questions or concerns, please feel free to contact the investigator or advisors at any time. They are available to address any questions you have

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Annex Ⅲ: Tables and graphs

Table 7: Multicollinearity check for each variable

Variable	VIF	1/VIF
Ventilation	1.96	0.509352
Blood	1.84	0.542739
ASA	1.75	0.571905
Vasopressor	1.71	0.584416
Gestation	1.65	0.607460
Surgery	1.53	0.653930
Weight	1.50	0.666099
Infection	1.38	0.722124
Pre-op NICU Admission	1.29	0.777631
Congenital	1.26	0.792186
Age	1.24	0.805669
Post op NICU Admission	1.22	0.821215
Urgency	1.21	0.827798
Maternal	1.16	0.863141
Temperature	1.09	0.913564
APGAR	1.08	0.921817
Hypoglycemia	1.06	0.941622
Mean VIF	**1.41**	

Table8: Schonfield residual test

Variable	Rho	chi^2	Df	Prob>chi2
Residancy	-0.00262	0.00	1	0.9807
Time	-0.22799	5.88	1	0.0153
Age	-0.06811	0.34	1	0.5606
Gestation	-0.07445	1.11	1	0.2922
Weight	-0.08277	1.02	1	0.3119
Sex	0.19817	4.36	1	0.0369
Congenital	0.23956	5.26	1	0.0218
APGAR	-0.17357	2.93	1	0.0867
Infection	-0.13473	1.49	1	0.2219
NICU	0.00569	0.00	1	0.9554
Urgency	-0.16510	2.11	1	0.1468
ASA	-0.09128	0.83	1	0.3611
Maternal	0.12573	1.56	1	0.2109
Surgery	0.00967	0.01	1	0.9250
Duration	0.17720	2.80	1	0.0941
Blood	-0.03668	0.11	1	0.7373
Temperature	0.09514	1.03	1	0.3092
Hypoglycemia	-0.14737	2.33	1	0.1270
NICU	0.09473	0.80	1	0.3704
Ventilation	0.01853	0.03	1	0.8673
Vasopressor	0.16476	2.09	1	0.1479
global test		**21.62**	**21**	**0.4215**

Table9: Socio-demographic factors of neonatal surgical patients in Addis Ababa public hospitals from January 2021 to December 2023, Ethiopia 2024

Variable	All Episodes (%) n=290(100)	Censored, n (%) n= 227 (78.28)	Event, n (%) n= 63 (21.72)
Residency			
Rural	74(25.52)	56(24.67)	18(28.57)
Urban	216(74.48)	171(75.33)	45(71.43)
Sex			
Male	163(56.21)	130 (57.27)	33 (52.38)
Female	127 (43.79)	97(42.73)	30(47.62)
Weight			
Under weight	47 (16.21)	40(17.62)	7(11.11)
Normal weight	187(64.48)	179(78.85)	8(12.70)
Over weight	56(19.31)	8(3.52)	48(76.19)
Age			
≤ 10 days	128(44.14)	76(33.48)	52(82.54)
Between10-20	120 (41.38)	111(48.90)	9(14.29)
≥20 days	42(14.48)	40(17.62)	2(3.17)
Gestational Age			
Pre term	60(20.6)	6(2.64)	54(85.71)
Term	192(66.21)	186(81.94)	6(9.52)
Post term	38(13.10)	35(15.42)	3(4.76)

Hint: underweight <2.5kg, normal weight 2.5-3.5 kg, overweight >3.5kg Preterm ≤37 weeks, Term 38-41 weeks post term ≥42 weeks

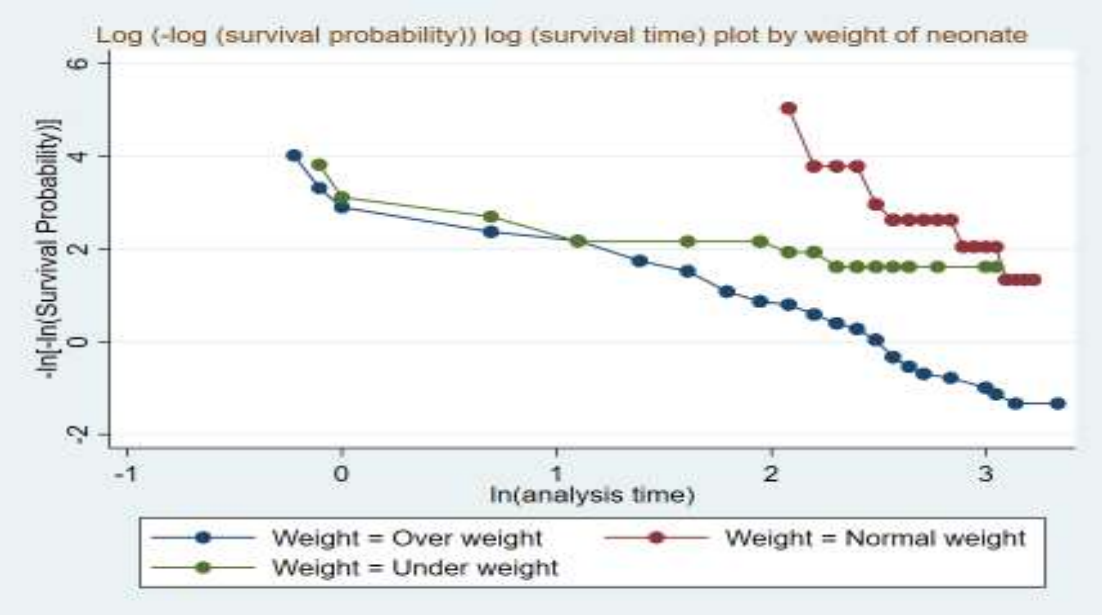
Table10: Clinical data of neonatal surgical patients in Addis Ababa public hospitals *from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.*

Variable	All Episodes (%) n=290(100)	Censored, n=227(78.37%)	Event, n=63(21.63%)
Timing of getting surgical intervention			
≤24 hr.	113(38.97)	108(47.58)	5(7.94)
24-48 hr.	102(35.17)	94(41.41)	8(12.70)
48-72 hr.	58(20.00)	23(10.13)	35(55.56)
≥72 hr.	17(5.86)	2(0.88)	15(23.81)
Presence of congenital anomaly			
Yes	209(72.07)	152(66.96)	57(90.48)
No	81(27.93)	75(33.04)	6(9.52)
Type of congenital anomaly			
None	70(24.14)	64(28.19)	6(9.52)
ARM	39(13.45)	38(16.74)	1(1.59)
CDH	6(2.07)	5(2.20)	1(1.59)
CHD	21(7.24)	12(5.29)	9(14.29)
CHD and Neural tube defect	4(1.38)	4(1.76)	0(0.00)
CHD and TEF	3(1.03)	0(0.00)	3(4.76)
Colonic Atresia	1(0.34)	1(0.44)	0(0.00)
Gastroschiasis	12(4.14)	7(3.08)	5(7.94)
Hydrocephalus	13(4.48)	10(4.41)	3(4.76)
Neural tube defect	82(28.28)	58(25.55)	24(38.10)
Omphalocel	14(4.83)	13(5.73)	1(1.59)
TEF with EA	25(8.62)	15(6.61)	10(15.87)
APGAR Score			
7-10	171(58.97)	126(55.51)	45(71.43)
4-6	111(38.28)	94(41.41)	17(26.98)
0-3	8(2.76)	7(3.08)	1(1.59)
Presence of infection			
Yes	79(27.24)	35(15.42)	44(69.84)
No	211(72.76)	192(84.58)	19(30.16)
Preoperative NICU admission			
Yes	127(43.79)	81(35.68)	46(73.02)
No	163(56.21)	146(64.32)	17(26.98)
Urgency of Surgery			
Emergency	72(24.83)	43(18.94)	29(46.03)
Elective	218(75.17)	184(81.06)	34(53.97)
American Society of Anesthesiologist Class			
ASA 2	168(57.93)	165(72.69)	3(4.76)
ASA 3	103(35.52)	62(27.31)	41(65.08)
ASA 4	19(6.55)	0(0.00)	19(30.16)
Presence of maternal coexisting disease			
Yes	103(35.52)	79(34.80)	24(38.10)
No	187(64.48)	148(65.20)	39(61.90)

Number of previous exposure to surgery			
None	234(83.15)	201(88.55)	33(52.38)
1 previous exposure	48(14.04)	26(11.45)	22(34.92)
2 and above previous exposure	8 (2.81)	0(0.00)	8(12.70)
Duration of Surgery			
Less than 1 hour	29(10.00)	26(11.45)	3(4.76)
1-2 hour	134(46.21)	123(54.19)	11(17.46)
2-3 hour	108(37.24)	71(31.28)	37(58.73)
Greater than 3 hour	19(6.55)	7(3.08)	12(19.05)
Amount of blood loss during operation			
Minor	204(70.34)	198(87.22)	6(9.52)
Sever	74(25.52)	28(12.33)	46(73.02)
Moderate	12(4.14)	1(0.44)	11(17.46)
Body temperature after operation			
Hypothermia	52(17.99)	22(9.73)	30(47.62)
Normothermia	156(53.98)	143(63.27)	13(20.63)
Hyperthermia	81(28.03)	61(26.99)	20(31.75)
Presence of low blood sugar(RBS) after operation			
Yes	65(22.41)	47(20.70)	18(28.57)
No	225(77.59)	180(79.30)	45(71.43)
Postoperative NICU admission			
Yes	220(75.86)	162(71.37)	58(92.06)
No	70(24.14)	65(28.63)	5(7.94)
Neonates on Mechanical Ventilation for prolonged time			
Yes	68(23.45)	20(8.81)	48(76.19)
No	222(76.55)	207(91.19)	15(23.81)
Neonates on vasopressor for prolonged time			
Yes	42(14.48)	9(3.96)	33(52.38)
No	248(85.52)	218(96.04)	30(47.62)

Table11: life table estimation of mortality among neonatal surgical patients

Interval		Total	Deaths	Lost	Survival	Error	[95% Conf. Int.]	
0	1	290	3	3	0.9896	0.0060	0.9681	0.9966
1	2	284	2	1	0.9826	0.0077	0.9588	0.9927
2	3	281	3	0	0.9721	0.0097	0.9450	0.9860
3	4	278	3	2	0.9616	0.0114	0.9317	0.9786
4	5	273	3	2	0.9510	0.0128	0.9187	0.9707
5	6	268	2	10	0.9438	0.0137	0.9098	0.9652
6	7	256	5	6	0.9251	0.0157	0.8874	0.9505
7	8	245	3	21	0.9133	0.0170	0.8733	0.9411
8	9	221	3	35	0.8998	0.0184	0.8570	0.9303
9	10	183	5	26	0.8733	0.0213	0.8246	0.9093
10	11	152	4	18	0.8489	0.0240	0.7948	0.8897
11	12	130	2	25	0.8345	0.0257	0.7769	0.8783
12	13	103	6	25	0.7791	0.0324	0.7075	0.8353
13	14	72	7	18	0.6926	0.0422	0.6014	0.7669
14	15	47	3	9	0.6437	0.0477	0.5419	0.7285
15	16	35	2	2	0.6058	0.0519	0.4963	0.6987
16	17	31	0	3	0.6058	0.0519	0.4963	0.6987
17	18	28	1	2	0.5834	0.0546	0.4688	0.6815
18	19	25	1	2	0.5591	0.0575	0.4394	0.6629
19	20	22	0	4	0.5591	0.0575	0.4394	0.6629
20	21	18	2	3	0.4913	0.0676	0.3539	0.6149
21	22	13	1	2	0.4504	0.0733	0.3042	0.5859
22	23	10	1	1	0.4030	0.0795	0.2489	0.5521
23	24	8	1	1	0.3492	0.0851	0.1908	0.5127
24	25	6	0	3	0.3492	0.0851	0.1908	0.5127
25	26	3	0	2	0.3492	0.0851	0.1908	0.5127
28	29	1	0	1	0.3492	0.0851	0.1908	0.5127



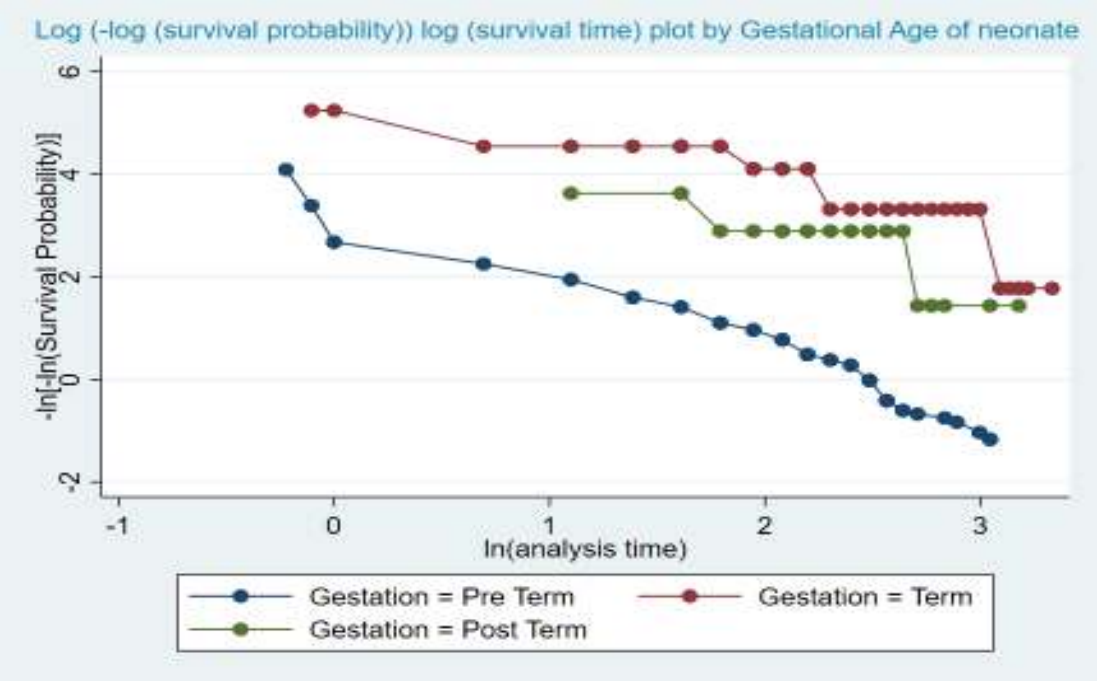
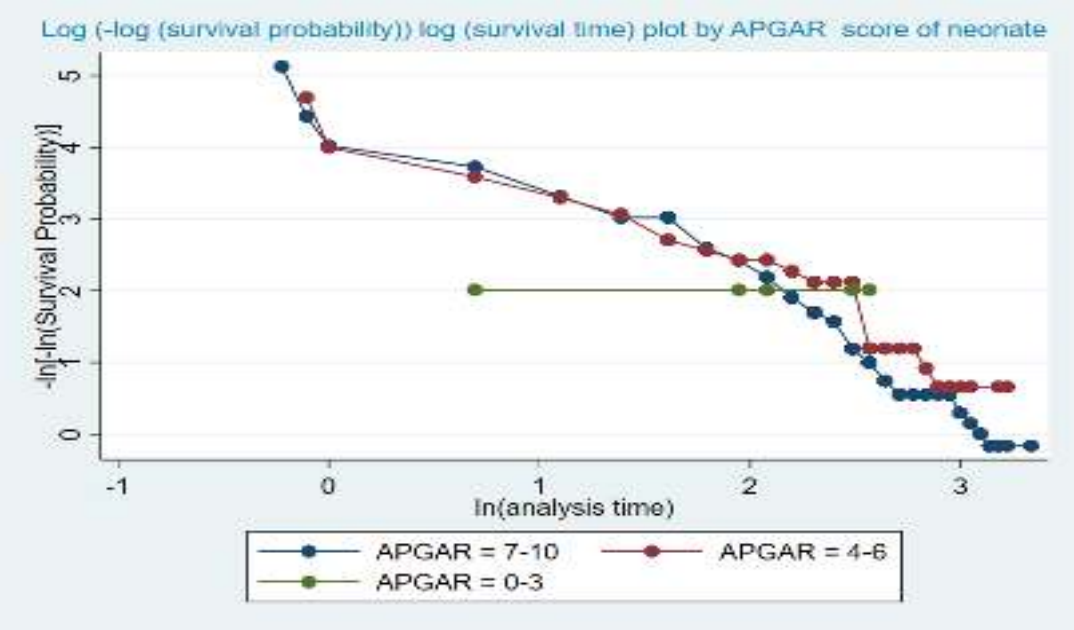


Figure10: Log (-log (survival probability)) log (survival time) plot by weight and Gestational Age of neonate respectively from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.



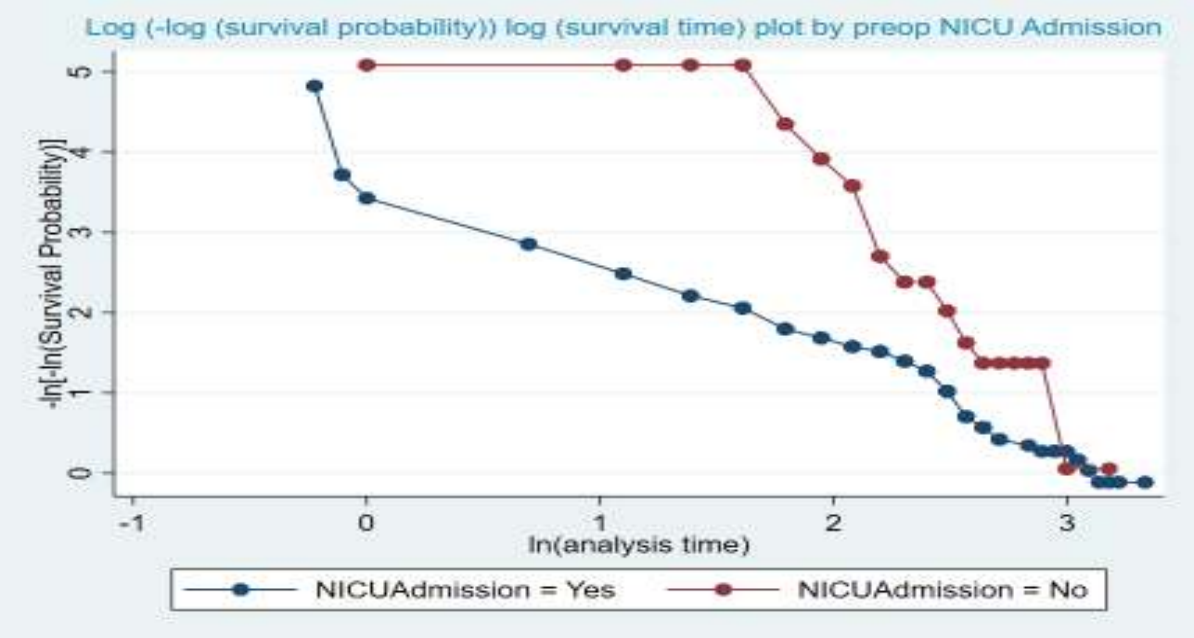


Figure11: Log (-log (survival probability)) log (survival time) plot by Apgar score and preoperative NICU status of neonate respectively from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.

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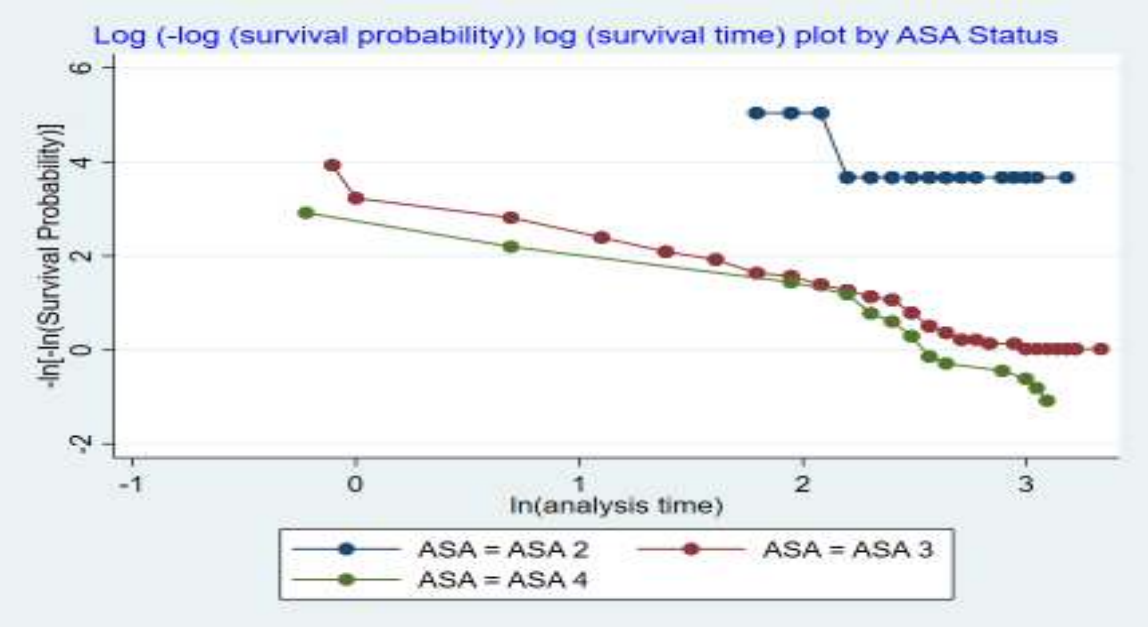

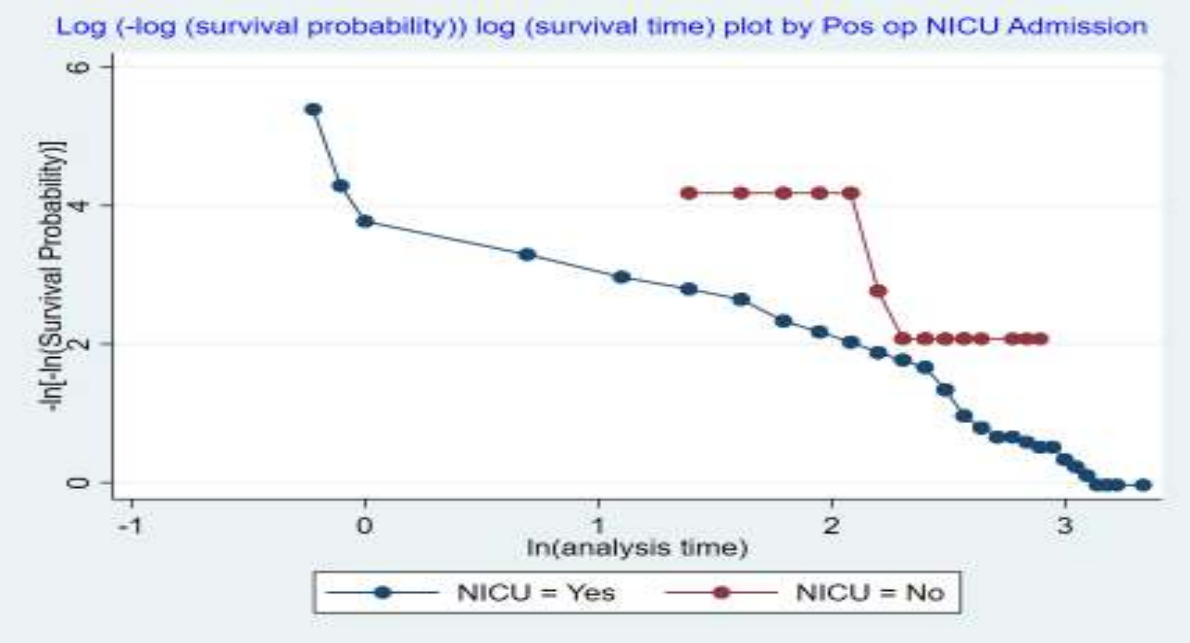

Figure12: Log (-log (survival probability)) log (survival time) plot by ASA Status and Post-operative NICU admission of neonate respectively from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.

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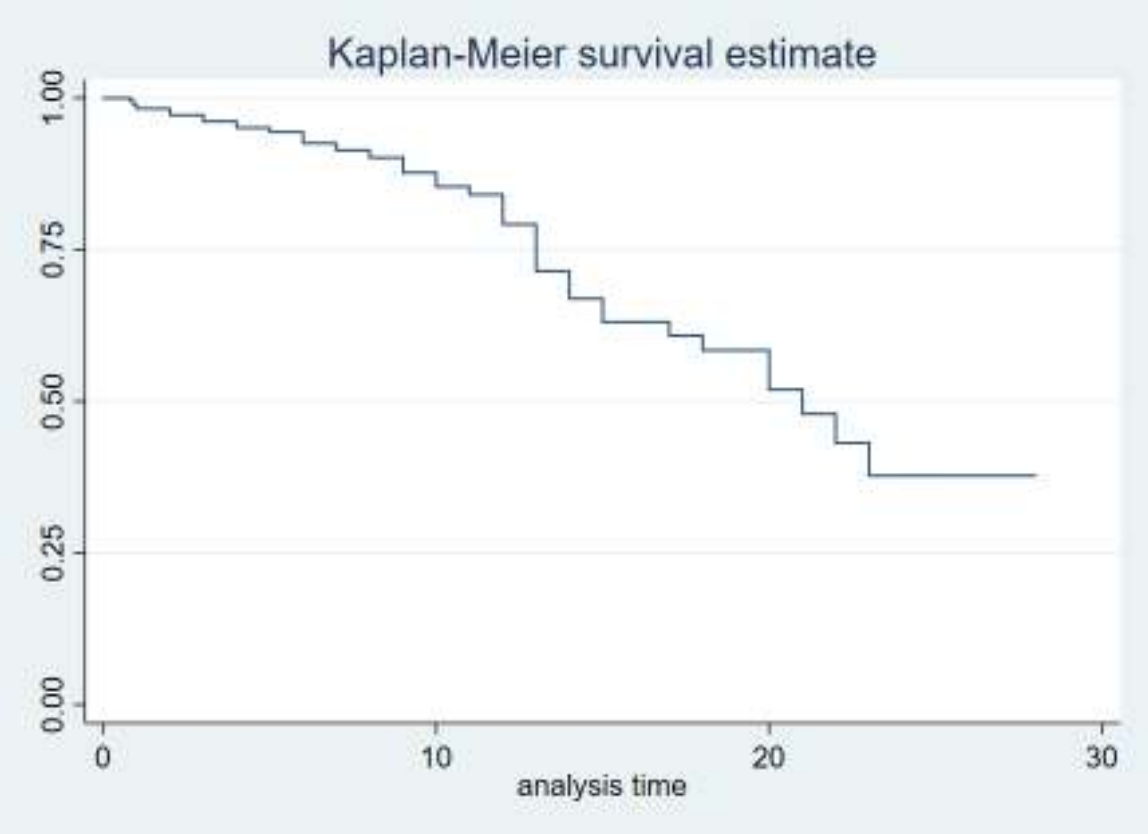


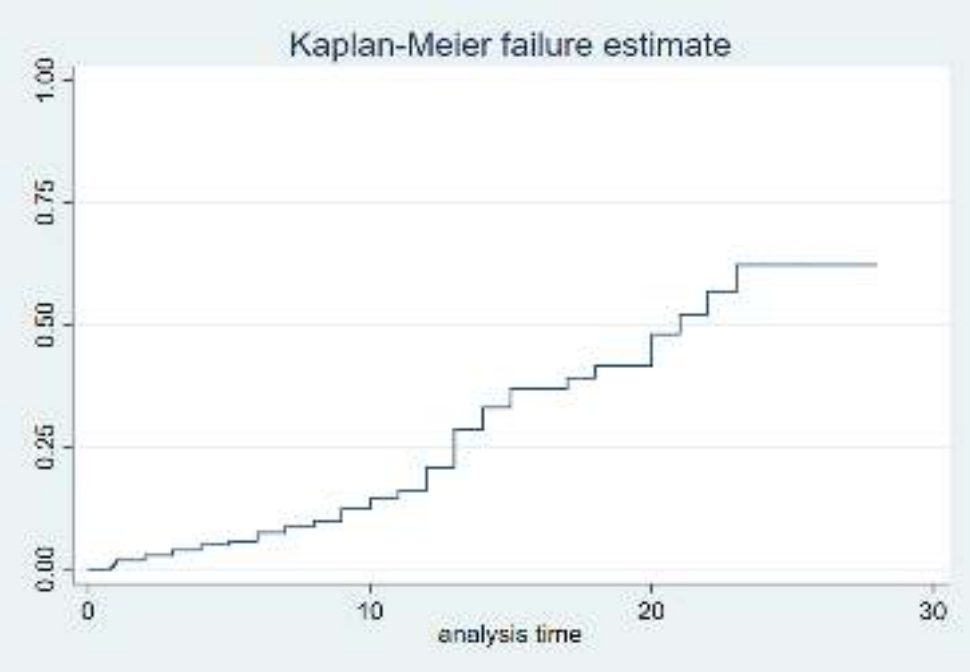
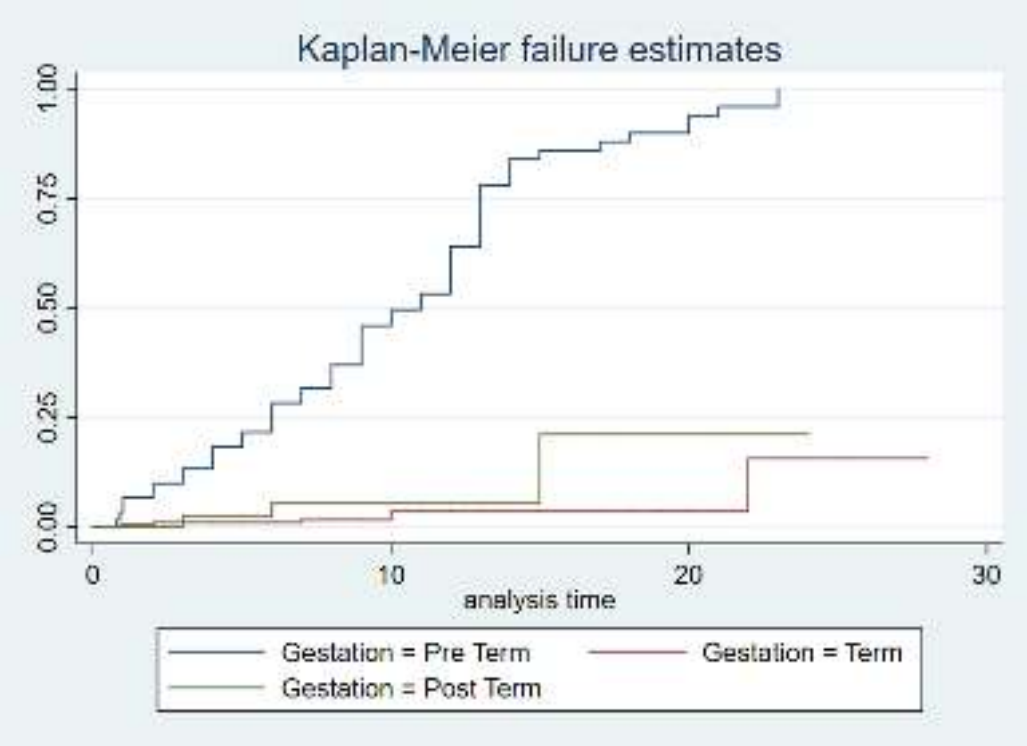


Figure13: Overall Kaplan-Meier Survival and failure estimate of neonatal surgical patients from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.



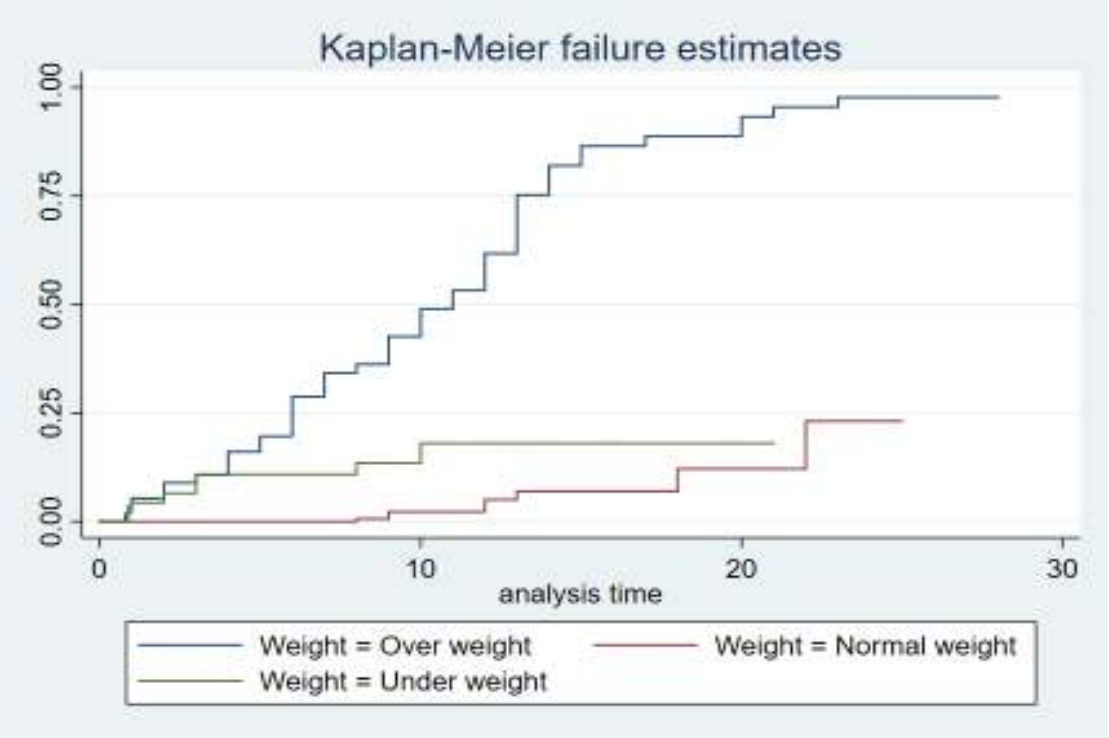
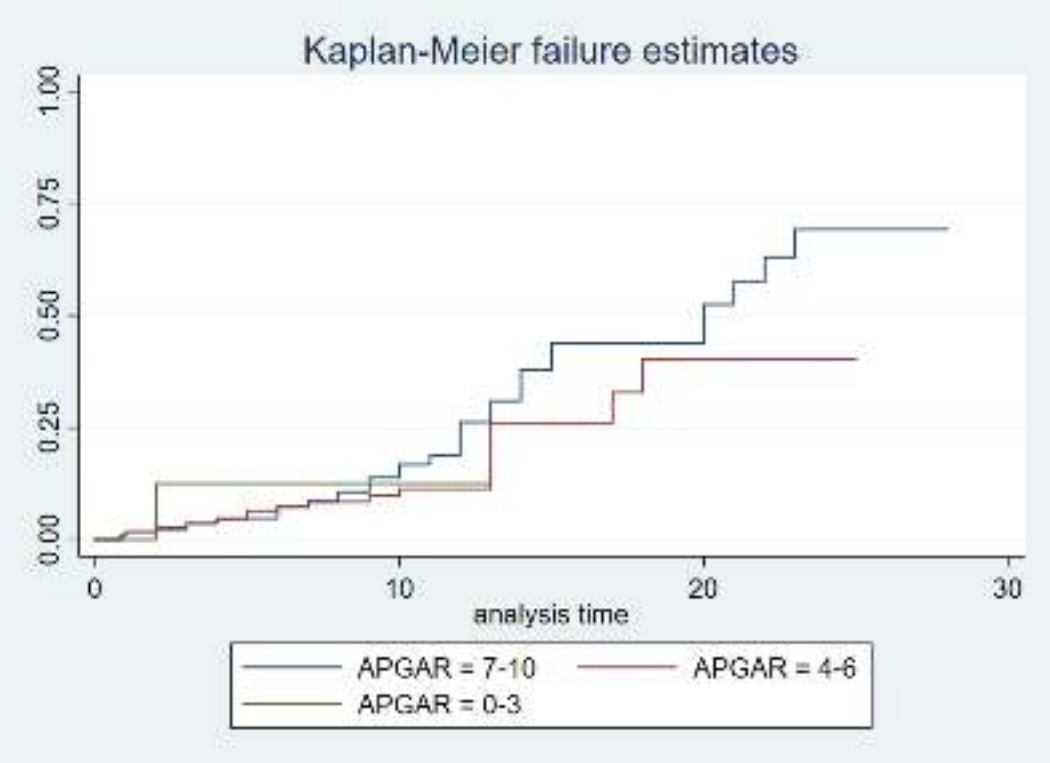


Figure14: Kaplan-Meier failure estimate of neonatal surgical patients based on gestational age and weight of neonate from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.



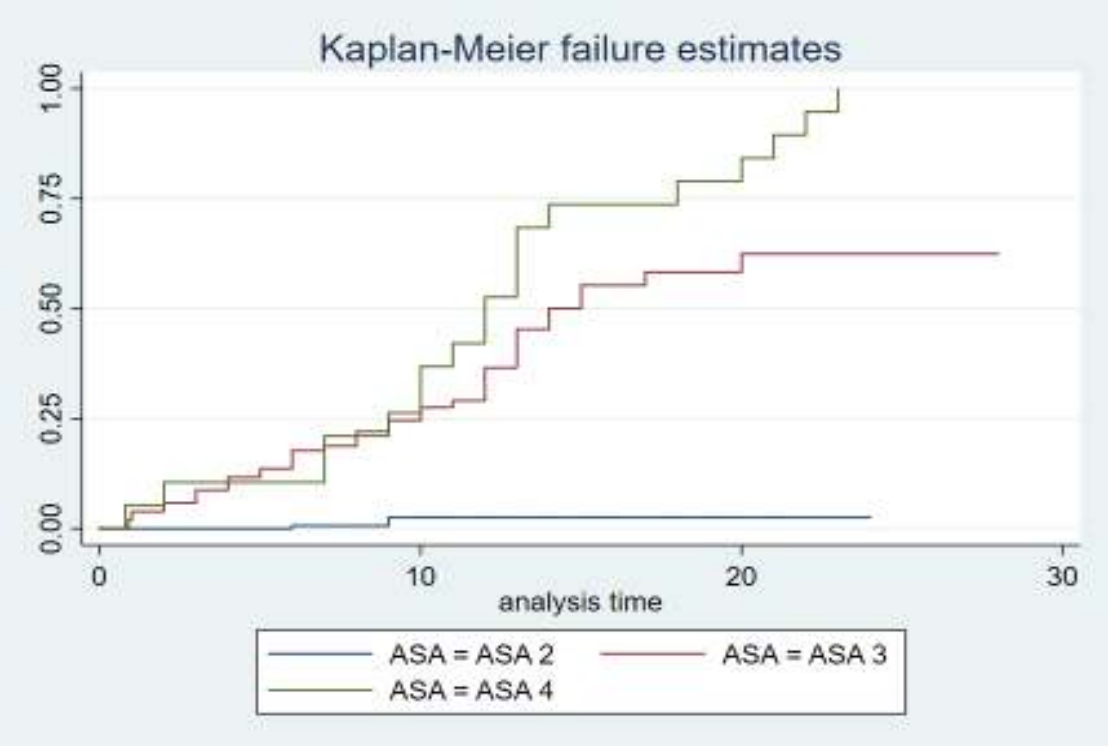
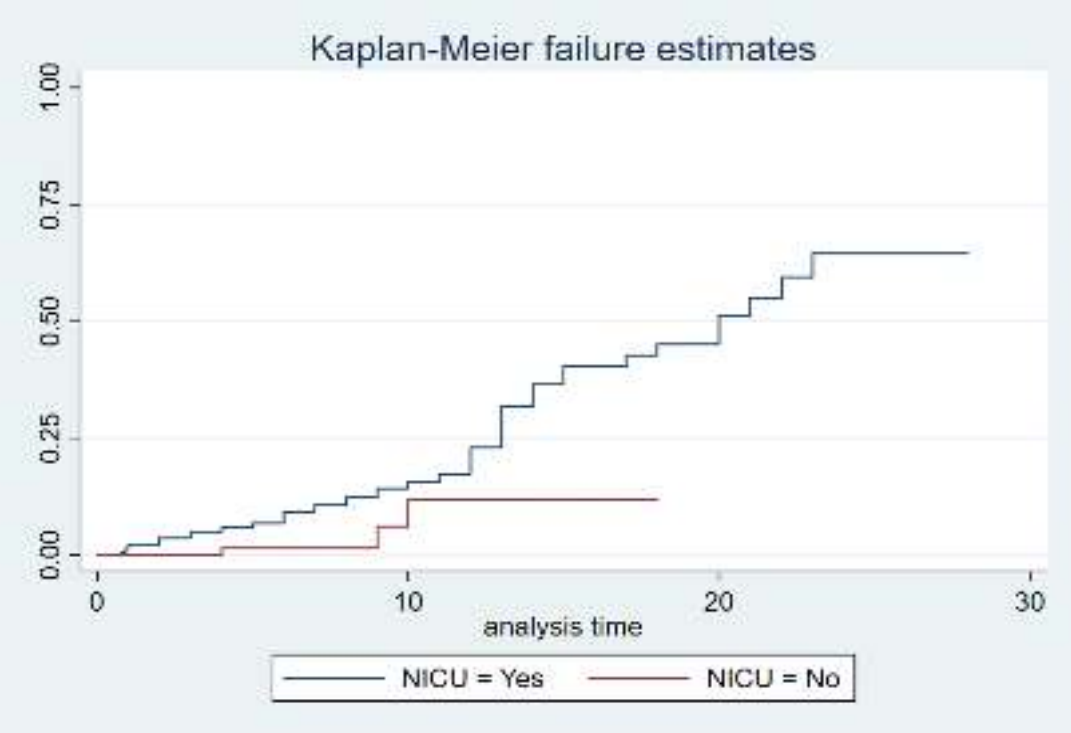


Figure15: Kaplan-Meier failure estimate of neonatal surgical patients based on Apgar score and ASA class of neonate respectively from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.



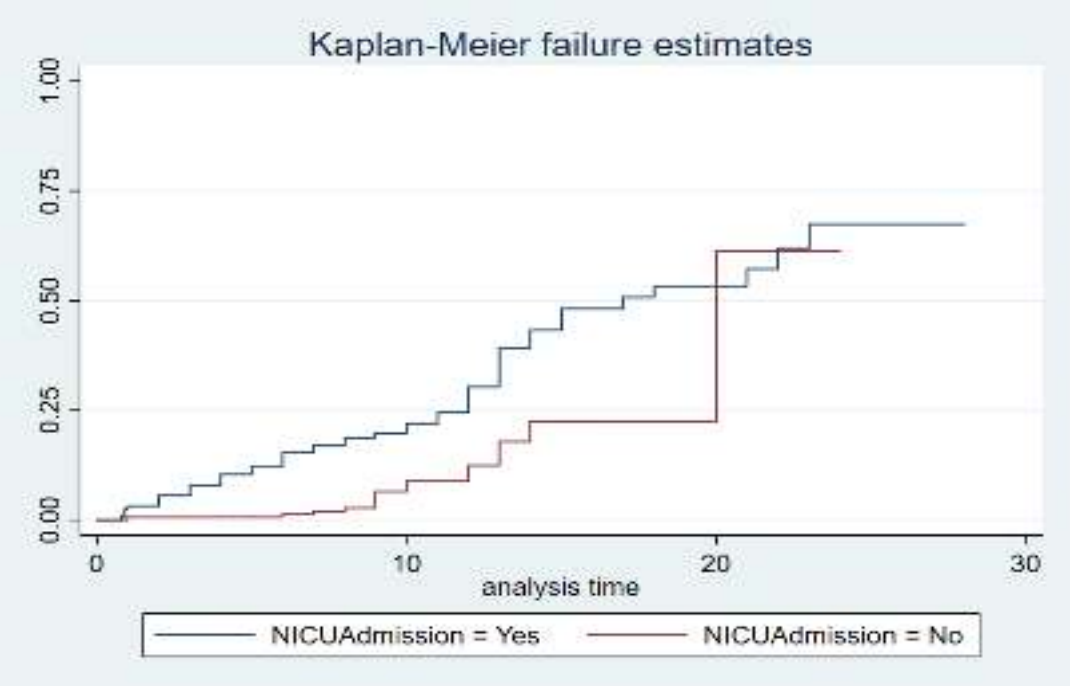
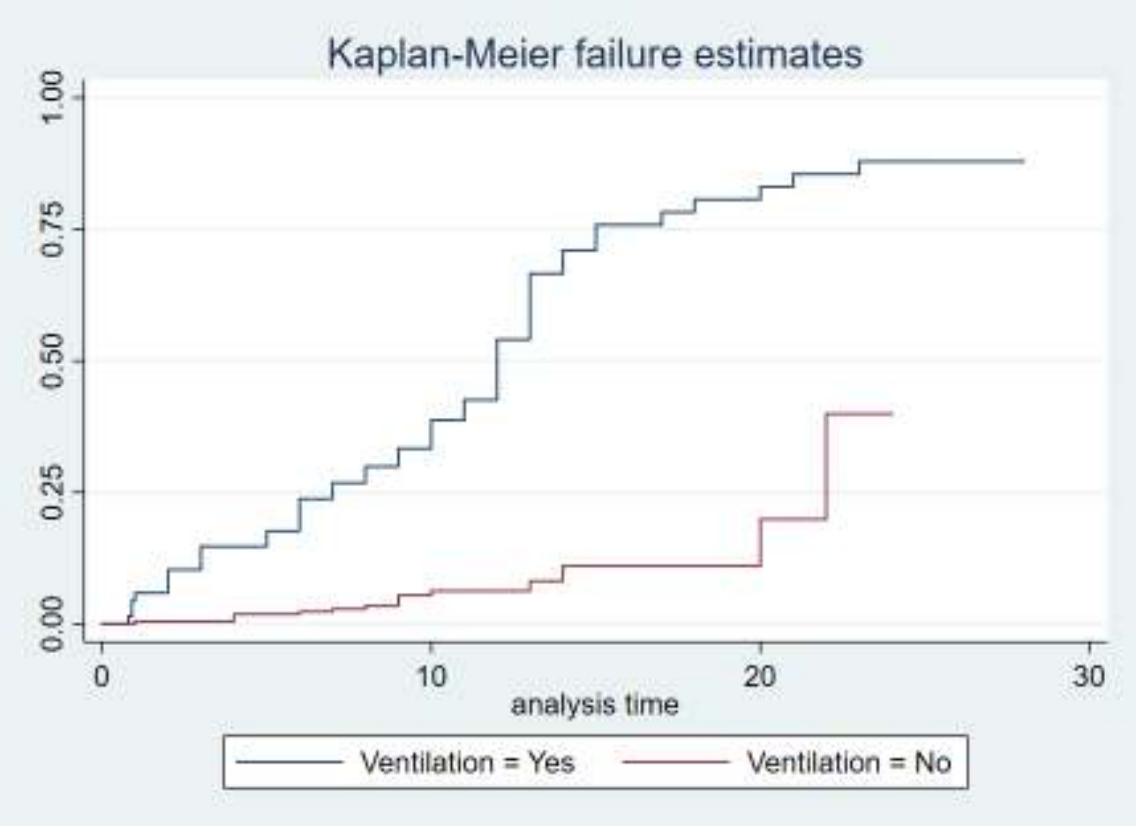


Figure16: Kaplan-Meier failure estimate of neonatal surgical patients based on postop and preop NICU admission of neonate respectively from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.



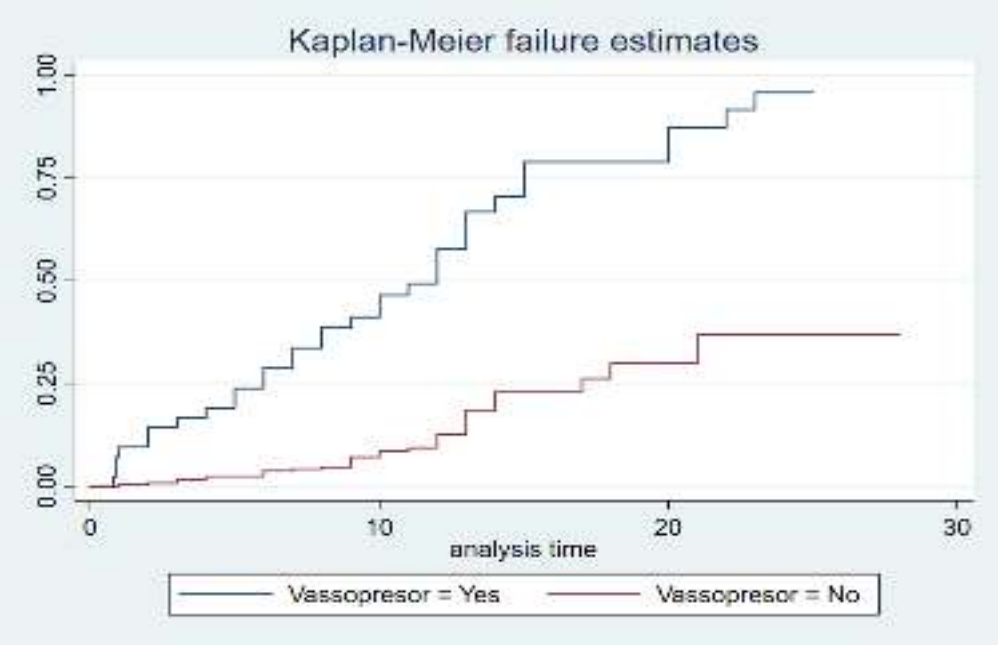


Figure17: Kaplan-Meier failure estimate of neonatal surgical patients based on postop mechanical ventilation and vasopressor of neonate respectively from January 1 2021 to December 31 2023 in Addis Ababa public hospitals, Ethiopia.

Table12: multivariable cox regression analysis for predictors of mortality among neonatal surgical patients in Addis Ababa public hospitals from January 2021- December 2023.

Variable	Category	Survival Status		Crude HR(95% CI)	P-value	Adjusted HR(95% CI)	P-value
		Censored	Event				
Time of getting surgical treatment	≤24 hr.	144	6	**1**			
	24-48 hr.	110	8	1.98(0.64, 6.14)	0.235	1.24(0.31, 5.10)	0.765
	48-72 hr.	23	46	14.39(5.55, 37.29)	0.000	1.69(0.45, 6.32)	0.429
	≥72 hr.	2	17	42.69(14.91,121.8)	0.000	3.44(0.71, 16.68)	0.125
Age of neonate	≤10 day	79	63	6.77(1.64, 27.89)	0.008	4.41(0.59,32.52)	0.145
	10-20 day	153	12	1.51(0.33 ,7.01)	0.595	2.55(0.30, 21.60)	0.389
	≥20 day	47	2	**1**			
Gestational age	Pre term	7	68	29.01(12.45, 67.59)	0.000	6.36(1.77, 22.81)	0.004**
	Term	236	6	**1**			
	Post term	36	3	2.42(0.60, 9.69)	0.211	2.53(0.49, 13.05)	0.270
Weight	Under weight	9	60	4.63(1.67, 12.83)	0.003	5.47(1.55, 19.24)	0.008*
	Normal	226	10	**1**			
	Over weight	44	7	20.95(9.9, 44.34)	0.000	1.44(0.55, 3.74)	0.445
Presence Of Congenital anomaly	Yes	160	64	2.73(1.17, 6.39)	0.020	1.38(0.41, 4)	0.575
	No	119	13	**1**			
APGAR	7-10	147	59	**1**			
	4-6	120	17	0.65(0.37, 1.13)	0.129	0.63(0.29, 1.33)	0.208
	0-3	12		0.71(0.09,5.18)	0.737	25.52(1.91,332.6)	0.013 *
Presence of infection	Yes	37	57	6.31(3.68,10.84)	0.000	2.09(0.97,4.78)	0.065
	No	242	20	**1**			
Preoperative NICU Admission	Yes	93	56	3.00(1.80, 4.99)	0.000	2.70(1.38, 5.73)	0.005*
	No	186	21	**1**			
Urgency of surgery	Emergency	52	32	2.76(1.67, 4.57)	0.001	1.37(0.59 , 2.99)	0.513
	Elective	227	45	**1**			
ASA class	ASA 2	215	3	**1**			
	ASA 3	64	54	19.37(5.98, 62.76)	0.000	4.95(1.01, 24.27)	0.049*
	ASA 4	0	20	36.92(10.84,125.6)	0.000	1.68(0.29, 9.86)	0.563
No of previous surgery Exposure	None	252	44	**1**			
	Only 1	26	24	2.97(1.72,5.81)	0.000	0.7(0.56, 1.26)	0.745
	≥2	1	9	7.60(3.45, 16.73)	0.000	0.9(.28, 2.79)	0.826
Amount of blood loss	Mild	250	6	**1**			
	Moderate	28	60	35.14(12.96, 95.31)	0.000	2.5(0.93, 19.44)	0.083
	Sever	1	11	20.52(8.75, 48.09)	0.000	3.3(1.17, 11.34)	0.088
Body Temperature	Hypothermia	22	41	5.66(2.94, 10.94)	0.000	1.8(0.57, 2.49)	0.173
	Normothermia	187	15	**1**			
	Hyperthermia	69	21	2.69(1.33, 5.41)	0.006	0.97(0.49, 2.49)	0.951
Hypoglycemia	Yes			1.77(1.02, 3.07)	0.042	0.81(0,38, 1.73)	0.601
	No			**1**			
Post op NICU Admission	Yes	190	71	2.63(1.05, 6.62)	0.039	0.19(0.05, 0.71)	0.021*
	No	89	6	**1**			
On mechanical Ventilation	Yes	20	58	9.01(5.01, 16.18)	0.000	1.15(0.71, 2.8)	0.763
	No	171	14	**1**			
On Vasopressor	Yes	9	40	5.95(3.62, 9.81)	0.000	1.6(0.68, 3.3)	0.183
	No	182	32	**1**			

Hint: *=Significant p<0.05, **Significant p<0.005

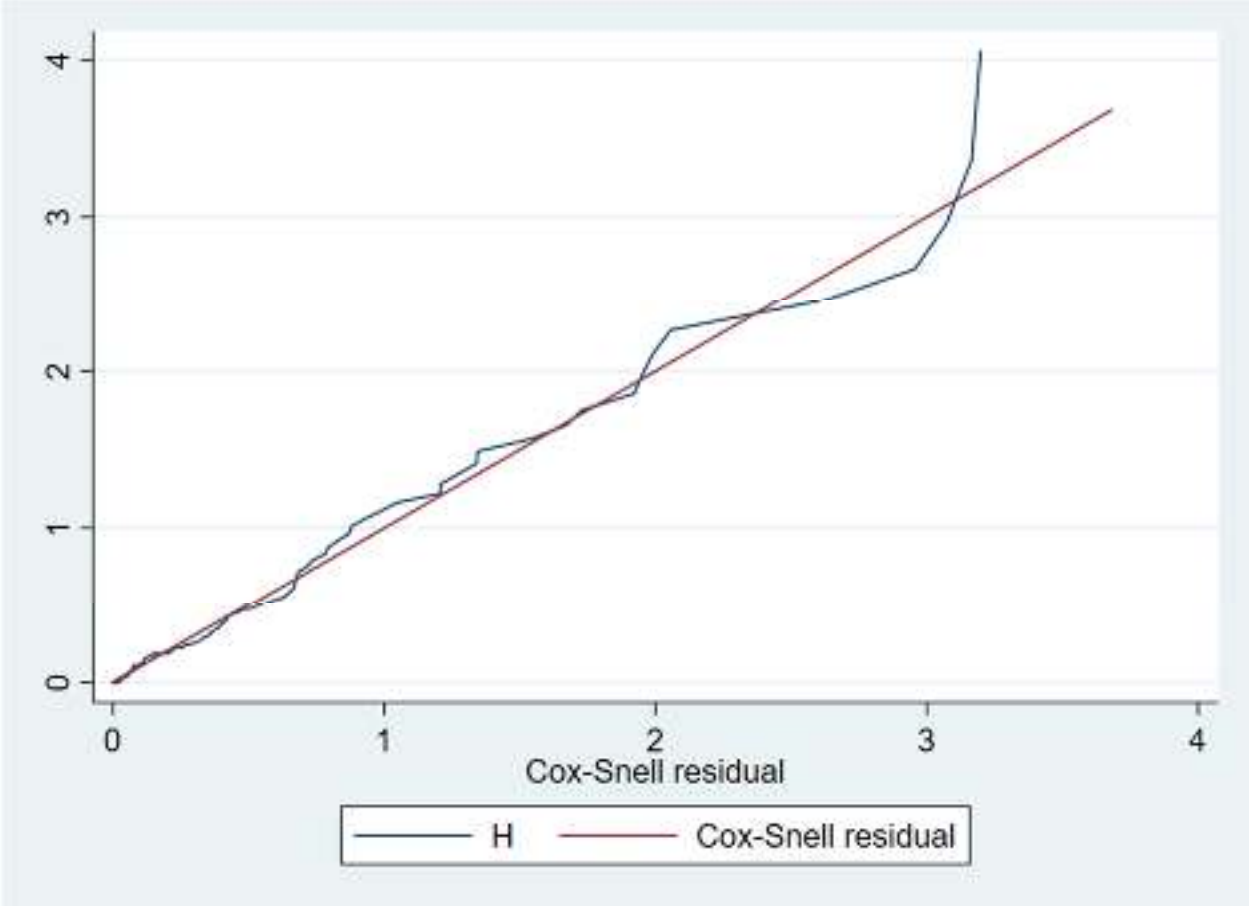


Figure18: cox-Snell residual test