COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

DEPARTMENT OF NURSING

TIME TO DEATH AND PREDICTORS AMONG NEONATES WITH OESOPHAGEAL ATRESIA ADMITTED AT TIKUR ANBESA SPECIALISED HOSPITAL, ADDIS ABABA, ETHIOPIA, 2021.

PRINCIPAL INVESTIGATOR: NATNAEL MOGES (BSC)

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

MAY, 2021.

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A RETROSPECTIVE FOLLOW UP STUDY

PRINCIPAL INVESTIGATOR: NATNAEL MOGES (BSC)

ADVISORS:

Dr. GIRUM SEBSBIE (PhD, ASSISTANT PROFESSOR)

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Full title	Time to death and predictors among neonates with oesophageal atresia admitted at Tikur Anbesa specialized hospital, Addis Ababa, Ethiopia, 2021.
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Duration of the project	From October 2020-May 2021.
Study area	Tikur Anbesa Specialised Hospital
Total cost	27,338 ETB.

APPROVAL SHEET

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I, the undersigned MSc student, declare that I have submitted my original work on a title Time to death and predictors among neonates with oesophageal atresia admitted at TASH, Addis Ababa, Ethiopia for the examination.

Submitted by:

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This thesis work has been submitted for examination with my approval as an advisor.

Approved by:

1. _____ _____ _____

Name of Major Advisor Signature Date

2. _____ _____ _____

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APPROVAL BY THE BOARD OF EXAMINATION

This thesis by **NATNAEL MOGES** is accepted in its present form by the board of examiners as satisfying thesis requirement for the degree of master's in neonatal nursing.

EXAMINER:

NAME	RANK	SIGNATURE	DATE

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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:

"Time to death and predictors among neonates with oesophageal atresia admitted at TASH, Addis Ababa, Ethiopia,2021."

Principal investigator

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This thesis work has been submitted for examination with my approval as an advisor.

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ABBREVIATION AND ACRONYMS

CHARGE	Coloboma, Heart defects, Atresia choanae, Retarded development, Genital hypoplasia, Ear defects/deafness
CI	Confidence Interval
COR	Crude Odds Ratio
GERD	Gastroesophageal Reflux Diseases
HR	Hazard Ratio
KID	Kid's Inpatient Database
LBW	Low birth weight
LMIC	Low- and Middle-Income Countries
MCHD	Major Congenital Heart Diseases
NICU	Neonatal Intensive Care Unit
NPO	Nothing by mouth
OA	Oesophageal Atresia
OR	Odds Ratio
PDT	Primitive Digestive Tube
PTSD	Parental post-traumatic stress disorders
TASH	Tikur Anbesa Specialised Hospital
TEF	Thoraco -oesophageal fistula
TPN	Total parenteral nutrition
VACTERL	Vertebral, Anorectal, Cardiac, Tracheal, oesophageal, Renal /genitourinary, limb

Table of Contents

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

Background -Esophageal atresia is a developmental defect of the upper gastrointestinal tract in which the continuity between the upper and lower esophagus is lost. In sub-Saharan Africa esophageal atresia has a higher mortality rate ranging from 30- 80%. In Ethiopia, the mortality of neonates with esophageal atresia is reported as 85.3%. To decrease the mortality rate, assessing time to death and predicors of esophageal atresia is crucial.

Objective -The objective of this study was to assess time to death and predictors among neonates with esophageal atresia admitted to Tikur Anbesa Specialized Hospital.

Methodology -An institutional-based retrospective follow-up study was conducted among 248 neonates diagnosed with esophageal atresia. Data was collected from February 10 to March 10 /2021 by reviewing medical charts of neonates diagnosed with OA who were registered from March 1/2011- February 30/2021 in TASH. A data extraction format was developed by reviewing different literature. Time to death was estimated by using the Kaplan-Meier failure curve and the time to death between different categorical variables was compared using the log-rank test. Bivariate and multivariable cox regression hazards models were fitted to identify the predictors of time to death. Hazard ratio with a 95% confidence interval was calculated and p-values < 0.05 were considered statistically significant.

Result

Among 225(90.7%) study subjects, 71.1% have died. Birth weight <2500g (AHR=1.49, 95%CI, 1.02 -2.21), sepsis (AHR=1.67,95%CI, 1.15 - 2.44), malnutrition (AHR=1.61, 95%CI, 1.03 - 2.58), time of fistula repair (AHR=3.72, 95%CI, 1.34- 10.38), diagnosis time (AHR=1.48, 95%CI, 1.01- 2.15) and dehydration (AHR=2.38, 95%CI, 1.63 - 3.46) were found to be significant predictors of time to death. The median time to death was 11 days (95%CI, 8.92-13.08).

Conclusion -In this study, the proportion of death among neonates diagnosed with esophageal atresia is high as compared to other studies. Among the deaths 76.9% have died within 14 days of admission. Early diagnosis, appropriate management of comorbidities, and timely surgical intervention will be helpful to overcome the high mortality rate.

Keywords: esophageal atresia, time to death, neonatal intensive care unit, Ethiopia

1. INTRODUCTION

1.1 Background

Congenital anomalies are the major cause of newborn morbidity, mortality, and disability in addition to adding to the burden of the health care system (1). It is estimated that about 20-30% of infant deaths occur due to congenital anomalies (2). Esophageal atresia associated with tracheoesophageal fistula (TEF) have been first described by Thomas Gibson in 1697. Cameron Haight made the first successful surgical repair of this malformation in 1941 following innumerable attempts by other surgeons (3). Esophageal atresia (EA) is a developmental defect of the upper gastrointestinal tract in which the continuity between the upper and lower esophagus is lost. EA can occur with or without tracheoesophageal fistula (TEF), abnormal communication between the trachea and the esophagus (4).

The etiology of esophageal atresia is not known but three primary theories attempt to explain the embryogenic origin of oesophageal anomalies(5–8). The first theory postulates that tracheoesophageal malformations come from tracheal growth failure; the second theory describes that failure in the development of a mesenchymal septum in the coronal plane of the primitive digestive tube (PDT). In these two theories, the origin of oesophageal atresia is a cellular reordering of the remaining distal PDT and the third concept combines elements of the first two and it is due to the loss of a portion of the previously formed tube as a result of reversion toward the main part of the embryo (7). Even if knowledge of the embryonic origin of esophageal anomalies is helpful for successful treatment, our understanding of the cause of this anomaly is still low (6,7).

EA classification is determined by the location of the atresia and the presence of any associated fistula to the trachea. The first classification was published by Vogt in 1929 and was modified by Gross in 1953. Thus, two classifications are used today. The primary types of congenital EA are EA with distal TEF (Vogt III b, Gross C), isolated EA without TEF (Vogt II, Gross A), TEF without atresia or H-type TEF (Vogt IV, Gross E), EA with proximal TEF (Vogt III a, Gross B) and EA with proximal and distal TEF (Vogt III c, Gross D). An understanding of these anatomical variants is vital to aid in medical and surgical management (9).

Infants with congenital forms of EA/TEF usually present shortly after birth with copious oral secretions, coughing, gagging, cyanosis, vomiting, and/or respiratory distress (4). The primary sign of EA in the delivery room is unable to insert an orogastric catheter beyond 11 or 12 centimeters(10). The confirmatory diagnosis of EA would be made with a simple chest X-ray using air as contrast in the proximal pouch to avoid aspiration of contrast fluid. If it is distal TEF air will be present in the stomach and causing abdominal distention also the air will be present on X-ray films (11).

The definitive management of neonates with oesophageal atresia is surgical. Surgical repair consists of the closure of the TEF and anastomosis of the oesophageal segments. Surgical repair may need to be delayed in infants with low birth weight, pneumonia, or other major congenital anomalies. When surgical repair is delayed, infants should be treated with parenteral nutrition and upper pouch suctioning until they become surgical candidates. Gastrostomy tube placement might also have importance. The most common complications after the surgical repair include leakage at the site of the anastomosis, recurrent fistula, structure formation, and gastroesophageal reflux (4).

There are no studies that have been done on time to death and predictors among neonates with oesophageal atresia in Africa including Ethiopia. As a result, it is challenging to write the data's related to time to death and predictors associated with time. Oesophageal atresia is a devastating and life-threatening condition in Ethiopia. So, attention should have to be given to control and reduce mortality from this anomaly by estimating time to death and identifying predictors associated with time.

1.2 Statement of the problem

Although esophageal atresia is one of the rare congenital anomalies, it is the most common congenital anomaly of the esophagus. This intricate malformation is still a difficult condition in pediatric surgical interventions(10,12). According to a population-based study conducted in 2012 on 23 European countries from the European database for surveillance of congenital anomalies the overall worldwide prevalence of EA is 2.4 (range 1.3–4.6) per 10,000 births (13,14). In France, a prospective population-based register was initiated in 2008 and included all the centers that care for EA patients. The register showed that the live-birth prevalence of EA was 1.8 per 10 000 births in the country (15,16). As different studies described that EA is a relatively common congenital malformation occurring 1 in 2500–3000 live births(17,18). International differences in the prevalence of EA across different geographical regions may also be attributable to differences in case identification methods, case definition, and case ascertainment (14).

Esophageal atresia is considered a fatal anomaly and neonatal emergency with significantly improved prognosis in industrialized countries. Recently, in developed countries due to the advancement of medical care; including neonatal and surgical procedures, the survival rate now exceeds 95% and an increasing number of patients reach adulthood (9,18,19). In addition to this 100% 1-week survival was reported for neonates without associated anomalies(20,21). Lower rates up to 87%, are reported for patients born with associated cardiac anomalies, very low birth weight (<1,500 g), and long-gap EA (22,23).

Oesophageal atresia accounts for 3% of intrauterine deaths and 27% of induced abortion among perinatally detected pregnancies (13,14,24). However, a majority of EA cases came up with live born. Among those around 55% of infants have associated birth defects or other anomalies (13). Nearly, 10% of patients have a non-random VACTERL association with undetermined genetic abnormalities that may under- lie this association (25,26),1% of patients also have CHARGE (coloboma, heart defects, atresia choanae, retarded growth and development, genital hypoplasia, and ear anomalies or deafness) syndrome (24), Edward and Down syndrome occurs in 6% and 3% of babies with EA, respectively (13,14,21). The presence of associated anomalies hastens the mortality rate of neonates with esophageal atresia ($p<0.05$) (27).

Mortality from EA in low- and middle-income countries (LMIC) is very high, ranging from 30 to 80%(28). In Sub-Saharan Africa, this anomaly is still accountable for high morbidity and mortality and raising several questions about the management of esophageal atresia (29,30). In the descriptive study conducted in Addis Ababa and Amhara region, the proportion of esophageal atresia among the overall congenital anomalies is 0.7% (31). Even though the prognosis of esophageal atresia is good in the developed world, the reverse is true in developing countries. Neonates with EA cases are increasing from time to time in Ethiopia and most neonates have died either before the surgical intervention or after surgical repair of the atresia due to different causes (19,32). There are also limited researches in Africa about oesophageal atresia and almost none in Ethiopia so studies should be done to further investigate this problem and to identify the predictors of mortality.

Whenever diagnosed, EA is a psychologically hurtful condition, and parents are at risk for developing traumatic stress reactions next to the diagnosis. Parental post-traumatic stress disorders (PTSD) harm infant and child development through their effects on parenting skills and parent-child interactions. EA children are also at risk for PTSD because of invasive and stressful procedures they undergo during the neonatal period. EA can have a long-term impact on children's psychological and social development (33). Neonates with EA have longer hospital stays for waiting for surgical intervention and most of their families are from low socioeconomic class as a result being economically deprived is a contributing factor for infants to have a poor prognosis(34).

various studies conducted so far in different countries to determine predictors of mortality such as low birth weight, prematurity, sepsis, aspiration pneumonia, delay in diagnosis, associated congenital anomalies, surgical repair within 24 hours(35–37). Despite this malnutrition, thrombocytopenia and dehydration were not well examined as a predictor of mortality in previous studies. Upon our clinical experience, these variables might have an association with mortality so further studies should be needed, and also there are no studies carried out in my study area. Therefore, this study will aim to determine time to death and predictors among neonates with esophageal atresia in Tikur Anbesa specialized hospital (TASH).

1.3 Significant of the study

Even though Oesophageal atresia is a rare congenital anomaly, it can cause severe complications and death. As different studies showed the survival of oesophageal atresia in developed countries is good while in sub-Saharan Africa it has a higher mortality rate including Ethiopia. As a result, to overcome this high mortality rate identifying the causes of mortality and making interventions accordingly will be helpful. This study was done to determine the time to death and to identify predictors of oesophageal atresia.

The input from this study will provide baseline data for;

For health care workers; it helps to know the time to death and predictors of OA, to make an intervention on the predictors, and to provide quality care to tackle the mortality. For health institutions; it helps to design new interventional projects to increase the survival of neonates with OA by designing strategies to prevent predictors of time to death. For policymakers; it helps to develop strategies and guidelines to improve the quality of care of neonates diagnosed with OA. For families, it provides knowledge about survival status and predictors of mortality. Lastly, findings from this study will serve as a baseline for further study.

2. LITERATURE REVIEW

2.1 Survival status among neonates with esophageal atresia

A 32 years review in Italy showed that survival status was traced for 91.7% of the 360 individuals so that the 25-year survival probability of patients affected by EA was 85.1% (95% CI, 80.8–89.4) with most cases of deaths occurring during the first months of life. 1-month, 3-month, and 12-month survival probabilities were respectively 92.7% (95% CI, 90.0–95.4) 90.9% (95% CI, 87.8–94.0) and 88.4% (95% CI, 84.9–91.9) (21). Furthermore, in a survival study conducted in Newcastle, survival for esophageal atresia between 1996 and 2014 among 120 cases 87% of the babies was survived (38).

In a retrospective review study in the united kingdom at Royal Manchester Children's Hospital among 248 cases of esophageal atresia, 89.7% survived and 11.3% have died (39). Moreover, the retrospective study conducted in Turkey from the data of the Turkish Esophageal Atresia Registry (TEAR) revealed that the overall survival rate was 81.09% and the mortality was 19.02% (40).

In a retrospective study conducted in the united states at Kid's Inpatient Database (KID) 4168 cases were recognized with a diagnosis of EA/TEF of them the overall in-hospital mortality was 9% (41). In another retrospective study conducted in Melbourne on esophageal atresia patients managed at the Royal Children's Hospital, among 650 patients 13.5% of them died during the study period. In this study, the mortality after and before discharge were 25% and 75.0% respectively (42). In addition, in the retrospective analysis at two major children's hospitals with fetal centers: The Advanced Fetal Care Center at Boston Children's Hospital in Boston and the Fetal Treatment Center at UCSF Benioff Children's Hospital in San Francisco of 253 patients with EA 5.1% experienced index admission mortality (43).

A retrospective cohort study was carried out in Nigeria at the University of Nigeria Teaching Hospital and Mother of Christ Specialist Hospital of 19 total patients managed for esophageal atresia overall survival rate was 31.6% (44). Another retrospective study conducted in Ghana from January 2007 to December 2014 at Korle-Bu Teaching Hospital revealed that of 85 cases of esophageal atresia 87.1% had undergone surgery. However, Surgical outcome was directed in 91% with an overall survival rate of 40.3% (45).

In addition to this, a retrospective study conducted in Tunisia at the department of pediatric surgery, Hedi Chaker Hospital 58 patients were treated for EA between 2007 and 2016 of the 76.2% was survived (46).

A retrospective review study in Algeria at Nefissa Hamoud University Hospital Center in Algiers indicated that of 86 patients with a diagnosis of EA 48% have died (22% babies died before surgery,46% deaths in early postoperative course, and 22% late deaths) (18). Also, a retrospective study conducted in Senegal at 2 Pediatric Surgery Departments in Dakar showed that among 49 patients diagnosed with esophageal atresia 78% (26% pre-operative,74% postoperative) were died (47). Moreover, in the retrospective cross-sectional study, which was conducted in Ethiopia at Tikur Anbesa specialized hospital among 34 cases of esophageal atresia, 85.3% have died and 14.7% were discharged alive (32).In this study, most (58.6%) of the cases died before surgical intervention and 41.4% died after surgical management.

2.2 Predictors of mortality among neonates with esophageal atresia

2.2.1 Sociodemographic and neonatal characteristics

In the retrospective study conducted in the United States at Kid's Inpatient Database (KID) 4168 cases were identified with a diagnosis of EA/TEF. Infants with LBW (1500-2500 g) and NBW (above 2500 g) had survival rate of 92% and 95% (P = 0.147) respectively. The survival rate for VLBW (1000-1499 g) and ELBW (< 1000 g) were 77% and 52% (P < 0.001) respectively. In this study Infants born within GA of 33-36 wk. and GA of 37 wk. or higher, had a survival rate of 92% and 95%(P= 0.522) and with GA of 28-32 wk. survival was 82% (P < 0.001) and <28 wk. 59% (P < 0.001) (41) but admission source(p=0.399) and gender(p=0.163) did not have association with mortality. Another retrospective single-center study conducted in Japan on 65 EA infants admitted to Shizuoka Children's Hospital described that birth weight of <1606 g (COR- 14.85; 95% CI - 2.29–96.57), gestational age of < 35 weeks (COR- 7.08; 95% CI - 1.16–43.05)and complex cardiac anomalies (COR, 12.75; 95% CI 1.99–81.39) were significant risk factors for death during hospitalization. However, being male was not a risk factor for death during hospitalization (COR 1.422; 95% CI 0.28-7.21) (48).

A retrospective multi-institutional cohort study of neonates with a diagnosis of EA/TEF conducted in Columbus concluded that among the total 3479 infants 83.5% had any other congenital anomaly other than oesophageal atresia or tracheoesophageal fistula. Of them, 183 (96.8 % from total 189 death) has been died due to associated congenital anomalies (p<.0001). In this study among the total 3479 infants, 69.6% were had congenital heart disease. Of them, 174 (92.1% from a total of 189 death) were died due to CHD (p<.0001), 20.3% had a gastrointestinal anomaly of them 28.6% were died (p=0.004), 26.4% had a musculoskeletal anomaly of them 39.7% died (p<.0001) and 6.1% had a genetic anomaly of them 19.6% died (p<.0001). Also, 37.0% were premature.Of the 60.0% were died (p<.0001) (49). Moreover, in a 10-year retrospective study conducted in Serbia on 60 new-borns who were treated for EA at the Mother and Child Health Institute (MCHI) in Belgrade, Republic of Serbia 41.3 % of cases had Associated anomalies. Among associated anomalies detected, the multiple (16.7 %), cardiac anomalies (13.3 %), musculoskeletal (5.0 %), urogenital (3.3 %), gastrointestinal (1.7 %) and chromosomal anomalies (1.7 %). The presence of associated anomalies considerably affected the death rate of these patients (p -0.006). In this study, the incidence of a type of oesophageal atresia was EA with distal TEF (83.3 %), EA with proximal TEF(6.7%) EA without TEF (6.7 %), and TEF without EA (3.3%) but the type of EA did not have any significant influence on the mortality of patients (27).

In the retrospectively reviewed study on EA/TEF patients born between 1995 and 2018 at the two major children's hospitals with fetal centers'; the Advanced Fetal Care Center at Boston Children's Hospital in Boston and the Fetal Treatment Center at UCSF Benioff Children's Hospital in San Francisco, index admission mortality by decade of birth were (4.4% from 1995 to 1999, 3.3% from 2000 to 2009, 7.4% from 2010 to 2018) on logistic regression analysis (1990s versus 2000s: p = 0.797; 1990s versus 2010s: p = 0.603; 2000s versus 2010s: p = 0.171). Multivariable logistic regression demonstrated that MCHD was the only significant independent predictor of index admission mortality (OR: 16.4; 95% CI: 3.3- 81.8; p = 0.001) while birth weight <1.5 kg and VACTERL association was not (OR 3.4; 95% CI: 0.6-20.2; p = 0.173) and (OR : 0.5 , 95% CI : 0.1-2.1 ,P=0.319) respectively (43).

According to a retrospective study carried out in Tunisia at the department of pediatric surgery Hedi Chaker Hospital being prematurity (OR = 5.4, 95% CI =1.13–25.80, P = 0.004), low birth weight (p = 0.023, 95% CI = 1.38– 35.47,OR = 7), cardiac malformations (OR = 10.5, CI 95% = 2.03–54.27, p = 0.006) and delayed diagnosis (OR = 10.11, p = 0.005, 95% IC = 2.005–50.980) were predictors for mortality of infants who had esophageal atresia while VACTERL association was not a predictor of mortality (p=0.236) (46). Furthermore, in retrospective study conducted in Algeria death was more common in patients with delayed diagnosis (P = 0.02), and premature patients (P < 0.02), and 80% of the patients who were admitted before 24 hours of age were survived. However, associated congenital anomalies, weight, and feeding history were not had significant association with mortality (18).

In the retrospective study conducted in Ethiopia prematurity (RR=1.238, 95% CI 1.026-1.494) and low birth weight (RR=1.333, 95% CI 1.035-1.717) were had a significant association with mortality of infants with esophageal atresia (32).

2.2.2 Maternal related characteristics

In the retrospective study conducted in Melbourne on esophageal atresia patients managed at the Royal Children's Hospital, the median age of the mothers was 31.5(17-43). Among 66 deaths before discharge maternal age influenced the mortality of neonates with esophageal atresia (p- 0.02) (42). In addition, in the retrospective study conducted in Italy, the overall prevalence of EA was significantly higher among children with mothers older than 35 years compared with those with younger mothers (p = 0.012) (21).

A study in Boston and San Francisco demonstrated that among the total 253 patients, 31.2% of them had a maternal history of polyhydramnios. According to this study prenatal diagnosis was not had a significant influence on mortality (OR:4.1, 95% CI: 0.9-17.7, P= 0.057) (43). In another retrospective study conducted in Korea at Asan medical center, 30% of the mothers were had a history of polyhydramnios, 12% of them had a prenatal diagnosis and 26% had a history of pregnancy-induced hypertension (5). In a retrospective study conducted in Algeria, Among 9 preoperative deaths, 67% of them were delivered from rural areas but a place of delivery was not significantly affected their survival (18).

2.2.3 Clinical related characteristics

A retrospective case-control study carried out in China at the Children's Hospital of Chongqing Medical University showed that in the univariate analysis, respiratory failure (p-0.000), postoperative sepsis (p-0.001), respiratory distress syndrome (p-0.001), and pneumothorax (p-0.018) were found in the non-survivor group than in the survivor group ($P<0.05$) while necrotizing enterocolitis (p- 0.331), pulmonary hemorrhage (p-0.088), atelectasis(p-1.00) and shock (p-0.032) was not had a significant influence on mortality. In the logistic regression analysis, respiratory failure (95% CI: 2.292–7.355, OR: 4.104) and postoperative sepsis (95% CI: 1.516–8.375, OR: 3.564) were associated with a high mortality rate (50). Another retrospective study conducted in Serbia revealed that sepsis significantly influenced the mortality of patients ($p<0.05$) (27).

A retrospective multi-institutional cohort study of neonates with a diagnosis of EA/TEF conducted in Columbus of the total 3479 patients 7.6% had malnutrition, the 14.8% was died due to malnutrition ($p=0.0001$) (49).

A retrospective study carried out in Nigeria showed that when compared the cases of esophageal atresia managed before September 2013 (Group A) with those managed from October 2013 (Group B) following improved anesthesia care and incorporation of cardia banding during gastrostomy, in Group A among 11 cases 90.9% have died of them, 30% were died due to uncontrolled sepsis and in Group B among 8 cases 37.5% died of them, 66.7% were died due to uncontrolled sepsis (44). In addition to this, in the retrospective study conducted in Algeria, among 9 preoperative deaths, 33% of them were died due to pneumonia (18). Furthermore, in the study conducted in Senegal, 36% of the cause of operative mortality was sepsis (47).

In the retrospective study conducted in Ethiopia, respiratory failure secondary to aspiration pneumonia was mentioned as a possible cause of death in 72.4% of the cases and sepsis in 27.6% of cases.

2.2.4 Treatment-related characteristics

In the retrospective study conducted in the united states, EA/TEF repair within 24 h of birth was determined to be the strongest predictor for higher mortality among all factors ($OR = 6.9$, $P < 0.001$) (41). Moreover, in a retrospective study conducted in Serbia on 60 newborns who were

treated for EA the birth-operative treatment time was between 5 hours and 7 days. In 50% of cases, the surgical treatment was performed in the first 24 hours after birth, and in 36.7% of cases during 25– 48 hours after birth revealed that birth-operative treatment time significantly influenced the mortality of the treated patients (P= 0.005) (27). In addition, a retrospective study conducted in Korea at Asan medical center, in the univariate analysis of variables affecting mortality of neonates with esophageal atresia days of operation (OR: 0.983, CI: 0.871-1.109, P=0.783) and days of hospitalization (OR:0.986, CI:0.968-1.003, P=0.109) did not have a significant association with mortality (5).

In a retrospective study conducted in Algeria among 66 patients who underwent primary anastomosis 39.4 % of them have died, 5 underwent stage anastomosis, 60% died and 3 underwent esophageal reconstitution, all were survived. According to the study type of surgery did not have a significant association with mortality of neonates with esophageal atresia (18). Another retrospective study conducted in Senegal described that the surgery-related mortality rate was 72% (47). Furthermore, in a retrospective review of records of infants with esophageal atresia in Ghana, among the 67 patients, the early primary repair was done in 35.8% with a survival rate of 45.8%. 17.9% had the initial procedure for delayed primary repair with a survival rate of 16.7% and the remaining 46.3% of patients had initial surgery for staged repair with a survival rate of 45.2% but there was no association between the type of surgery and the surgical outcome (P = 0.183) (45).

Conceptual framework

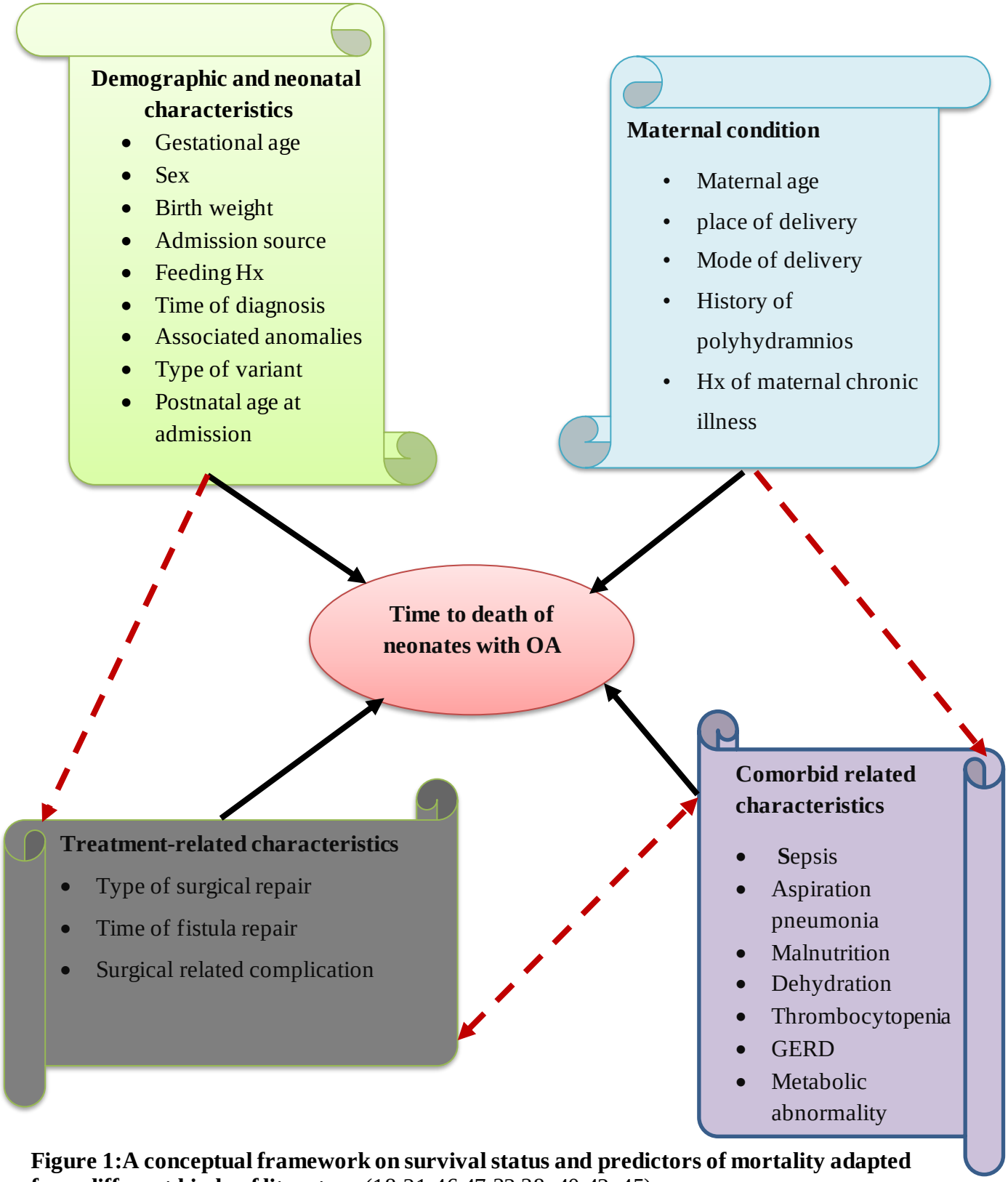

Figure 1:A conceptual framework on survival status and predictors of mortality adapted from different kinds of literature (18,21,46,47,32,38–40,42–45).

3.OBJECTIVE

3.1 General objective

To assess time to death and predictors among neonates with esophageal atresia admitted to Tikur Anbesa specialized from March 1/2011- February 30/2021.

3.2 Specific Objective

1) To determine the survival status of neonates diagnosed with OA admitted at TASH
2) To estimate the median time to death of neonates with esophageal atresia admitted at TASH.
3) To identify the predictors of time to death among neonates with esophageal atresia admitted at TASH.

4. METHODS AND MATERIALS

4.1 Study area and period

The study was conducted in Tikur Anbesa Specialized Teaching Hospital in Addis Ababa Ethiopia. TASH is found in Addis Ababa city, the capital of Ethiopia. TASH is a teaching, central tertiary comprehensive referral hospital and has approximately more than 800 beds, gives diagnostic, and treatment services for about 370,000-400,000 patients per year. It is the largest and best-known public hospital, which was built in the early 1960s. It has the very best highest concentration of healthcare facilities and trained healthcare practitioners in the country. Data was collected from February 10 to March 10 /2021 by reviewing medical charts of neonates diagnosed with OA who were registered from March 1/2011- February 30/2021 in TASH. TASH is the single largest referral hospital in Ethiopia and it is the only hospital that serves as a management center for neonates having esophageal atresia in Ethiopia.

4.2 Study design

An institutional-based retrospective follow-up study was conducted at TASH

4.3 Populations

4.3.1 Source population

The source population comprises all medical charts of neonates with oesophageal atresia at Tikur Anbesa specialized hospital during the study period.

4.3.2 Study population

The study population comprises all medical charts of neonates with esophageal atresia at Tikur Anbesa specialized hospital from March 1/2011- February 30/2021.

4.4 Inclusion and exclusion criteria

4.4.1 Inclusion criteria

All eligible medical charts of neonates with oesophageal atresia at Tikur Anbesa specialized hospital from March 1/2011- February 30/2021 were included.

4.4.2 Exclusion criteria

Medical charts with incomplete information (discharge date and outcome status) were excluded from the study.

4.5 Sample size determination

The sample size is can be calculated using a sample size calculation formula for the survival analysis using STATA version 16 statistical software by considering associated major predictors of time to death in neonates with esophageal atresia. However, no study in Ethiopia determines predictors associated with time to death.

As a result, all neonates diagnosed with OA (225) who had a complete chart admitted to TASH NICU from March 2011to February 2021 were included as study subjects. We used the whole cases as sample size as it was not possible to use the sample size calculation formula of survival analysis for this study as there was no known relative hazard and censoring rate of our variables from the previous study in the same setups.

4.6 Variables

4.6.1 Dependent variable

- Time to death of neonates with OA

4.6.2 Independent variables

- **Sociodemographic and neonatal characteristics: -** postnatal age at admission, weight, GA, sex, time of diagnosis, admission source, feeding history, associated congenital anomalies, type of OA
- **Maternal related characteristics: -** maternal age, place of delivery, mode of delivery history of polyhydramnios, Hx of maternal chronic illness
- **Clinical comorbid conditions: -** sepsis, aspiration pneumonia, malnutrition, thrombocytopenia, dehydration, GERD, metabolic abnormality
- **Treatment-related characteristics: -** type of surgical repair, time of fistula repair, surgical related complication

4.7 Operational definitions

Oesophageal atresia - Neonates diagnosed by a health care provider with confirmed X-ray results and documented on the chart as OA was taken as esophageal atresia.

Time to death - refers to the median time of total length of hospital stay

Censored- refers to neonates with esophageal atresia discharged or against for medical treatment or EA cases lost during treatment for unknown status.

Event -is considered to be the death of neonates with esophageal atresia while in the hospital and whose death report was recorded.

Incidence density rate – It was computed by dividing the number of events by total follow-up time in person-days.

Survival time - The number of days the child stayed in the hospital from admission until death or discharged or lost to follow-up or against medical advice.

Co-morbidities - Newborns with EA and have other illnesses.

Malnutrition – Neonates with OA whose serum albumin level is low to age or kept NPO for a prolonged time or edematous and documented on the chart as malnutrition.

Dehydration - Neonates with OA who had sign and symptom of dehydration and documented on the medical chart as dehydration

Sepsis- Neonates with OA who had sign and symptom of infection and documented on the chart as sepsis

4.8 Data collection tool and procedure

4.8.1 Data collection tool

A data extraction format was adapted by reviewing related literature (18,21,46,47,32,38–40,42–45) to collect the required individual information from the relevant documents. The data extraction format consists of the demographic and neonatal characteristics (postnatal age at admission, weight, GA, sex, time of diagnosis, admission source, feeding history, associated congenital anomalies, type of variant), maternal related characteristics (maternal age, mode of delivery, history of polyhydramnios, place of delivery, Hx of maternal chronic illness), clinical comorbid conditions (sepsis, aspiration pneumonia, malnutrition, thrombocytopenia, GERD, dehydration, metabolic abnormality) ,treatment-related characteristics (type of surgical repair, time of fistula repair, surgical related complication) , outcome and total length of hospital stay .

4.8.2 Data collection procedure

All available information on patient records was checked and the data extraction format was prepared in English to extract all the relevant information from patients' charts. The initial time for the chart review was since the diagnosis of EA and the end time is the date of death, date of recovery, date of loss to follow up, date of against, and 28 days of postnatal age. All charts of babies with EA admitted in TASH from March 2011 to February 2021 were retrieved from the registration books and the charts of all study subjects were selected based on the eligibility criteria. Death was confirmed by a death summary note and registration book. One supervisor and two data collectors were recruited.

4.9 Data quality Assurance

To keep data quality supervisors and data collectors were trained for one day on how and what information they should collect from the targeted data sources. Data extraction forms checked before data collection for completeness and consistency using a 13(5 %) pretest of randomly selected charts at Tikur Anbesa specialized hospital and any faults found during the process were corrected and modified by the principal investigator. The completeness and consistency of the collected data were checked daily during data collection and after data collection. All data were examined for completeness and consistency during data cleaning, storage, and analysis. Whenever there are incompleteness and ambiguity of recording, the filled information formats were cross-checked with source data soon. Individual records with incomplete data were excluded.

4.10 Data processing and analysis

Data were coded, cleaned, and entered by Epi-data (version 4.6.0.2) and exported to STATA (version 16) for further analysis. Exploratory data analysis was carried out to check the levels of missing values, possible outliers, and multicollinearity. Descriptive statistics were used to describe the frequency, percentage, and rate then, after checking the distribution of the data's median was calculated. The life table was constructed to estimate the probabilities of death over time. Kaplan–Meier curve was used to estimate the survival curve from the observed survival times and a comparison of two survival curves was done using the log-rank test.

Bivariate Cox regression analysis was conducted to assess the effect of each independent variable on the outcome variable. Variables with a P-value < 0.25 in the bivariate cox regression

analysis were included in the multivariable Cox regression analysis to identify the independent predictors of mortality. All statistical tests were considered significant at 0.05 or 5%. The Cox regression model for its fitness to the data and proportional hazard assumptions were checked by using the Schoenfeld residuals test. Finally, results were summarized and presented using text, table, percentage, and graphs.

4.11 Ethical clearance

Ethical clearance was obtained from the Ethical Review Committee of Addis Ababa University College of Health Sciences. Then, data was collected after getting consent from TASH. As the study was conducted through a review of medical records, there will not be harmful to individual patients and no consent was obtained from the mothers or caregivers of the study subjects. No information obtained from the medical records was disclosed to any third person. Patient Identification variables such as name weren't used in the study. This study wasn't inflicting harm on or expose neonates to unnecessary risk as a result of reviewing their medical records. All data of study participants were kept confidential.

4.12 Dissemination of research finding

The findings of the study will be submitted and presented to Addis Ababa University. The dissemination will also go to the TASH, the federal ministry of health, and other health institutions. Besides, efforts will be made for the publication of the research in a reputable journal.

5.RESULT

Out of 248 records of neonates diagnosed with OA admitted in the last 10 consecutive years (2011-2021) at Tikur Anbesa specialized hospital, Addis Ababa, Ethiopia,225 (90.7%) records of neonates with OA were enrolled in this study.

5.1 Sociodemographic and neonatal characteristics of the study participants

The post-natal age at admission ranges from 30 min to 19 days with mean postnatal age of 3.3 days (SD ± 2.93) and more than half of neonates have postnatal age of 2 days at admission. The mean time of diagnosis was 2.98(SD ±2.76) days and more than half 133(59.1%) were diagnosed with oesophageal atresia after two days of birth. Almost all 219(97.3%) of neonates were referral cases and 90(%) of them were referred from the Oromia region.

Out of 225 neonates in the cohort, 123(54.7%) were females. Regarding gestational age 168(74.7%), neonates were terms. About 140(62.2%) neonates had normal birth weight. Among 225 participants,193(88.5%) had proximal oesophageal atresia with distal TEF (type A) (**Table1**). From the total reviewed records,92(40.9 %) of neonates had associated congenital anomalies. Among those 60 (65%) had congenital heart diseases (**Figure 2).**

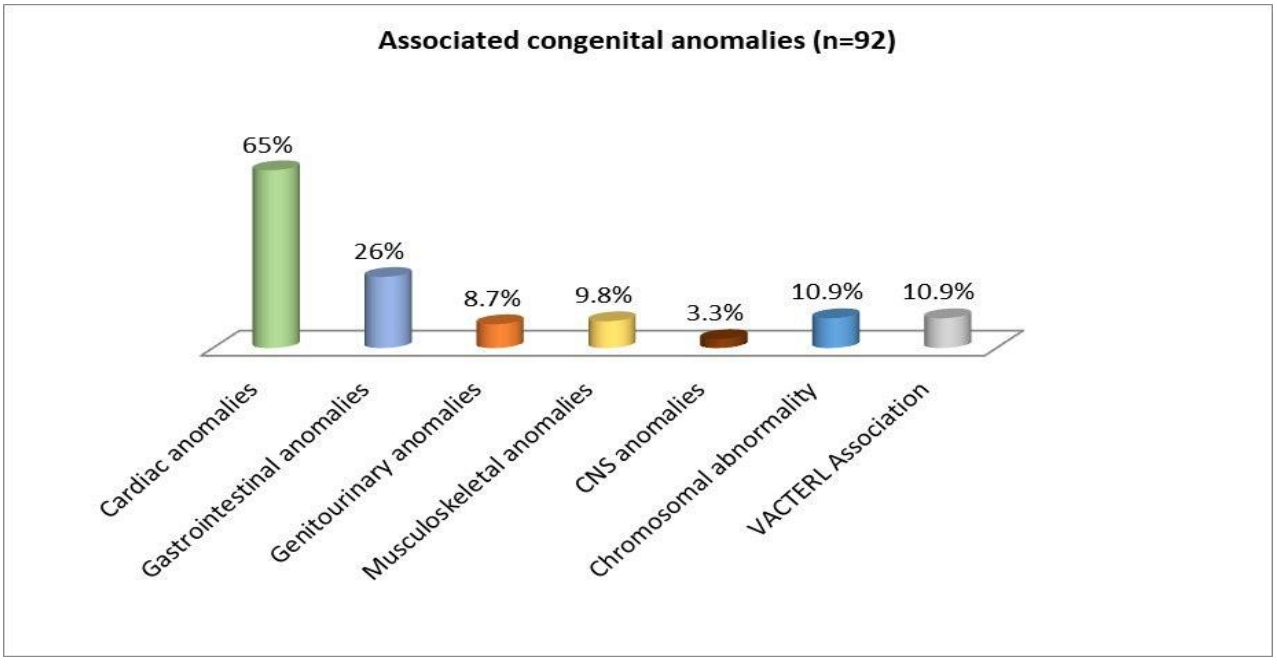

Figure 2: Shows distribution of associated congenital anomalies in neonates with oesophageal atresia in Tikur Anbesa specialized hospital from March 2011 to February 2021(n=225)

Table 1: Socio-demographic and neonatal characteristics of neonates with esophageal atresia admitted to Tikur Anbesa specialized hospital, Addis Ababa, Ethiopia; from March 2011 to February 2021 (n=225)

Socio-demographic and neonatal characteristics	Category	Frequency number (%)
Region	Addis Ababa city	83(36.9)
	Amhara	27(12)
	Oromia	90(40)
	SNNPR	25(11.1)
	Other	5 (2.2)
Admission source	Inborn	6(2.7)
	Out born	219(97.3)
Postnatal age at admission	<1day	68(30.2)
	1-2day	35(15.6)
	>2day	122(54.2)
GA	28-36wk	53(23.6)
	37-42wk	168(74.7)
	>42wk	4(1.8)
Sex	Male	102(45.3)
	Female	123(54.7)
Weight	2500-4000g	140(62.2)
	1500-2500g	77(34.2)
	1000-1500g	8(3.6)
Type of variants (n=218)	Type A	18(8)
	Type B	3(1.3)
	Type C	193(88.5)
	Type D	4(1.8)
Feeding Hx	Yes	91(40.4)
	No	134(59.6)
Time of Dx	< 48 hr	92(40.9)
	>48 hr	133(59.1)

5.2 Maternal related characteristics of study subjects

Among the 225 study participants, a significant majority (84.9%) of mother's ages were ranging from 18-35 years. About 168(74.7%) of the mothers were born via spontaneous vaginal delivery and a significant majority 214(95.1%) them were born at a health facility. Twenty-seven (12%) mothers had a chronic illness. About 51(22.7%) of mothers had a history of polyhydramnios (**Table 2**).

Table 2: Maternal related characteristics of neonates diagnosed with esophageal atresia admitted to Tikur Anbesa specialized hospital, Addis Ababa, Ethiopia; from March 2011 to February 2021(n=225)

Maternal related characteristics	Category	Frequency number (%)
Maternal age	<18yr	4(1.8)
	18-35yr	191(84.9)
	>35yr	30(13.3)
Place of delivery	Home	11(4.9)
	Health facility	214(95.1)
Mode of delivery	SVD	168(74.7)
	C/S	57(25.3)
History of polyhydramnios	Yes	51(22.7)
	No	174(77.3)
History of maternal chronic illness	Yes	27(12)
	No	198(88)

5.3 Clinical comorbid related conditions of the study subjects

Among all neonates selected for the study, the most common clinical comorbidities accompanied with oesophageal atresia were aspiration pneumonia 203(90.2%) of this,49.6% was diagnosed at admission,30.7% after admission and 9.3% before admission, sepsis 77(34.2%), thrombocytopenia 100(45.7%) and malnutrition 126(59.1%) **(Table 3).**

Table 3: Clinical comorbid related characteristics of neonates diagnosed with esophageal atresia admitted to Tikur Anbesa specialized hospital, Addis Ababa, Ethiopia; from March 2011 to February 2021(n=225)

Clinical comorbid conditions	Category	Frequency number (%)
Sepsis	Yes	77(34.2)
	No	148(65.8)
Aspiration pneumonia	Yes	203(90.2)
	No	22(9.8)
Malnutrition (n=213)	Yes	126(59.1)
	No	87(40.9)
Thrombocytopenia (n=219)	Yes	100(45.7)
	No	119(54.3)
GERD	Yes	42(18.7)
	No	183(81.3)
Dehydration	Yes	94(41.8)
	No	131(58.2)
Metabolic abnormality	Yes	18(8)
	No	207(92)

5.4 Treatment-related characteristics of study subjects

Among the study subjects, surgical intervention was done for 119(52.7%) neonates with oesophageal atresia. Primary repair was done for 105(88.2%) of the neonates diagnosed with OA. About 13(10.9%) of the neonate had a surgical-related complication. Of this,10(8.4%) had an anastomotic leak and 3(2.5%) had surgical site infection (**Table 4).**

Table 4: Treatment-related characteristics of neonates diagnosed with esophageal atresia admitted to Tikur Anbesa specialized hospital, Addis Ababa, Ethiopia; from March 2011 to February 2021(n=225).

Treatment-related characteristics	Category	Frequency number (%)
Surgical intervention	No	106(47.3)
	Yes	119(52.7)
Time of fistula repair (n=119)	<=72hr	23(19.3)
	>72hr	96(80.7)
Type of surgical repair (n=119)	Primary repair	105(88.2)
	Gastrostomy	14(11.8)
Surgical related complication (n=119)	Yes	13(10.9)
	No	106 (89.1)

5.5 Survival status of neonates diagnosed with oesophageal atresia

Two hundred twenty-five neonates with OA have followed a total of 2933 neonate-days with a minimum of 1 hour to a maximum of 28 days, with a median time to death of 11days (95% CI, 8.92-13.08).

Out of 225 study subjects, 160 (71.1%) neonates died. Of this, 104(65%) have died before surgery and 56(35%) died after surgery. Among the deaths 75(46.9%) died within the first 7 days of admission,48 (30%) died within the second week of admission. About 65(28. 9%) of them were censored with 18(8%) against,40(17.8%) discharged and 7(3.1%) lost to follow-up. The incidence death rate of neonates diagnosed with oesophageal atresia is found to be 5.5 (95% CI, 0.05 - 0 .06) per 100-neonates day. The cumulative probability of failure at the end of the first day was 0.44%, at fifth to sixth days was 25.64%, at 20–21 days was 65.51% and at the end of the follow-up was 71.56%.

5.6 Kaplan-Meir failure estimates for neonates diagnosed with esophageal atresia time to Death

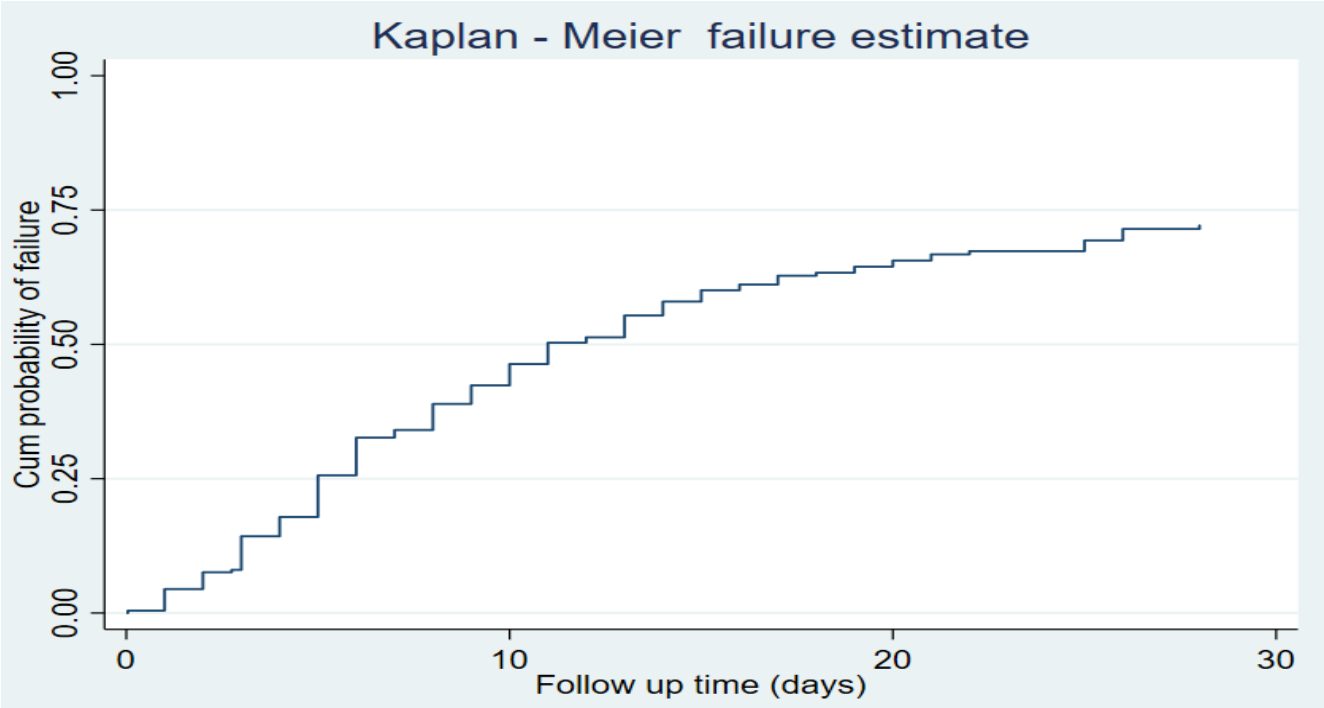

Figure 3: Kaplan-Meier failure curve of neonates with esophageal atresia admitted in NICU at Tikur Anbesa specialized Hospital from March 2011 to February 2021(n=225)

The median time to death of the entire cohort was 11 days (95% CI, 8.92-13.08). comparing the median time to death according to birth weight showed that there was a significant difference (P<0.05) in median time to death of normal birth weight 14 days (95% CI, 9.05-18.96), low birth weight 8 days (95% CI, 4.75-11.25) and very low birth weight 3days (95% CI. 1.66-4.34) neonates.

Concerning comorbid diseases median time to death for neonates who had dehydration 8 days (95% CI, 6.15-9.85) and without dehydration 20 days (95% CI 10.50-29.50). similarly, the median time to death was significantly different for neonates with malnutrition 9 days (95% CI, 7.20-10.79) and without malnutrition 29 (95% CI, 15.67-42.33).

Table 5: Kaplan-Meir survival estimates for esophageal atresia with different covariates at NICU of Tikur Anbesa specialized Hospital from March 2011 to February 2021(n=225).

Covariate	Category	Median time to death in days			
		Estimate	95% CI	Log rank X2 value	P-value
Birth weight	2500-4000g	14	9.05-18.96	41.931	.000
	1500-2500g	8	4.75-11.25		
	1000-1500g	3	1.66-4.34		
Gestational age	37-42wk	13	10.24-15.76	10.004	.007
	28-36wk	6	2.72-9.28		
	>42wk	11	-		
Admission source	Out born	11	8.94-13.06	4.194	.041
	Inborn	-	-		
Associated congenital anomalies	Present	11	8.64-13.37	1.625	.202
	Absent	11	7.44-14.56		
Place of delivery	Home	6	2.76-9.24	5.993	.014
	Health facility	13	10.80-15.20		
History of maternal chronic illness	Yes	9	7.08-10.92	1.869	.172
	No	13	10.55-15.45		
Aspiration pneumonia	Present	11	8.92-13.08	4.495	.034
	Absent	-	-		
Sepsis	Yes	9	6.78-11.22	2.820	.093
	No	14	11.32-16.68		
Dehydration	Present	8	6.15-9.85	43.072	.000
	Absent	20	10.50-29.50		
Malnutrition	Present	9	7.20-10.79	35.527	.000
	Absent	29	15.67-42.33		
Thrombocytopenia	Yes	8	5.38-10.62	31.579	.000
	No	25	18.04-31.96		
Metabolic abnormality	Yes	8	1.07-14.93	3.122	.077
	No	12	9.78-14.22		
Diagnosis time	<48hr	14	8.18-19.82	3.239	.072
	>48hr	10	7.90-12.10		
Timing of surgery	<72hr	-	-	97.596	.000
	>72hr	26	20.80-31.20		
	No	6	5.15-6.86		

Regarding treatment-related conditions, a significant median time to death has been observed in neonates undergoing surgery after three days of admission 26 days (20.80-31.20) and those without surgical intervention 6 days (95% CI, 5.15-6.86) **(table 5)**

Failure functions among different groups of neonates with esophageal atresia

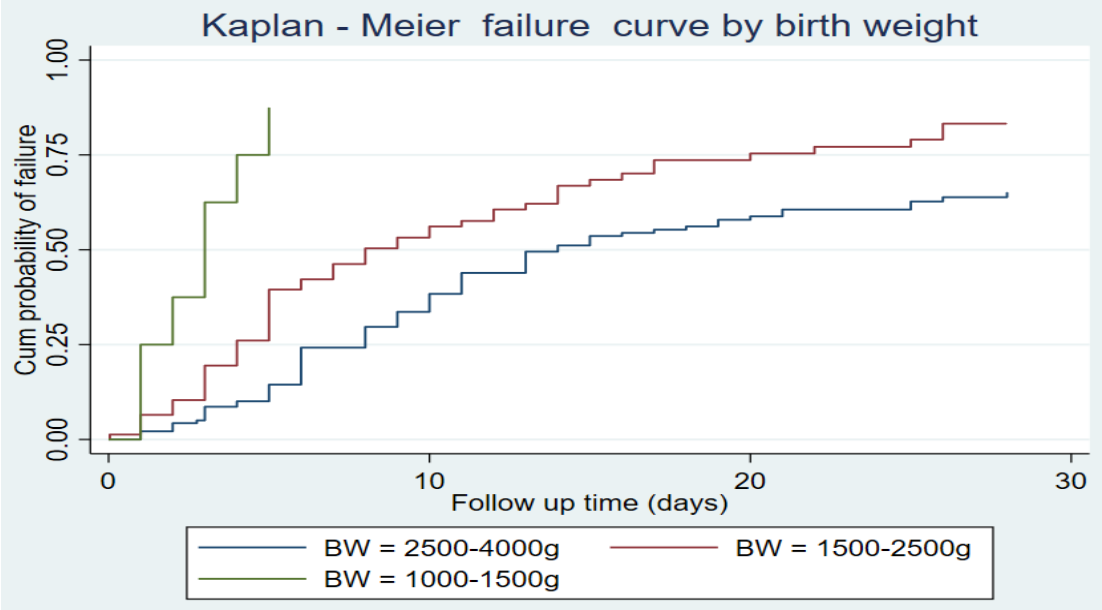

Figure 4: Kaplan-Meier failure curve by birth weight of neonates with esophageal atresia admitted in NICU at Tikur Anbesa specialized Hospital from March 2011 to February 2021(n=225).

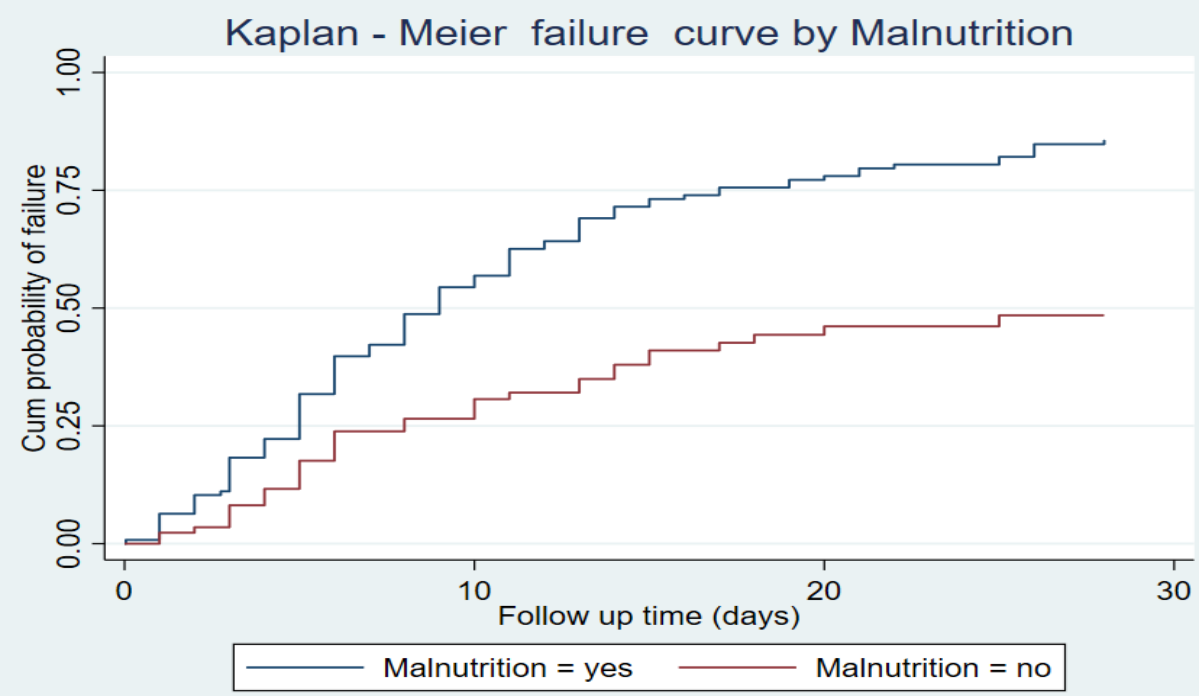

Figure 5: Kaplan-Meier failure curve by malnutrition of neonates with esophageal atresia admitted in NICU at Tikur Anbesa specialized Hospital from March 2011 to February 2021(n=225).

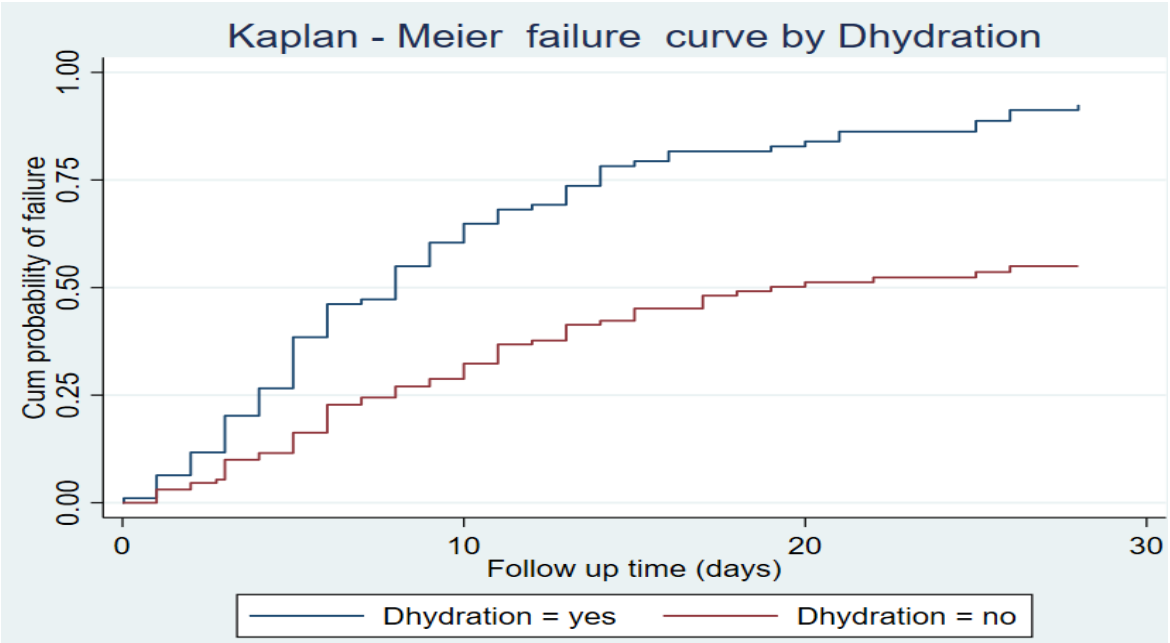

Figure 6: Kaplan-Meier failure curve by dehydration of neonates with esophageal atresia admitted in NICU at Tikur Anbesa specialized Hospital from March 2011 to February 2021(n=225).

5.7 Predictors of time to death in neonates with esophageal atresia

Bivariate and multivariate cox regression was used for analysis to identify predictors of time to death for neonates with esophageal atresia from admission to discharge/death in the neonatal intensive care unit. Findings from the bivariate analysis showed that birth weight, gestational age admission source, associated anomalies, delivery place, history of maternal chronic illness, sepsis, aspiration pneumonia, malnutrition, thrombocytopenia, dehydration, time of diagnosis timing of surgery, metabolic abnormality, and type of variant were associated with time to death of neonates diagnosed with esophageal atresia with p-Value <0.25 **(Table 6).**

However, in the multi-variable analysis birth weight, sepsis, dehydration, malnutrition, time of diagnosis and time of fistula repair were had a statistically significant association with time to death of neonates with esophageal atresia with p-Value <0.05 **(Table 7).**

The hazard of death among neonates who had very low birth weight was 3.9 times higher as compared to normal birth weight neonates (AHR =3.90, 95%CI (1.36- 11.17)). Similarly, the risk of death among neonates who had low birth weight was increased by 49 % as compared to those who had normal birth weight neonates (AHR =1.49, 95%CI (1.02 - 2.20)).

Table 6: Bivariate Cox regression model for predictors of time to death among neonates with esophageal atresia admitted in NICU at Tikur Anbesa specialized from March 2011 to February 2021(n=225).

Covariates		Died (%)	Censored (%)	CHR and 95% CI	P-value
GA	28-36 wk.	54(24)	10(4.4)	1.65(1.19-2.30)	**0.003***
	37-42 wk.	102(45.3)	51(22.7)	1	
	>42 wk.	4(1.8)	4(1.8)	0.92(0.34-2.50)	0.872
Sex	Male	74(32.9)	28(12.4)	1	0.783
	Female	86(38.2)	37(16.4)	0.96(0.70-1.30)	
BW	2500-4000g	91(40.4)	49(21.8)	1	**0.001***
	1500-2500g	62(27.6)	15(6.7)	1.78(1.28-2.46)	
	1000-1500g	7(3.1)	1(0.4)	8.17(3.62-18.43)	**0.000***
Admission source	Inborn	2(0.9)	4(1.8)	1	**0.071***
	Out born	158(70.2)	61(27.1)	3.63(0.90-14.71)	
Postnatal age at admission	<24hr	47(20.9)	21(9.3)	1	0.571
	24-48hr	27(12)	8(3.6)	1.15(0.71-1.84)	
	>48hr	86(38.2)	36(16)	0.90(0.62-1.28)	0.534
Time of diagnosis	<48 hr	58(25.8)	34(15.1)	1	**0.084***
	>48 hr	102(45.3)	31(13.8)	1.33(0.96-1.83)	
Feeding history	yes	61(27.1)	30(13.3)	0.92(0.67-1.27)	0.612
	No	99(44)	35(15.6)	1	
Associated anomalies	Yes	75(33.3)	17(7.6)	1.21(0.89-1.66)	**0.221***
	No	85(37.8)	48(21.3)	1	
Maternal age	<18yr	4(1.8)	0	1.35(0.50-3.66)	0.556
	18-35yr	136(60.5)	55(24.4)	1	
	>35yr	20 (8.9)	10(4.4)	1.30(0.81-2.09)	0.269
History of polyhydramnios	Yes	39(17.3)	12(5.3)	1.20(0.84-1.72)	0.324
	No	121(53.8)	53(23.6)	1	
Place of delivery	Home	10(4.4)	1(0.4)	2.15(1.13-4.09)	**0.020***
	Health facility	150(66.7)	64(28.4)	1	
Mode of delivery	SVD	116(51.6)	52(23.1)	1	0.439
	C/S	44(19.5)	13(5.8)	1.15(0.81-1.62)	
History of maternal chronic illness	Yes	15(6.7)	3(1.3)	1.43(0.84-2.44)	**0.190***
	No	145(64.4)	62(27.6)	1	
Aspiration pneumonia	No	9(4)	13(5.8)	1	**0.045***
	Yes	151(67.1)	52(23.1)	2.0(1.02-3.90)	
Malnutrition	Yes	117(52)	9(4)	2.80(1.94-4.04)	**0.000***
	No	38(16.9)	49(21.8)	1	

Bivariate Cox regression model for predictors of time to death among neonates with esophageal atresia admitted in NICU at Tikur Anbesa specialized from March 2011 to February 2021(n=225) (continued)

Covariates		Died (%)	Censored (%)	CHR and 95% CI	P-value
Thrombocytopenia	Yes	87 (38.7)	13(5.8)	2.39(1.73-3.30)	**0.000***
	No	67(29.8)	52(23.1)	1	
GERD	No	29(12.9)	13(5.8)	1	0.647
	Yes	131(58.2)	52(23.1)	0.91(0.61-1.36)	
Sepsis	No	103(45.8)	45(20)		**0.106***
	Yes	57(25.3)	20(8.9)	1.30(0.94-1.81)	
	No	151(67.1)	61(27.1)	1	**0.000***
Dehydration	Yes	88(39.1)	6(2.7)	2.69(1.96-3.69)	
	No	72(32)	59(26.2)	1	**0.089***
Metabolic abnormality	Yes	15(6.7)	3(1.3)	1.59(0.93-2.72)	
	No	145(64.4)	62(27.6)	1	0.275
Surgical related complication	Yes	11(9.2)	2(1.7)	0.69(0.35-1.35)	
	No	88(74)	18(15.1)	1	
Time of fistula repair	<=72 hr	5(2.2)	18 (8)	1	0.223
	>72 hr	59(26.2)	37 (16.4)	1.76(0.71-4.40)	
	No repair	96 (42.7)	10(4.4)	7.61(3.08-18.80)	**0.000***
Type of surgery	Primary repair	51(42.9)	54(45.4)	1	0.251
	Gastrostomy	12(10)	2(1.7)	1.44(0.77-2.72)	
Type of variant	Type A	16(7.3)	2(0.9)	3.13(0.72-13.64)	**0.128***
	Type B	2(0.9)	1(0.5)	1.94(0.27-13.8)	0.507
	Type C	136(62.5)	57(26.1)	2.03(0.5-8.21)	0.320
	Type D	2(0.9)	2(0.9)	1	

*** show a significant association between predictors and time to death (P < 0.25)**

This finding showed that the risk of death among neonates who did not have surgical intervention was 3.73 times higher as compared to those who underwent surgical intervention before three days (AHR; 3.73, 95% CI (1.34-10.38)). Even though there is no significant association, the risk of death among neonates who underwent surgery after three days of admission was increased by 13 % as compared to those who underwent surgery before three days of admission.

The hazard of death for neonates with esophageal atresia who did not have malnutrition is decreased by 39% as compared to its counterpart (AHR=1.61, 95%CI, 1.03 -2.58).

Table 7: Multivariate Cox regression model for predictors of time to death among neonates with esophageal atresia admitted in NICU at Tikur Anbesa specialized Hospital from March 2011 to February 2021(n=225)

Covariates		Died (%)	Censored (%)	AHR and 95% CI	P-value
GA	28-36 wk.	54(24)	10(4.4)	0.97(0.63-1.50)	0.883
	37-42 wk.	102(45.3)	51(22.7)	1	
	>42 wk.	4(1.8)	4(1.8)	2.00(0.68-5.90)	0.208
BW	2500-4000g	91(40.4)	49(21.8)	1	
	1500-2500g	62(27.6)	15(6.7)	**1.49(1.02-2.21)**	**0.049***
	1000-1500g	7(3.1)	1(0.4)	**3.90(1.36-11.17)**	**0.011***
Admission source	Inborn	2(0.9)	4(1.8)	1	0.110
	Out born	158(70.2)	61(27.1)	3.37(0.76-14.97)	
Time of diagnosis	<48 hr	58(25.8)	34(15.1)	1	
	>48 hr	102(45.3)	31(13.8)	**1.48(1.01-2.15)**	**0.043***
Associated anomalies	Yes	75(33.3)	17(7.6)	0.97(0.67-1.39)	0.851
	No	85(37.8)	48(21.3)	1	
Place of delivery	Home	10(4.4)	1(0.4)	1.78(0.87-3.62)	0.113
	Health facility	150(66.7)	64(28.4)	1	
History of maternal chronic illness	Yes	15(6.7)	3(1.3)	1.75(0.99-3.10)	0.056
	No	145(64.4)	62(27.6)	1	
Aspiration pneumonia	No	9(4)	13(5.8)	1	0.937
	Yes	151(67.1)	52(23.1)	1.03(0.49-2.19)	
Malnutrition	Yes	117(52)	9(4)	**1.61(1.03-2.58)**	**0.047***
	No	38(16.9)	49(21.8)	1	
Thrombocytopenia	Yes	87 (38.7)	13(5.8)	1.27(0.87-1.84)	0.212
	No	67(29.8)	52(23.1)	1	
Sepsis	No	103(45.8)	45(20)	1	**0.008**
	Yes	57(25.3)	20(8.9)	**1.67(1.15-2.44)**	
	No	151(67.1)	61(27.1)	1	
Dehydration	Yes	88(39.1)	6(2.7)	**2.38(1.63-3.46)**	**0.000***
	No	72(32)	59(26.2)	1	
Metabolic abnormality	Yes	15(6.7)	3(1.3)	1.40(0.77-2.53)	0.271
	No	145(64.4)	62(27.6)	1	
Time of fistula repair	<=72 hr	5(2.2)	18 (8)	1	0.813
	>72 hr	59(26.)	37 (16.4)	1.13(0.41-3.14)	
	No repair	96 (42.7)	10(4.4)	**3.73(1.33-10.38)**	**0.012***
Type of variant	Type A	16(7.3)	2(0.9)	2.17(0.44-10.66)	0.339
	Type B	2(0.9)	1(0.5)	1.44(0.18-11.81)	0.731
	Type C	136(62.5)	57(26.1)	1.69(0.38-7.44)	0.487
	Type D	2(0.9)	2(0.9)	1	

***Statistically significant predictor of death (P < 0.05)**

The risk of death of neonates with oesophageal atresia who diagnosed after two days of life was 1.48 times higher as compared to neonates diagnosed before two days of life. AHR=1.48, 95% CI (1.01-2.15)). Neonates with oesophageal atresia who had dehydration were 2.38 times increase risk of death (AHR=2.38, 95%CI (1.63 - 3.46)). Neonates with oesophageal atresia who had no sepsis were 33% less likely to die than neonates who had sepsis (AHR=1.67,95%CI (1.15 - 2.44)).

5.8 Test of proportional hazard assumption by Schoenfeld's residuals

Testing the proportional hazard assumption is vital for the interpretation and use of fitted proportional hazard models. Therefore, in this study goodness-of-fit (GOF) particularly the Schoenfeld residuals proportional hazard assumption test for the individual covariates and the global test was used. If P-Value < 0.05, then the proportional hazard assumption is violated. From the Table below, each covariate (P-Value > 0.05) and all of the covariates simultaneously (Global test for Cox proportional hazard P-Value=0.3298> 0.05) met the proportional hazard assumption.

Table 8: **Test of proportional hazard by Schoenfeld residuals for each predictor as well as a global test**

Predictor	rho	Chi2	Df	Prob>chi2
Birth weight	0.05312	0.48	1	0.4896
GA	-0.04157	0.31	1	0.5786
Admission source	0.04031	0.23	1	0.6336
Associated congenital anomalies	-0.10907	2.09	1	0.1480
Aspiration pneumonia	-0.04499	0.35	1	0.5556
Sepsis	-0.05623	0.49	1	0.4846
Metabolic abnormality	-0.09644	1.47	1	0.2247
Thrombocytopenia	0.05460	0.57	1	0.4500
Dehydration	-0.10018	1.79	1	0.1804
Time of fistula repair	-0.13006	2.99	1	0.0838
Malnutrition	-0.16407	5.51	1	0.189
Diagnosis time	-0.03748	0.24	1	0.6242
Delivery place	-0.03031	0.15	1	0.7003
History of maternal chronic illness	-0.07604	0.83	1	0.3608
Type of variant	-0.03519	0.19	1	0.6650
Global test		**15.74**	**15**	**0.3783**

6. DISCUSSION

The study aimed to determine the survival of neonates with esophageal atresia and to identify predictors of time to death. From the total of 225 neonates with esophageal atresia included in the study,71.1% of neonates have died,17.8% discharged,8% against medical advice and 3.1% lost to follow-up.

The proportion of death among neonates diagnosed with esophageal atresia admitted at NICU of Tikur Anbesa specialized hospital was 71.1%. Based on this finding the mortality of neonates diagnosed with esophageal atresia at TASH was very high as compared to the survival status of neonates with OA in western countries which was more than 95 %.

This finding is comparable with the study conducted in Nigeria reported 68.4% (44). This finding was lower than the study conducted in Senegal 78% and Ethiopia 85.3%. (32,47). This discrepancy might be due to the health-seeking and utilization behavior of the community are improved and accessibility of trained health care providers are comparatively increased, study period, study design and sample size. However, this finding was significantly higher than the studies conducted in the united states 9%, Melbourne 13.5% and Boston 5.1% (41–43). This difference might be due to the presence of advanced medical and surgical care of neonates with esophageal atresia in western countries and one of the possible reasons for this discrepancy may be the unavailability of total parenteral nutrition (TPN) and mechanical ventilation in the NICU of TASH.

The causes of time to death were not a single problem rather a combination of problems lead to death and the major ones were sepsis, malnutrition, dehydration, low birth weight, time of diagnosis and time of fistula repair.

In this study, sepsis had a statistically significant association with the time to death of neonates diagnosed with OA. This study was supported by studies conducted in Senegal and Saudi Arabia (47,51). This finding is also supported by Clinical evidence that sepsis could be due to maternal (premature rupture of membrane) or neonatal (impaired host defense) factors and due to delay making a diagnosis. Moreover, sepsis might be due to a break in the infection prevention strategies and techniques. Sepsis could complicate the babies with OA and prolong surgical intervention as a result it fastens their time to death. This finding was lower than a study conducted at Dr. Sardjito Hospital in Indonesia. The difference might be due to the study design (52).

This finding showed that neonates diagnosed after two days of life had a significant association with time to death as compared to their counterparts. The possible reason might be due to the consequence of

delay in making diagnosis patients may complicated to severe pneumonia due to aspiration, dehydration, sepsis and dependence on mechanical ventilation and death. Even though neonates with esophageal atresia should be diagnosed during the antenatal period or within hours of birth, in our study area almost all study subjects were referred from different health institutions in the country to TASH. As a result, the chance of having delayed diagnosis, aspiration pneumonia, dehydration and sepsis is higher as compared to developed countries. This could hurt their survival. This finding was supported by the study conducted in Turkey and Tunisia (46,53).

Dehydration was significantly associated with the time to death of neonates diagnosed with OA. This finding is supported by a clinical practice that neonates with esophageal atresia had decreased fluid intake, inadequate breastfeeding and excessive secretion due to the atresia in the esophagus. This condition will lead the neonate to dehydration and untreated dehydration in neonates may end up with life-threatening complications including hypovolemic shock, heat injury, kidney failure, seizure due to electrolyte imbalance and death. This finding is supported by a study in Kenya (54).

This study showed that a neonate diagnosed with OA whose weight <2500g had a significant association with time to death. This finding was lower than the study conducted in Tunisia at the department of pediatric surgery, Hedi Chaker Hospital. The reason behind could be neonates with LBW and VLBW are likely to be preterm as a result they will have chance of preterm related complications which might hasten time to death. The difference might be due to the study population and study design. This finding negates the study conducted in Boston and San Francisco which revealed that birth weight did not have an association with mortality (43). This discrepancy might be due to variable categorization and study design.

In this finding being malnourished is a predictor of time to death of neonates diagnosed with OA. This finding was supported by clinical evidence that neonates with esophageal atresia had feeding difficulties. As a result of these difficulties, neonates will have low calorie and immunity, growth and development will be affected. In our study area, there is no access to total parenteral nutrition and patients kept NPO for a prolonged time. As a consequence of this, patients with esophageal atresia are at high risk to be malnourished. Being malnourished is one of the reasons for delaying to do a surgical intervention. As result, it increases the risk of mortality. This finding is also supported by in multi-institutional cohort study conducted in Columbus (49).

This study showed that the risk of death among neonates who had no surgical intervention is higher than those who had surgical intervention before three days of admission. This finding was supported by a clinical practice that surgical intervention should be done early as soon as possible. This finding is also supported by the study conducted in St Zahra Hospital, Isfahan, Iran (55). However, in Tikur Anbesa specialized hospital, a significant majority of neonates diagnosed with esophageal atresia had a surgical time of above three days. This can increase the risk of acquiring clinical comorbidities which contribute more to delaying the surgical time. As a result of this, the risk of mortality will be increased. In our study in 50% of the cases, the time of fistula repair was 9 days which is longer than the study conducted in Serbia which was in the first 24 hours. This is described that there was a delay in surgical intervention in TASH. This delay might be due to a delay in diagnosing the problem, associated anomalies and clinical comorbidities.

7. LIMITATION AND STRENGTH OF THE STUDY

7.1 Strength of the study

This study tried to review the medical records of neonates diagnosed with esophageal atresia for the last 10 years to increase the sample size and to decrease the effect of seasonal variations. In addition, this research included malnutrition, thrombocytopenia and dehydration as independent variables which were not well investigated in the previous studies. The first study conducted nationally on time to death and predictors among neonates diagnosed with OA.

7.2 Limitation of the study

The study was based on secondary data so analysis of predictors for time to death was limited by the information that could be obtained from the patients' charts. During the follow-up time, any death recorded on the medical chart was taken as death (event) due to esophageal atresia. Because of the exclusion of incomplete medical charts, there might be Selection bias.

8. CONCLUSION AND RECOMMENDATION

8.1 Conclusion

The proportion of death among neonates diagnosed with esophageal atresia in Tikuranbesa specialized hospital is high compared to studies. The median time to death was 11 days. 76.9 % have died within 14 days of admission. low birth weight, sepsis, malnutrition, time of fistula repair, time of diagnosis, dehydration were predictors of time to death in neonates diagnosed with OA.

8.2 Recommendation

Based on the finding of this study, the following recommendations were forwarded to concerned bodies.

To Federal Ministry of Health (FMOH)

As already known, currently, there is only one treatment center for neonates diagnosed with esophageal atresia at TASH. FOMH should expand the treatment centers other than TASH because almost all cases of OA were referral cases and the majority were died due to delay in surgical intervention. FMOH should also incorporate the standard of care for neonates diagnosed with OA in the national guidelines.

To Tikur Anbesa Specilized Hospital (TASH)

TASH had better strengthen the treatment strategies of neonates diagnosed with OA by supplying the equipment needed for intervention like mechanical ventilation, Suction machine and isolated Operation room for timely surgical intervention and should make availability of total parenteral nutrition in the hospital.

To health care workers

Health care professionals should better work to diagnose esophageal atresia early and refer the patient to where the treatment center is available for better intervention. NICU workers have to work intensively by following the standard of care protocol and surgical intervention has to be done early as soon as possible. Suctioning has to be done by NICU nurses, physicians rather than parents of a neonate.

Lastly, for the researchers; a prospective study to address variables that are not well documented on the chart like genetic components, esophageal gap has to be investigated.

9. REFERENCES

1. Organization WH, (U.S.) C for DC and P, Systems IC for BDM. Birth defects surveillance: a manual for programme managers. Geneva PP - Geneva: World Health Organization; 2014. 124 p.
2. Ahmed AM, Abd S, Abd AA, Hamid E, Hassan M. Assessment of Risk Factors for Fetal Congenital Anomalies among Pregnant Women at Cairo University Hospitals. J Am Sci [Internet]. 2011;7(12):899–908. Available from: http://www.americanscience.org
3. Mortell AE, Azizkhan RG. Esophageal atresia repair with thoracotomy: the Cincinnati contemporary experience. Semin Pediatr Surg. 2009;18(1):12–9.
4. Scott DA. Esophageal Atresia / Tracheoesophageal Fistula Overview 1 . Clinical Characteristics of EA / TEF. GeneReviews. 2019;1–10.
5. Seo J, Kim DY, Kim AR, Kim DY, Kim SC, Kim IK, et al. An 18-year experience of tracheoesophageal fistula and esophageal atresia. Korean J Pediatr. 2010;53(6):705–10.
6. De Jong EM, Felix JF, De Klein A, Tibboel D. Etiology of esophageal atresia and tracheoesophageal fistula: "Mind the gap." Curr Gastroenterol Rep. 2010;12(3):215–22.
7. Ioannides AS, Copp AJ. Europe PMC Funders Group Embryology of oesophageal atresia Normal embryogenesis. Semin Pediatr Surg. 2009;18(1):2–11.
8. El-Gohary Y, Gittes GK, Tovar JA. Congenital anomalies of the esophagus. Semin Pediatr Surg. 2010;19(3):186–93.
9. Pinheiro PFM, e Silva ACS, Pereira RM. Current knowledge on esophageal atresia. World J Gastroenterol. 2012;18(28):3662–72.
10. Fernando P, Pinheiro M, Cristina A, Pereira RM, Fernando P, Pinheiro M, et al. Current knowledge on esophageal atresia. 2012;18(28):3662–72.
11. McDuffie LA, Wakeman D, Warner BW. Diagnosis of Esophageal Atresia with Tracheoesophageal Fistula: Is There a Need for Gastrointestinal Contrast? J Pediatr [Internet]. 2010;156(5):852. Available from: http://dx.doi.org/10.1016/j.jpeds.2009.10.030
12. Mortell AE, Azizkhan RG. Esophageal atresia repair with thoracotomy : the Cincinnati contemporary experience. YSPSU. 2009;18(1):12–9.

13. Pedersen RN, Calzolari E, Husby S, Garne E, Andersen HC. Oesophageal atresia : prevalence , prenatal diagnosis and associated anomalies in 23 European regions. Arch Dis Child. 2012;97:227–32.
14. Nassar N, Leoncini E, Amar E, Arteaga-Vázquez J, Bakker MK, Bower C, et al. Prevalence of esophageal atresia among 18 international birth defects surveillance programs. Birth Defects Res Part A - Clin Mol Teratol. 2012;94(11):893–9.
15. Sfeir R, Bonnard A, Khen-Dunlop N, Auber F, Gelas T, Michaud L, et al. Esophageal atresia: Data from a national cohort. J Pediatr Surg. 2013;48(8):1664–9.
16. Schneider A, Blanc S, Bonnard A, Khen-dunlop N, Auber F, Breton A, et al. Results from the French National Esophageal Atresia register : one-year outcome. 2014;4–9.
17. Nassar N, Leoncini E, Amar E, Arteaga-vázquez J. HHS Public Access. 2015;94(11):893–9.
18. Bouguermouh D, Salem A. Original article Esophageal atresia : a critical review of management at a single center in Algeria. Dis esophagus. 2014;1–6.
19. Tröbs RB, Finke W, Bahr M, Roll C, Nissen M, Vahdad MR, et al. Isolated tracheoesophageal fistula versus esophageal atresia – Early morbidity and short-term outcome. A single institution series. Int J Pediatr Otorhinolaryngol. 2017;94:104–11.
20. Donoso F, Kassa AM, Gustafson E, Meurling S, Lilja HE. Outcome and management in infants with esophageal atresia – A single centre observational study. J Pediatr Surg. 2016;51(9):1421–5.
21. Cassina M, Ruol M, Pertile R, Midrio P, Piffer S, Vicenzi V, et al. Prevalence, characteristics, and survival of children with esophageal atresia: A 32-year population-based study including 1,417,724 consecutive newborns. Birth Defects Res Part A - Clin Mol Teratol. 2016;106(7):542–8.
22. Jason P. Sulkowski, MD1, 2, Jennifer N. Cooper, PhD1, Joseph J. Lopez, MD1 Y, Jadcherla, BS1, Alissabeth Cuenot, MD1, Peter Mattei, MD3, Katherine J. Deans, MD MHSc1, 2, and Peter C. Minneci, MD MHSc1 2. Morbidity and Mortality in Patients with Esophageal Atresia. Surgery. 2014;156(2):1–17.
23. Powell L, Frawley J, Crameri J, Teague WJ, Frawley GP. Oesophageal atresia: Are "long gap" patients at greater anesthetic risk? Paediatr Anaesth. 2018;28(3):249–56.
24. van Lennep M, Singendonk MMJ, Dall'Oglio L, Gottrand F, Krishnan U, Terheggen-

Lagro SWJ, et al. Oesophageal atresia. Nat Rev Dis Prim. 2019;5(1).
25. Solomon BD. VACTERLVATER Association (2011). 2011;1–12.
26. Stoll C, Alembik Y, Dott B, Roth MP. Associated anomalies in cases with esophageal atresia. Am J Med Genet Part A. 2017;173(8):2139–57.
27. Vukadin M, Savic D. Analysis of Prognostic Factors and Mortality in Children with Esophageal Atresia. 2015;82(July):586–90.
28. Alslaim HS, Banooni AB, Shaltaf A, Novotny NM. Tracheoesophageal fistula in the developing world: are we ready for thoracoscopic repair? Pediatr Surg Int. 2020;36(5):649–54.
29. Fall M, Mbaye PA, Horace HJ, Wellé IB, Lo FB, Traore MM, et al. Oesophageal atresia: Diagnosis and prognosis in Dakar, Senegal. Afr J Paediatr Surg. 2015;12(3):187–90.
30. Bandré E, Niandolo K, … AW-A de pediatrie, 2010 U. Oesophageal atresia: management in Sub Saharian countries. europepmc.org [Internet]. 2010 [cited 2020 Nov 1];2. Available from: https://europepmc.org/article/med/20034771
31. Taye M, Afework M, Fantaye W, Diro E, Worku A. Congenital anomalies prevalence in Addis Ababa and the Amhara region , Ethiopia : a descriptive cross-sectional study. Ethiop J Pediatr. 2014;1–11.
32. Amare M, Habtamu A. Assessment Of The Outcomes Of Neonates With The Diagnosis Of Esophageal Atresia And / Or Tracheoesophageal Fistula Admitted To Tikur Anbessa Specialized Hospital- Neonatal Intensive Care Unit. Ethiop J Pediatr. 2013;13.
33. Caplan A. Psychological impact of esophageal atresia: Review of the research and clinical evidence. Dis Esophagus. 2013;26(4):392–400.
34. Rozensztrauch A, Śmigiel R, Błoch M, Patkowski D. The Impact of Congenital Esophageal Atresia on the Family Functioning. J Pediatr Nurs. 2020;50(xxxx):e85–90.
35. Vukadin M, Savic D, Malikovic A, Jovanovic D, Milickovic M, Bosnic S, et al. Analysis of Prognostic Factors and Mortality in Children with Esophageal Atresia. Indian J Pediatr. 2015;82(7):586–90.
36. Aminde LN, Ebenye VN, Arrey WT, Takah NF, Awungafac G. Oesophageal atresia with tracheo-oesophageal fistula in a preterm neonate in Limbe, Cameroon: Case report & brief literature review. BMC Res Notes. 2014;7(1):2–5.

37. Ekenze SO, Ajuzieogu O V., Nwankwo EP. Effect of cardia banding and improved anaesthetic care on outcome of oesophageal atresia in a developing country. J Trop Pediatr. 2018;64(6):539–43.
38. Hartley MJ, Smith NPM, Jaffray B. Statistical modelling of survival for babies with oesophageal atresia. J Pediatr Surg [Internet]. 2016;51(7):1110–4. Available from: http://dx.doi.org/10.1016/j.jpedsurg.2015.11.016
39. Peters RT, Ragab H, Columb MO, Bruce J, MacKinnon RJ, Craigie RJ. Mortality and morbidity in oesophageal atresia. Pediatr Surg Int. 2017;33(9):989–94.
40. M.O., Oztan¨ 1, T.Soyer2, C.I. Oztorun¨ 3, B.Fırıncı4 C. UD, Z. D¨ok¨umc¨u6, G.G.Bahadır7, I.Akkoyun8, B.D. Demirel9, A. Karaman10, I. C¸ iftc¸i11, H.Ilhan12 AP, O.¨ Ozden¨ 14, S.Yalc¸ın15, A.Oral16, G.T. Tekant17, G.Kıyan18, B.Erginel19, U.¨ G¨uvenc¸20 AOE, N. Ert ¨urk22 AY. survival rates of infants with Esophageal atresia :data of Turkish esophageal registery. Int Soc Dis esophagus. 2019;107.
41. Wang B, Tashiro J, Allan BJ, Sola JE, Parikh PP, Hogan AR, et al. A nationwide analysis of clinical outcomes among newborns with esophageal atresia and tracheoesophageal fistulas in the United States. J Surg Res [Internet]. 2014;190(2):604–12. Available from: http://dx.doi.org/10.1016/j.jss.2014.04.033
42. Tanny SPT, Fearon E, Hawley A, Critical N, Cert C, Brooks J, et al. Predictors of Mortality after Primary Discharge from Hospital in Patients. J Pediatr [Internet]. 2019;1–6. Available from: https://doi.org/10.1016/j.jpeds.2019.12.031
43. Lazow SP, Aribindi VK, Staffa SJ, Pluchinotta FR, Schecter SC, Cauley RP, et al. Predictors of index admission mortality and morbidity in contemporary esophageal atresia patients. 2020;2–8.
44. Ekenze SO, Ajuzieogu O V, Nwankwo EP. Effect of cardia banding and improved anaesthetic care on outcome of oesophageal atresia in a developing country. J ofTropical Pediatr. 2018;(January):1–5.
45. Aa H, Osei-nketiah S, Hesse AAJ, Appeadu-mensah W, Glover-addy H, Etwire VK, et al. Management of oesophageal atresia in a developing country : Is primary repair forbidden ? African J Paediatr Surg AJPSpediatrics Surg. 2016;13(3):114–9.
46. Ammar S, Sellami S, Sellami I, Hamad AB, Jarraya A, Zouari M, et al. Management of esophageal atresia and early predictive factors of mortality and morbidity in a

developing country. Dis esophagus. 2019;1–6.

47. Mbaye Fall1, Papa Alassane Mbaye2, Haingonirina Joelle Horace1, Ibrahima Bocar Wellé1, Faty Balla Lo1, Mamadou Mour Traore1, Marie Diop1, Oumar Ndour2 GN. Oesophageal atresia: Diagnosis and prognosis in Dakar, Senegal Mbaye. African J Paediatr Surg AJPSpediatrics Surg. 2015;12(3):187–90.
48. Yamoto M, Nomura A, Fukumoto K, Takahashi T, Nakaya K, Sekioka A. New prognostic classification and managements in infants with esophageal atresia. Pediatr Surg Int [Internet]. 2018;0(0):8. Available from: http://dx.doi.org/10.1007/s00383-018-4322-5
49. Jason P. Sulkowski, MD1, 2, Jennifer N. Cooper, PhD1, Joseph J. Lopez, MD1, Yamini Jadcherla, BS1, Alissabeth Cuenot, MD1, Peter Mattei, MD3, Katherine J. Deans, MD MHSc1, 2, and Peter C. Minneci, MD MHSc1 2. Morbidity and Mortality in Patients with Esophageal Atresia. Surgery [Internet]. 2014;156(2):1–7. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3624763/pdf/nihms412728.pdf
50. Li X, Jiang Y, Wang X, Yu J, Li L. A scoring system to predict mortality in infants with esophageal atresia. Medicine (Baltimore). 2017;1–6.
51. Al-Salem AH, Kothari M, Oquaish M, Khogeer S, Desouky MS. Morbidity and mortality in esophageal atresia and tracheoesophageal fistula: A 20-year review. Ann Pediatr Surg. 2013;9(3):93–8.
52. Purniti PS. Paediatrica Indonesiana. 2011;51(4):207–12.
53. Karakus SC, Ozokutan BH, Bakal U, Ceylan H, Sarac M, Kul S, et al. Delayed diagnosis: An important prognostic factor for oesophageal atresia in developing countries. J Paediatr Child Health. 2016;52(12):1090–4.
54. Akech S, Rotich B, Chepkirui M, Ayieko P, Irimu G, English M. The prevalence and management of dehydration amongst neonatal admissions to general paediatric wards in Kenya-a clinical audit. J Trop Pediatr. 2018;64(6):516–22.
55. Davari HA, Hosseinpour Dr. M, Nasiri GM, Kiani G. Mortality in esophageal atresia: Assessment of probable risk factors (10 years' experience). J Res Med Sci. 2012;17(6):540–2.

10. ANNEXES

Annex I: Information Sheet

This tool was prepared for the collection of socio-demographic, neonatal, maternal, clinical comorbid, treatment and treatment and outcome-related information that is important for the assessment of survival status and predictors of mortality among neonates with esophageal atresia admitted in neonatal intensive care units of TASH, Addis Ababa, Ethiopia, 2021. All this information was retrieved from the individual patient card without mentioning the name of the clients. This information was collected by health care providers (BSc Nurses) possibly working in the NICU clinic of the hospitals.

Lastly, for further information and concern contact this address.

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Annex II: Data extraction tool

Data collection date ----------

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

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

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

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

	Is baby has OA **Yes** ☐ ☐ **If no stop filling the questioner)** **If yes type of OA_____**		
	Part I: Socio demographic characteristic		
No	**Socio demographic and neonatal information**	**Possible answers**	**Remark**
101	Date of birth	_____/_____/_____ **E.C**	
102	Place of residency	_____	Hometown
103	Postnatal age at admission	_____days _____ hours	
104	sex	1. male 2. female	
105	Birth weight	_____ in grams	Admission weight **
106	Gestational age	_____ weeks _____days	
107	Admission source	1. Inborn 2. Out born	
108	Time of diagnosis	_____days _____ hours	
109	History of Feeding	1.yes 2. no	
110	Associated anomalies	1.yes 2. no If yes, specify _____	
	Part -II maternal related characteristics		
201	Age of the mother	_____ in years	
202	History of polyhydramnios	1. Yes 2. No	
203	Place of delivery	1. home 2. health facility	

204	Modes of delivery	1. Spontaneous vaginal delivery 2. Cesarian section	
205	History of chronic illness	1.yes 2. no If yes, specify _____	
Part III: clinical comorbid conditions			
301	Sepsis	1. Yes 2. No	
302	Aspiration pneumonia	1. Yes 2. No	If no skip Q. no = 303
303	If yes	1.before admission 2. after admission 3.at admission	
304	Malnutrition	1. Yes 2. No	
306	Thrombocytopenia	1. Yes 2. No	
307	Gastroesophageal reflex diseases (GERD)	1. Yes 2. No	
308	Metabolic abnormality	1. Yes 2. No	
309	Dehydration	1. Yes 2. No	
Part IV: Treatment related characteristic			
401	Time of fistula repair	_____ days _____hours	
402	Type of surgical repair	_____	
403	Surgical related complications	1. yes 2. No if yes, specify _____	
Part V: Outcomes of the neonates and length of hospitalization			
601	Final outcome	1.Died 2. Discharged 3. Lost to follow-up 4. Against medical advice If died 1. Before surgery 2. After surgery	
602	Length of hospitalization	Total hospital stays _____	

****** - In the case of absent birth weight, you can use the weight at admission.