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# Time to Death and Predictors Among Neonates Admitted With Respiratory Distress at Felege Hiwot Comprehensive Specialized Hospital, Bahir Dar, Northwest Ethiopia, 2022

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BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCE

SCHOOL OF HEALTH SCIENCES

DEPARTMENT OF PEDIATRICS AND CHILD HEALTH NURSING

# TIME TO DEATH AND PREDICTORS AMONG NEONATES ADMITTED WITH RESPIRATORY DISTRESS AT FELEGE HIWOT COMPREHENSIVE SPECIALIZED HOSPITAL, BAHIR DAR, NORTHWEST ETHIOPIA, 2022

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A THESIS SUBMITTED TO DEPARTMENT OF PEDIATRICS AND CHILD HEALTH NURSING, SCHOOL OF HEALTH SCIENCES, BAHIR DAR UNIVERSITY FOR THE PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS IN PEDIATRIC AND CHILD HEALTH NURSING.

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MASTER OF SCIENCE THESIS SUBMISSION FORM

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Time to death and predictors among neonates admitted with respiratory distress at Felege Hiwot Referral Hospital, Bahir Dar, Northwest Ethiopia.

By: Selamsew Kindie Nega (BSc.)

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## DECLARATION FORM

I declare and affirm by my signature that, this thesis entitled Time to death and predictors of mortality among respiratory distress neonates admitted to Felege Hiwot Comprehensive Specialized Hospital, northwest Ethiopia 2022: retrospective follow up study is my original work and all the sources that I have used throughout the thesis have been indicated and acknowledged using complete references.

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## ABBREVIATIONs AND ACRONYMS

| | |
|---|---|
| AHR | Adjusted Hazard Ratio |
| AIC | Akaike Information Criteria |
| ANC | Antenatal Care |
| APGAR | Appearance, Pulse, Grimace, Activity, Respiratory |
| BIC | Bayesian Information Criteria |
| CHD | Congenital Heart Disease |
| CHR | Crud Hazard Ratio |
| CS | Cesarian Section |
| DM | Diabetes Mellites |
| FHCSH | Felege Hiwot Comprehensive Specialized Hospital |
| FR. | Frequency |
| HC | Health Center |
| HIV/AIDS | Human Immune Virus/ Acquired Immunodeficiency Syndrome |
| HR | Hazard Ratio |
| IAD | Instrumental Assisted Delivery |
| MAS | Meconium Aspiration Syndrome |
| NICU | Neonatal Intensive Care Unit |
| RD | Respiratory Distress |
| RDS | Respiratory Distress Syndrome |
| SVD | Spontaneous Vaginal Delivery |
| TTN | Transient Tachypnea of Neonate |
| WHO | World Health Organization |

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# ABSTRACT

**Introduction:** Respiratory distress is the most significant cause of neonates in need of resuscitation and neonatal intensive care unit admission. It is one of the leading causes of early neonatal mortality, mainly in middle-and low-income countries. Besides this fact, time to death and its predictors among neonates with respiratory distress are not addressed.

**Objective:** To assess time to death and predictors among neonates admitted with respiratory distress at Felege Hiwot Comprehensive Specialized Hospital, Northwest Ethiopia, 2022.

**Methods and materials:** An institution-based retrospective follow-up study was employed among 475 records of neonates admitted with respiratory distress at Felege Hiwot comprehensive specialized Hospital from January 2019 to December 2021. Data was extracted from neonatal records after being selected through a simple random sampling technique. Data was entered into Epi-data before being exported to Statistical and Data Version 16. A failure probability table and the Kaplan-Meier failure function were computed. The assumption was checked by Schoenfeld residual test. A Weibull regression model was fitted to identify predictors of time to death among neonates admitted with respiratory distress. All variables in the bivariable analysis with p-values less than 0.15 were included in the multivariable Weibull regression model. The hazard ratio with a 95% confidence interval was reported and statistical significance was declared at a p-value of 0.05.

**Results:** The mean time to death of neonates with respiratory distress was 5.34±0.162 days. Of all deaths, 90% of death occurred within 7 days during the follow-up and the overall incidence rate was 54 deaths per 1000 neonate days from diagnosis with respiratory distress. Being male (AHR: 1.64, 95%, CI: 1.08,2.50), birth weight <2500 gram(AHR: 1.9, 95%, CI: 1.06), 3.27, not cry at birth (AHR: 2.7, 95%, CI: 1.56, 4.50), preterm (AHR: 2.42, 95%, CI: 1.33, 4.40), obstetric complications (AHR: 1.96; 95%, CI: 1.20, 3.13) and referred neonates (AHR: 1.82; 95%, CI: 1.10, 3.01) were predictors of time to death

**Conclusion and recommendations:** The risk of death was higher during the early neonatal period. Sex of the neonate, birth weight, not crying at birth, preterm, obstetric complications, and source of referral were predictors of time to death for neonates with respiratory distress. As soon as the diagnosis is set, it is better to transfer to a neonatal intensive care unit for better management.

***Keywords*:** *Respiratory distress, Time to death, predictors, Neonate, Ethiopia*

# 1. INTRODUCTION

## 1.1. Background

Respiratory distress (RD) in the neonates is defined as; a respiratory rate greater than 60 or less than 30 breaths per minute, nasal flaring, central cyanosis in room air, chest retraction, and grunting (1, 2). As a result, the presence of at least two of these clinical criteria, regardless of the cause, would indicate respiratory distress (3). It occurs immediately after birth due to abnormal respiratory function during the transition from fetal to neonatal life (4). It is one of the most common causes of admission and respiratory failure in neonates (5).

The causes of respiratory distress are diverse and multisystemic and can be classified as pulmonary and non-pulmonary in origin (6).  Pulmonary origins are the most commonly occurring including transient tachypnea of the newborn (TTN), respiratory distress syndrome (RDS) (7), meconium aspiration syndrome (8), congenital pneumonia, birth asphyxia (9-11). Other uncommon and rare causes are tracheoesophageal fistula, cysts, congenital lobar emphysema, pulmonary hypoplasia, and congenital heart disease (12).

Transit tachypnea of the newborn is a self-limiting benign condition that occurs shortly after birth and can present in term and late preterm neonates due to a delay in the clearance of fetal lung fluid after birth(13).  Respiratory distress syndrome  is also known as hyaline membrane disease, which is common in premature neonates due to a lack of alveolar surfactant (12). Meconium aspiration syndrome  respiratory distress occurs soon after birth in a neonate born from a meconium-stained milieu (14).

The progress, the level of care, and outcome of neonatal respiratory distress are determined by various predictors, including; birth weight, gestational age, and the severity of respiratory compromise (15). Early diagnosis of the causes is very important in the management of neonatal distress for better clinical outcomes (16). When there is a suspicion of respiratory distress after initial resuscitation and stabilization, it is critical to use a detailed history, physical examination, radiographic and laboratory findings to determine a more specific diagnosis and appropriate timely management (17).Irrespective of the etiology of RD the management is the same (18). The treatment of neonates with respiratory distress should be based on generalized supportive management like intranasal oxygen, and disease-specific treatment, and for severe cases, ventilator support may be used (19).

The outcome of neonatal respiratory distress is poor when the intervention is not appropriate and immediate (20). The mortality rate was high and responsible for about 20% of neonatal mortality (21). It is a very common neonatal problem and it causes death of more than one third of those affected (22).

## 1.2. Statement of the problem

Based on the United Nations report 2020, in the first 28 days of life, neonates are exposed to the highest risk of dying, at a global rate of 17 death per 1000 live births (23, 24). Sub-Saharan Africa had the highest neonatal mortality rate (27 deaths per 1,000 live births)(25). Based on the mini demographic health survey 2019, Ethiopia is one of the countries with high neonatal mortality of neonates, 33 per 1000 live birth (26). About 20.3% of neonatal mortality was observed in the Amhara region, which is higher than in other regions (27).

Respiratory distress in neonates takes a lion's share of neonatal mortality, particularly in low- and middle-income countries (20). Globally. around one in every ten neonates require respiratory assistance immediately after birth due to transitional problems or respiratory disorders, and about one of every hundred neonates needs resuscitation (14, 17). It is the most significant cause of neonates in need of resuscitation and neonatal intensive care unit (NICU) admissions (6). The severity of RD varies with gestational age, and a recent study found that 42.2% of term, 54.4% of preterm, and 3.4% of post-term neonates were affected (28).

Among neonates admitted at neonatal intensive care units with RD the mortality rate is 12.5%-60% in the world (21, 22, 29-31). In Nepal, RD accounted for 6.55% of all total live deliveries and 30.83% of all NICU admissions (32). The study conducted in South Asian countries was responsible for 30.77%-34.3% of NICU admissions and contribute 12.5%-21.5% of mortality (33, 34). In Africa, studies found that 26.2%-60% of neonates were admitted due to RD, and 26.2%-36.6% died (22, 35, 36). In a study conducted in Cameroon, 90% of mortality occurred within 7days (36). In Ethiopia, 34-42.9% of neonates admitted were due to RD (37, 38). Even though a study shows that RD shares a high neonatal mortality rate in Ethiopia, there is no data on the mortality rate of respiratory distress in Ethiopia (27).

The severity of neonatal respiratory distress can be assessed by Downe's score, which includes respiratory rate, retraction, grunting, cyanosis, and air entry (39). Different risk factors predispose to respiratory distress in neonates, including; low gestational age, an increasing number of Caesarean sections, meconium-stained amniotic fluid, gestational diabetes, maternal chorioamnionitis, or prenatal ultrasonographic findings, such as oligohydramnios or structural lung abnormalities (17, 40, 41). Even though the risk factors are preventable, the prevalence and mortality rate of neonatal respiratory distress is still alarming, particularly in low- and middle-income countries (36).

Respiratory distress is not identified and treated promptly, it can led to short-or long-term complications (14). Study done Nigeria 8 % of neonates admitted with RD were discharged with complications (22). Short-term complications like, hypoglycemia, anemia, hypernatremia, and late include gastroesophageal reflux, feeding intolerance, growth failure, apnea, sudden death as well as developmental and neurologic deficits (8). According to the study, 1.9 % of preterm neonates with RDs developed cerebral palsy later in life (42). It also exposes the neonates to respiratory failure, cardiopulmonary arrest, and even death (16). It was 2-4 times more at risk of death in comparison to a newborn without respiratory distress (11). It puts pressure on the country's economy because of its magnitude; implementing the specified newborn and child survival interventions requires a total of United States $1.16 billion ( 23.2 billion Ethiopian Birr) during a five-year period (2015–2020) (43, 44).

Ethiopia implements different national and global indicators to overcome neonatal mortality and morbidity, like the Maternal and Child Survival Program (45), National Newborn and Child Survival Strategy (43), Sustainable Development Goal (SGDs) (46) and Every Women and Every Child initiative (47). Federal Ministry of Health has given due emphasis to the expansion of quality high-impact neonatal interventions in health centers and Hospitals, including establishing basic newborn care units (newborn corners) at health centers and NICUs at Hospitals (39).

Today, despite advances in clinical diagnosis and management, neonatal mortality in our country has remained increasing(26). In Ethiopia, plan in the National Newborn and Child Survival Strategy is to reduce neonatal mortality to 11/1000 live births in 2020 (44). However, neonates continue to die of easily preventable and treatable diseases for which low cost and effective interventions exist (38). Based on available evidence, there is no data related to RD in neonates, mainly time to death and significant predictors. To improve the outcome of neonates with RD, it is vital to have precise data on when high mortality occurs. Therefore, this study assessed time to death and predictors among neonates admitted with respiratory distress in the neonatal intensive care unit of Felege Hiwot comprehensive specialized Hospital, Northwest Ethiopia.

### 1.3. Significance of the study

The well-being of neonates determines the health of the next generation and can help predict future public health challenges for families, communities, and the medical care system. Moreover, healthy birth outcomes and early identification and treatment of health conditions among infants can prevent death or disability and enable children to reach their full potential. Studying the time to death and its predictors among neonates admitted with RD is important with other related studies to update preventive guidelines and treatment protocols to reduce the mortality of neonates due to preventive causes. The results of the study will be used to improve the health outcome of neonates by providing data for health care providers to prevent and intervene timely. Since nurses are the first to detect tachypnea ( the first sign of respiratory distress) (48), this will determine the most vulnerable time and they are used as a guideline for prioritizing intervention to prevent RD-related death.

It will be used for health policymakers as an impute to document gaps and in designing attainable interventions to increase the survival rate of neonates and prevent complications due to respiratory distress in neonates. Finally, the findings of this study will be used as reference for researchers who have an interest to carry out further investigations.

# 2. LITERATURE REVIEW

## 2.1. Time to death

In the study done in Kenya among neonates with RD, there were 72.3% deaths during the study period, with 58% occurring within the first 10 days of life, and the Mortality rate at day 10 was 61% (49). In a study conducted in Cameroon, 90% of mortality occurred within 7days (36). A prospective study was conducted in Sri Lanka among neonates with respiratory distress; 3.5% died within the first 2 hours of birth (50).

The magnitude of mortality among neonates with RD is different in different studies. A prospective cohort study conducted in India revealed that the overall mortality of neonates was 12.5% (29). Another prospective study conducted in India found that the mortality rate of neonates with RD was 21.5% (21). In Nepal, of neonates admitted with respiratory distress to NICU, 4.5-12.8% died (32, 51). In Iraq, of neonates admitted to NICU due to RD, 19.3% were died (30). A recent retrospective study conducted in Yemen found that approximately half (49.2%) of neonates were died (40).

In African countries, there are different studies conducted on the mortality of neonates having respiratory distress. A retrospective study conducted in Egypt the mortality rate was 26.2% of neonates admitted with respiratory distress (52). The other study conducted in Nigeria found that the mortality rate was 36.6% of those admitted with respiratory distress (53). In a retrospective follow-up study done in Cameroon, the overall neonatal respiratory distress mortality was 24.5% (36). Another prospective cohort study done in Sudan shows that 36% of admitted neonates die due to RD (35).

### 2.2. Predictors of mortality among neonates with respiratory distress

There are different predictors of mortality among neonates admitted with respiratory distress neonates. Based on the previous study, the predictors were grouped as, neonatal predictors, socio demographic and obstetric, and maternal medical disorders related predictors.

#### 2.2.1. Neonatal-related predictors

Male sex is a non-modified predictor of mortality in neonates with RD, according to studies conducted in India, Pakistan, and Cameroon. (34, 35, 54). The other findings in India revealed that birth weight of less than 1620 gm, GA less than 31 weeks, and an APGAR score of less than 6 at five minutes were significant predictors associated with neonatal mortality (15, 55). Birth weight of less than 1000 gm, an APGAR score of less than 3 at five minutes, and small GA were identified as predictors of mortality in India (31). In a prospective study conducted in Colombia, the risk factor associated with mortality was a first-minute Apgar score of less than 6 (50). In a study conducted in Cameroon APGAR score less than 7 at the 1st minute, prematurity, and birth weight ≥ 4000 grams are the predictors of neonatal respiratory distress mortality (36).

In Misan University, Iraq; a neonate who was born preterm was one of the predictors of mortality among respiratory distress neonates (11). In an Iran finding show when neonates' NICU stay was extended by one day, mortality decreased by 18.5 percent, while the likelihood of death in patients requiring mechanical ventilation increased to 33.497 times (32). In Cameroon an APGAR score of 7 at the first minute, prematurity, and birth weight of 4000 gram were found to be predictors of neonatal respiratory distress mortality (31). Crying newborns who are breathing at delivery are not breathing after 1 and 5 minutes and are at risk of predischarge mortality(56).

#### 2.2.2. Obstetric -related predictors

In India, the study found that vaginal delivery was a predictor of neonatal mortality than deliver through cesarean sectioning among neonates with respiratory distress (31). Study in Egypt pre-eclampsia, oligohydramnios, and C.S delivery were the identified significant predictors of mortality among respiratory distress neonates (52). A study done in India identified that antenatal history of per vaginal bleed, meconium liquor, and prolonged rupture of the membrane (PROM) were significant predictors of mortality among those respiratory distress neonates (55). The other prospective follow-up study conducted at in Iraq mothers delivered through vaginal and multiple pregnancies were the identified predictors (11). In Cameroon shows that elective cesarean delivery was an independent predictor of respiratory distress in neonates (36). The finding in Nigeria neonates born out of the hospital or referred from other health center has high significance predictors of neonatal mortality due to RD (22).

#### 2.2.3. Maternal medical-related predictors

Study in Egypt maternal diabetes was the identified significant predictor of mortality among respiratory distress neonates (52). Another prospective study showed that maternal hypertension increases the risk of neonatal respiratory distress mortality (57).

### 2.3. Conceptual framework

The conceptual framework was developed from different literature to show the relationships of neonatal related predictors, socio demographic and obstetric predictors, and medical disorders of the mother and time to death due to respiratory distress. The predictors are conceptualized from different literatures that have significance to neonatal mortality due to RD. It also shows the effects of one independent variables to the other using the Brocken line (11, 22, 31, 34, 36).

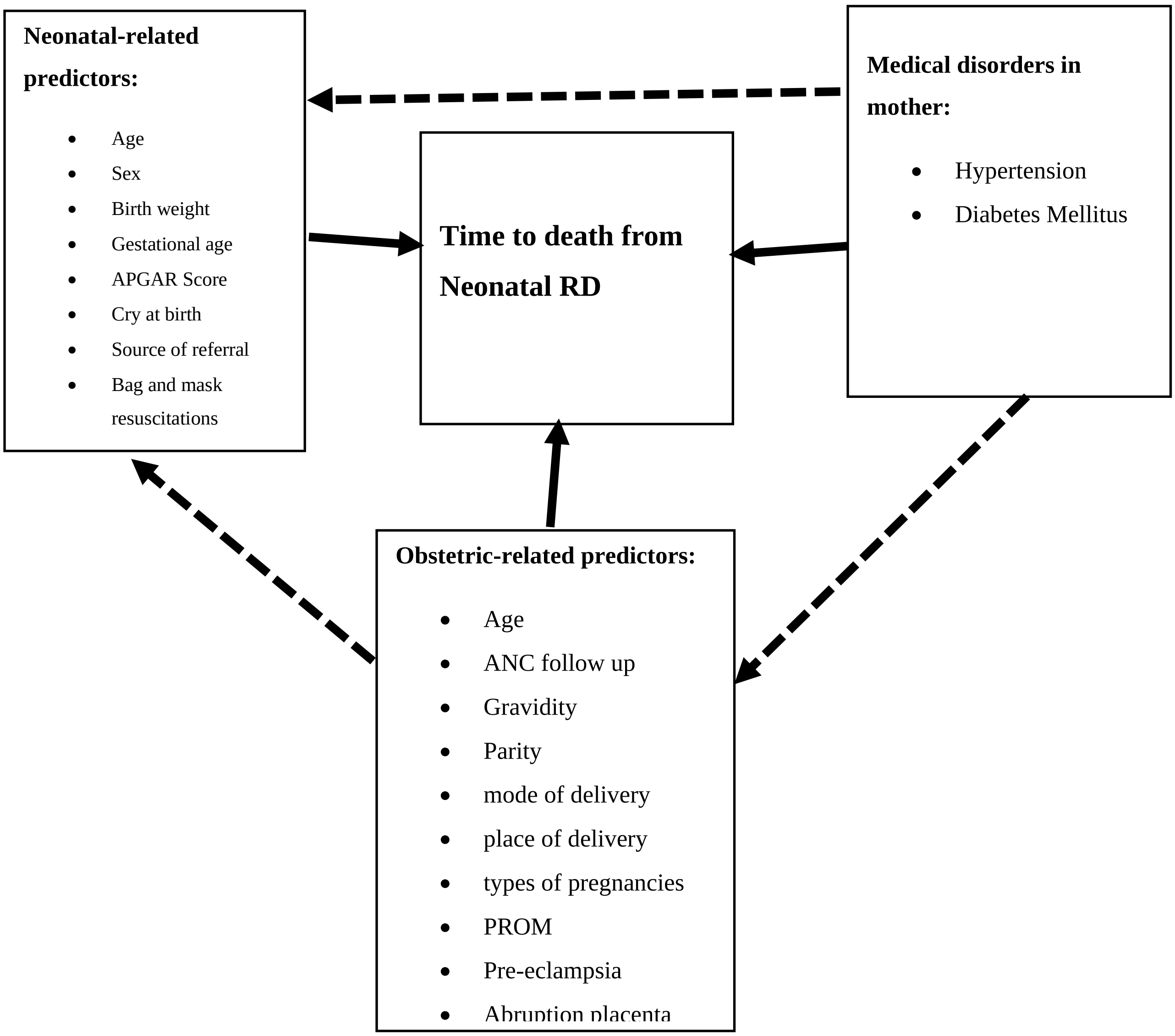


Figure 1: Conceptual framework to show the association between time to death and independent predictors of neonates admitted with respiratory distress, Bahir Dar, Northwest Ethiopia, 2022

# 3. OBJECTIVE

## 3.1. General objective

To assess time to death and predictors among neonates admitted with respiratory distress in Felege Hiwot Comprehensive Specialized Hospital, Bahir Dar, Northwest Ethiopia, 2022

## 3.1. Specific objectives

To determine the time to death among neonates admitted with respiratory distress

To identify predictors of mortality among neonates admitted with respiratory distress

# 4. METHODS AND MATERIALS

## 4.1. Study setting and period

This study was conducted at Felege Hiwot Comprehensive Specialized Hospital, which is located in Bahir Dar City, the capital of Amhara regional state. Which is located 565km away from Addis Ababa, capital City of Ethiopia. Currently, the city has one comprehensive specialized Hospital, one comprehensive specialized teaching Hospital, and one primary public Hospital (58). Felege Hiwot Comprehensive Specialized Hospital is among the three Hospitals which has 410 beds and serve more than 5 million people. The NICU ward is one of the departments that contains about 71 beds with average annual admission of 2100 neonates. From January 2019 to December 2021, about 1765 neonates were admitted with the diagnosis of respiratory distress. Currently, the ward has 35 nurses, 8 general practitioners, and 3 pediatricians. The study was conducted from January, 2019 to December, 2021 among neonates admitted with respiratory distress and the charts were retrieved from May 2022 to June 2022.

## 4.2. Study design

An institution-based retrospective follow-up study was conducted

### 4.3. Population

### 4.3.1. Target population

All neonates admitted with respiratory distress in FHCSH

### 4.3.2. Study population

All neonates admitted with respiratory distress at Felege Hiwot Comprehensive Specialized Hospital from January 2019 to December 2021.

### 4.3.3. Study subjects

All neonates admitted with respiratory distress whose charts were selected with a simple random sampling technique from study population.

## 4.4. Eligibility criteria

### 4.4.1. Inclusion criteria

Neonates who were admitted to FHCSH with the diagnosis of respiratory distress from January 2019 to December 2021.

### 4.4.2. Exclusion criteria

Neonates admitted to FHCSH from January 2019 to December 2021 with respiratory distress whose medical record numbers were not recorded and unreadable in the registration book.

### 4.5. Sample size determination and procedure

### 4.5.1. Sample size determination

To determine the sample size predictors of neonatal mortality among respiratory distress were considered. By using STATA version 16 software, the sample size was determined by assuming a two-sided significance level (α) of 5%, a 95% confidence interval, power of 80%, a hazard ratio, the probability of an event, and a proportion of withdrawal of 10%. The largest sample size was observed in birth weight after calculating from various predictors (Table 1).

Table 1: Sample size calculation for predictors of mortality among neonates with respiratory distress, Bahir Dar, Northwest Ethiopia, 2022

| Variable | | Probability event | HR | Sample size | Reference |
|---|---|---|---|---|---|
| Birth weight | <2500gm | 0.153 | 2 | 475 | (36) |
| | ≥2500 | | | | |
| APGAR score at 5 minutes | <7 | 0.082 | 4.29 | 201 | (36) |
| | ≥7 | | | | |
| Place of delivery | Out born | 0.37 | 1.96 | 209 | (22) |
| | Inborn | | | | |
| Gestational age | <31weeks | 0.2 | 7.93 | 41 | (59) |
| | ≥31 weeks | | | | |

The maximum sample size was taken after calculating the predictors of RD mortality from the study done in Cameroon(36). The final sample size was 475.

### 4.5.2. Sampling procedures

The study participants were selected from the registration books. The records of neonates admitted with respiratory distress in the neonatal intensive care unit from January, 2019 to December, 2021 were listed using the medical record number. The sampling frame was prepared using the medical record number. The study participants were selected by using a simple random sampling technique using a computer-generated method by SPSS version 25. Then, using the medical record number, the charts were retrieved from the patient record catalog. Finally, the data was extracted from the selected medical charts.

### 4.6. Variables of the study

### 4.6.1. Dependent variable

Time to death from neonatal RD

### 4.6.2. Independent variables

**Neonatal related predictors:** age, gestational age, sex, birth weight, APGAR score, cry at birth, source of referral, history of bag and mask resuscitation at birth

**Socio demographic and obstetric related predictors of the mother:** age, residence, ANC follow up, gravidity, parity, mode of delivery, onset of labor, types pregnancies, place of delivery, PROM, preeclampsia, abruption placenta, and breastfeeding initiation within one hour

**Medical disorders in mother:** Hypertension, diabetes mallets

### 4.7. Operational definitions

**Event:** Death among neonates with respiratory distress during the study period.

**Censored:** Neonates referred, against, unknown outcome or discharged for any reason before the event (death) occurred during the study period.

**Time to death:** The interval in days between diagnosis with respiratory distress to the occurrence of death

**Follow up time:** The time starting from diagnosis with respiratory distress until either an event or censorship occurs

**Medical disorders in mother:** Any history of medical diagnosis in the mother as it has been registered on the neonate's medical record

**Time origin**: At the time of diagnosis of the neonates with respiratory distress at NICU

**Time scale**: Days from the diagnosis of a neonate with respiratory distress.

**Respiratory distress:** Is diagnosed based on the presence of two or more; abnormal respiratory rates, expiratory grunting, nasal flaring, chest wall recessions, and cyanosis, in their files.

**Failure status:** Is the outcome of the RD neonate, either death or censored.

**Failure time**: Measures the follow-up time from a defined starting point/from diagnosis of RD up to the occurrence of the outcome/last neonatal period

## 4.8. Data collection procedures and tools

Neonate's records were reviewed using their medical record number identified in the registration books. Their charts were reviewed and data was extracted using an English data extraction checklist by two trained BSC nurses and supervised by one BSc nurse. The semi-structured data extraction checklist tool was adopted by considering neonatal-related predictors, maternal socio demographic and obstetric-related predictors, and medical disorders of mothers from different literatures.

## 4.9. Quality assurance

Data quality was assured thorough training of both the supervisor and data collectors for one day about how and what information they should collect from the exact data sources. Data extraction forms were checked for their completeness and any missing information before data collection. During data collection, the supervisor and principal investigator checked the collected data for completeness on a daily basis and provided prompt feedback. A pretest was done on 5% (24) of the study sample in Felege Hiwot Comprehensive Specialized Hospital. The data was not added to analysis. After the pretest, the necessary corrections were made on the checklist, like avoiding APGAR at 10 minutes and Mechanical ventilation related in the checklist because it was not recorded on the chart and rearrangements of sequence. During the data extraction period, about 62 randomly selected charts were incomplete or major variables were missing, and the charts were replaced with new, randomly selected ones until the sample size was saturated. Missing variables were checked on daily and managed accordingly. Based on the data study unit having missing value greater than 10% the variables considered as incomplete data and after enter in to Epi data variables with missing value greater than 10% of the sample size was removed from the analysis. The principal investigator carefully entered and thoroughly cleaned the data before the beginning of the analysis.

## 4.10. Data processing and analysis

Data were checked manually for completeness and entered into Epi-data software version 4.6.0.6 Then, the data were transported to STATA version 16 and cleaned before analysis. Descriptive findings were presented in tables, figures, and in text form. Incidence density rate (IDR) was calculated for the entire study period. Failure probability table and Kaplan–Meier failure function were computed. Kaplan Meier with log-rank test was used to compare survival time between categories of different predictors. A multicollinearity test was done through spearman rank correlation based on the result. APGAR scores at 1 minute and at 5 minutes (rho 0.954) were correlated. The variable APGAR score at 1 minute was omitted due to their correlation. The proportional hazard (PH) assumption was checked graphically through Kaplan Meier (log-log) and by global and detailed Schoenfeld residuals tests. Based on this test, the model was fitted with a *p*-value of $> 0.05$ and a global test result of 0.1947 (appendix). The AIC and BIC of Cox regression and parametric regression (exponential, Weibull, and Gompertz) models were compared by taking the baseline hazard distribution assumptions into account. The distribution with the lowest AIC or BIC a was considered the best model. The Weibull regression model was chosen to fit the data set based on lowest AIC. Weibull regression model assumption was checked through log – log of survival time against log of analysis time and the graph was straight and parallel. The association between predictors and the outcome variable (time to death) was assessed by the Weibull regression model. As variable selection precedes model diagnostics, all variables in the bivariable analysis with p-values less than 0.15 were included in the multivariable Weibull regression model. The Likelihood Ratio test was used to diagnose the model. Since the likelihood ratio test was significant (p-value$<0.05$), the model was adequate (p-value 0.0008). Statistically significant predictors for time to death were identified based on the adjusted hazard ratio and its 95% confidence interval at a p-value $\leq 0.05$.

### 4.11. Ethical considerations

Ethical clearance was obtained from college of medicine and health science, Bahir Dar University institutional review board (IRB) protocol number 401/2022 after approval of the proposal. A letter was obtained from college of medicine and health science chief academic and research director to Felege Hiwot comprehensive specialized referral hospital. Data collection was started after getting permission from FHCSH. To keep confidentiality names and unique card numbers were not included in the collection checklist and all collected data was coded and locked in a separate room before being entered into the computer. After entering into the computer, the data was locked by password and the data were not disclosed to any person other than the principal investigator. All information collected from the charts were kept strictly and confidentially.

### 4.12. Dissemination of the results

The results of the study will be submitted to Bahir Dar University College of Medicine and Health Sciences, Department of Pediatrics and Child Health Nursing. The findings will be distributed to Felege Hiwot Comprehensive Specialized Hospital, Amhara health bureau, and other responsible organizations working on the related areas to use as a baseline for intervention. The study will be presented at a related conference. The result will be submitted to the international or national p journal for publication.

# 5.RESULTS

## 5.1. Socio-demographic and Obstetric Characteristics of Mothers of Neonates

A total of 475 charts of neonates admitted in the NICU were reviewed. The mean age of the mothers of neonate with respiratory distress was 28.61±5.4 years and more than three quarters, 375 (78.85%) of them were between the age of 20 and 35 years. The majority, 419 (88.21%), of mothers attended ANC and approximately 30% of mothers had at least one complication during the index pregnancy. Nearly 87% of the mothers had a singleton pregnancy and for about 94% of the mothers, the labor was of spontaneous onset. More than half, 57% of mothers had a spontaneous vaginal delivery and about 62% of the births occurred at Hospitals (Table 2).

Table 2: Socio-demographic and obstetric characteristics of mothers of neonates with respiratory distress admitted at FHCSH, Northwest Ethiopia, 2022 (n=475)

| Variables | Category | Total | | Death | | Censored | |
|---|---|---|---|---|---|---|---|
| | | FR. | % | FR. | % | FR | % |
| maternal age (year) | <20 | 14 | 2.9 | 3 | 0.6 | 11 | 2.3 |
| | 20-35 | 375 | 80 | 108 | 22.7 | 267 | 56.3 |
| | ≥35 | 86 | 18.1 | 26 | 5.5 | 60 | 12.6 |
| Residence | Rural | 230 | 48.4 | 97 | 20.4 | 133 | 28 |
| | Urban | 245 | 51.6 | 40 | 8.4 | 205 | 43.2 |
| Had ANC follow up | Yes | 419 | 88.2 | 101 | 21.3 | 318 | 66.9 |
| | No | 56 | 11.8 | 36 | 7.6 | 20 | 4.2 |
| Parity | I | 265 | 55.8 | 72 | 15.2 | 193 | 40.6 |
| | II-V | 200 | 42.1 | 63 | 13.3 | 137 | 28.8 |
| | ≥V | 10 | 2.1 | 2 | 0.4 | 8 | 1.7 |
| Types of Pregnancy | Single | 411 | 86.5 | 96 | 20.2 | 315 | 66.3 |
| | Twin | 64 | 13.5 | 41 | 8.6 | 23 | 4.9 |
| Onset of labor | Elective CS | 5 | 1 | 2 | 0.4 | 3 | 0.6 |
| | Spontaneous onset | 461 | 97.1 | 132 | 27.8 | 329 | 69.3 |
| | Induced | 9 | 1.9 | 3 | 0.6 | 6 | 1.3 |
| Place of delivery | Home | 28 | 5.9 | 24 | 5.1 | 4 | 0.8 |
| | Health center | 166 | 34.9 | 77 | 16.2 | 89 | 18.7 |
| | Hospital | 281 | 59.2 | 36 | 7.6 | 245 | 51.6 |
| Mode of delivery | SVD | 273 | 57.5 | 54 | 11.4 | 219 | 46.1 |
| | CS | 145 | 30.5 | 65 | 13.7 | 80 | 16.8 |
| | IAD | 57 | 12 | 18 | 3.8 | 39 | 8.2 |
| Maternal chronic disease | Yes | 110 | 23.2 | 68 | 14.3 | 42 | 8.8 |
| | No | 365 | 76.8 | 69 | 14.5 | 296 | 62.3 |
| History of bad obstetric diagnosis | Yes | 154 | 32.4 | 99 | 20.8 | 55 | 11.6 |
| | No | 321 | 67.6 | 38 | 8 | 283 | 59.6 |

SVD: spontaneous vaginal delivery, CS: cesarean sectioning, IAD: Instrumental assisted delivery

### 5.2. Characteristics of neonates admitted with respiratory distress

More than half 53% of neonates admitted with respiratory distress were males, and about 37% were preterm births. More than two third 67.4% of neonates cried immediately at birth and about 42.5% of neonates were birth weight of less than 2500 gram. About three fourth (75.1%) of neonates admitted with respiratory distress was put on respiratory support on admission. Neonates with respiratory distress only 17% were resuscitated with bag and mask and nearly 15% had less than three APGAR score at five minutes. Regarding source of referral more than half (54.1%) of neonates with respiratory distress admitted through referral (Table 3).

Table 3: Characteristics of neonates admitted with respiratory distress at FHCSH, Northwest Ethiopia, 2022 (n=475)

| Variables | Category | Total | | Death | | Censored | |
|---|---|---|---|---|---|---|---|
| | | FR | % | FR | % | FR | % |
| Sex | Male | 251 | 52.8 | 100 | 21 | 151 | 31.8 |
| | Female | 224 | 47.2 | 37 | 7.8 | 187 | 39.4 |
| Age of neonate in days | <7 | 454 | 95.6 | 131 | 27.6 | 323 | 68 |
| | ≥7 | 21 | 4.4 | 6 | 1.3 | 15 | 3.1 |
| Gestational age at birth in complete week | <37 | 175 | 36.9 | 111 | 23.4 | 64 | 13.5 |
| | ≥37 | 300 | 63.1 | 26 | 5.4 | 274 | 57.7 |
| Source of referral | Inborn | 218 | 45.9 | 21 | 4.4 | 197 | 41.5 |
| | Out born | 257 | 54.1 | 116 | 24.4 | 141 | 29.7 |
| Birth weight | <2500 | 202 | 42.5 | 112 | 23.6 | 90 | 18.9 |
| | ≥2500 | 273 | 57.5 | 25 | 5.3 | 248 | 55.2 |
| APGAR score at 1 minute | <3 | 71 | 14.9 | 63 | 13.2 | 8 | 1.7 |
| | 3-6 | 141 | 29.7 | 56 | 17.8 | 85 | 17.9 |
| | ≥7 | 263 | 55.4 | 18 | 3.8 | 245 | 51.6 |
| APGAR score at 5 minutes | <3 | 36 | 7.5 | 33 | 6.9 | 3 | 0.6 |
| | 3-6 | 101 | 21.4 | 72 | 15.2 | 29 | 6.2 |
| | ≥7 | 338 | 71.1 | 32 | 6.7 | 306 | 64.4 |
| Cry at birth | Yes | 320 | 67.4 | 26 | 5.5 | 294 | 61.9 |
| | No | 155 | 29.6 | 111 | 23.4 | 44 | 6.2 |
| On respiratory support on admission | Yes | 357 | 75.1 | 107 | 22.5 | 250 | 52.6 |
| | No | 118 | 24.9 | 30 | 6.4 | 88 | 18.5 |
| Bag and mask resuscitation at birth | Yes | 81 | 17 | 22 | 4.6 | 59 | 12.4 |
| | No | 394 | 83 | 115 | 24.3 | 279 | 58.7 |
| Initiation BF within 1 hour | Yes | 96 | 20.2 | 16 | 3.4 | 80 | 16.8 |
| | No | 379 | 79.8 | 121 | 25.5 | 258 | 54.3 |

Fr: Frequency, BF: Breast Feeding

### 5.3. Time to death among neonates admitted with respiratory distress

In this study the median time to death was not determined due to the largest observation is censored observation. Accordingly, the mean ±standard deviation time to death among neonates died was 5.34±0.163 days. The mean time to death of neonates with respiratory distress was different across categories of maternal and neonatal related characteristics. For instance, the mean time to death of male and female neonates with respiratory distress was 10.3 and 17.1 days respectively.

### 5.4. The incidence of Failure/Death of Neonates admitted with respiratory distress

During the follow up period about 475 neonatal charts were reviewed. The lowest and highest length of follow up were 1 and 22 days respectively and the total person-time risk was 2,537 neonate days. Among the neonates followed, 137 (28.8%, 95%, CI: 20.8, 33.1) died during the follow-up period and that accounts the neonatal mortality rate (NMR) 288 per 1000 live births (Figure 2). The overall death incidence rate in this study was 54 (95% CI 45.67, 63.84) per 1000 neonate days from diagnosis with respiratory distress to death. The incidence rate across different categories was different. As an example, the incidence rate of mortality regarding term and preterm gestational age was 1.42 per 100 neonate days (95 % CI: 0.56, 2.08) and 15.7 per 100 neonate days (95% CI: 13.1, 18.3) respectively (Table 4).

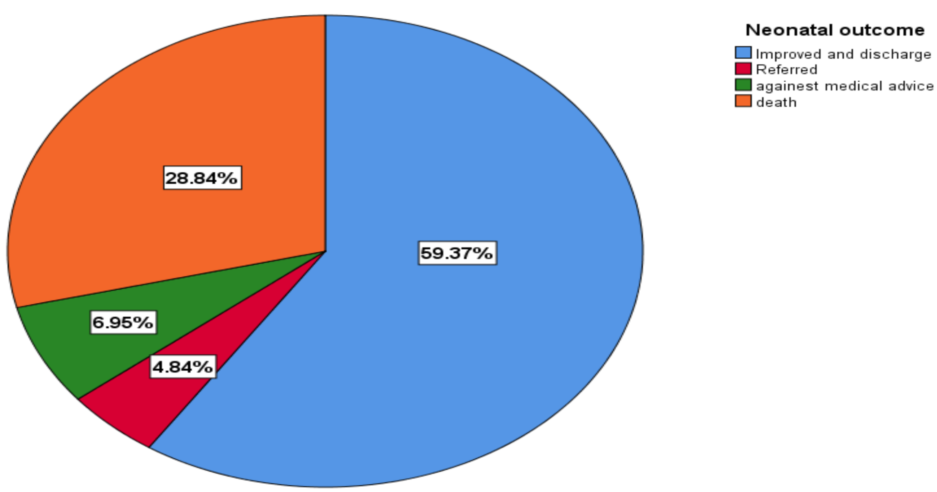


Figure 2: Proportions of outcomes among neonates admitted with respiratory distress in FHCSH, Bahir Dar, Northwest Ethiopia, 2022 (n=475)

### 5.5. Failure estimate of time to death

From all deaths, about 41% of the neonates died in the first 24 hours, nearly 78% died in the first 3 days, almost 90% of the neonatal deaths occurred in the first 1 week of life and the rest 10% deaths occurred up to 13 days from diagnosis of respiratory distress. The probability of failure during the follow-up time from date of diagnosis with respiratory distress to death was also presented by the failure curve. Accordingly, during the first 3 days, the graph went up sharply increasing showing a higher probability of neonatal death. Also, between days 3 and 7, the probability of death continued to increase moved upward. In 7 up to day 13 the graph increases upward and showed that neonatal death with respiratory distress remained continued. In the remaining days of the follow-up period, the graph became straight indicating the likelihood of neonatal death remained stable with virtually no deaths occurring (Figure 3). Life table also done (Appendix 3)

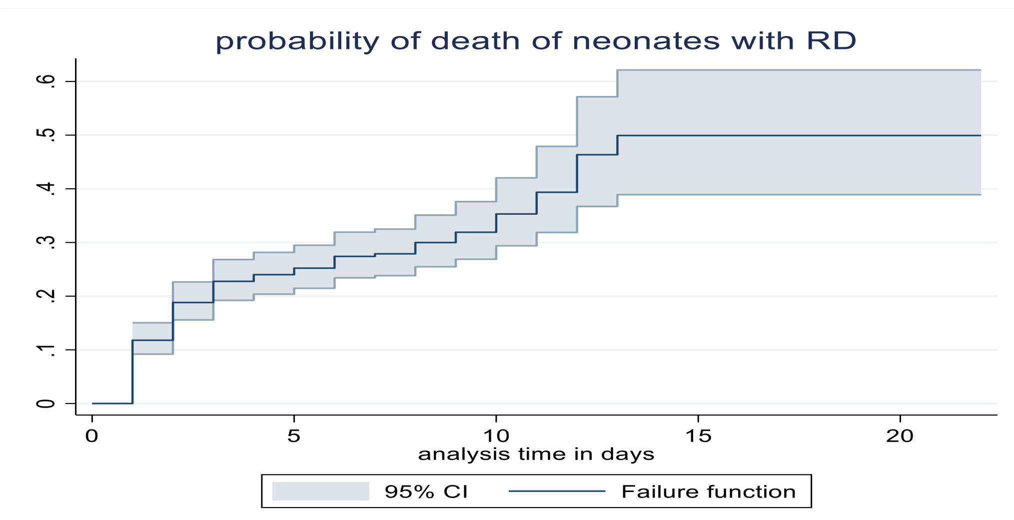


Figure 3:Summary of Kaplan–Meier failure estimate of neonates admitted with respiratory distress at FHCSH, Northwest Ethiopia, 2022 (n=475)

### 5.4. Predictors of time to death among neonates with respiratory distress

The log-rank test was used to estimate failure probability between categories of different predictor variables revealed that the failure pattern among neonates with respiratory distress was significantly different as there is a highly significant difference among failure curves. The Kaplan-Meier together with the log-rank test shows the relations of each predictor on the neonatal mortality among neonates with respiratory distress (Table 4). Among twenty independent variables fifteen are significant at p-value <0.15.

Table 4:Log-rank test for equality of different categorical predictors of neonates admitted with respiratory distress at FHCSH, Bahir Dar, Northwest Ethiopia, 2022 (n=475)

| Variables | Category | Event | Incidence per 100 days (95% CI) | $X^2$ | p-value |
|---|---|---|---|---|---|
| Residence | Rural | 97 | 8.87 (7.27, 10.87) | 38.31 | 0.021 |
| | Urban | 40 | 2.77 (2.03,3.51) | | |
| ANC follow up | Yes | 101 | 4.31 (3.55, 5.24) | 51.88 | 0.031 |
| | No | 36 | 2.85 (2.22, 3.48) | | |
| Types of pregnancy | Single | 96 | 4.14 (3.39, 4.89) | 64.81 | <0.001 |
| | Twin | 41 | 8.64 (4.7, 12.57) | | |
| Place of delivery | Home | 24 | 23.5 (16.6,30.4) | 109.96 | <0.001 |
| | HC | 77 | 10 (9.5, 12.4) | | |
| | Hospital | 36 | 2.17 (1.56, 3) | | |
| Mode delivery | SVD | 54 | 3.45 (2.64, 4.5) | 30.58 | <0.001 |
| | CS | 65 | 9.75 (7.64, 11.68) | | |
| | IAD | 18 | 5.94 (3.74, 9.43) | | |
| Obstetric Complications | Yes | 99 | 15.5 (12.78,18.9) | 112.2 | <0.001 |
| | No | 38 | 13 (11. 5, 15.5) | | |
| Maternal chronic disease | Yes | 68 | 14.5 (11.5, 18.5) | 81.58 | 0.004 |
| | No | 69 | 3.3 (2.63, 4.22) | | |
| APGAR score at 1’ | <3 | 63 | 15.12 (11.14, 21.14) | 122.5 | 0.006 |
| | 3-6 | 56 | 7.8 (6.06, 10.25) | | |
| | ≥7 | 18 | 1.1 (0.7, 1.76) | | |
| APGAR score at 5 min | <3 | 33 | 33.6 (23.9, 47.3) | 118.49 | <0.001 |
| | 3-6 | 72 | 18.4(14.6, 23.1) | | |
| | ≥7 | 32 | 1.5 (1.1, 2.21) | | |
| Sex | Male | 100 | 8.5 (7.02, 10.38) | 34.36 | <0.001 |
| | Female | 37 | 2.7 (1.96,3.74) | | |
| Birth weight | <2500 | 112 | 13 (10.7, 15.6) | 125.91 | <0.001 |
| | ≥2500 | 25 | 1.5(1.01,2.21) | | |
| Gestational age | <37 | 111 | 15.7(13.1, 18.9) | 17.4 | <0.001 |
| | ≥37 | 26 | 1.42 (0.97, 2.08) | | |
| Cry immediately at birth | Yes | 26 | 1.3 (0.9, 1.95) | 125.8 | <0.001 |
| | No | 111 | 9.01 (7.32, 11.7) | | |
| Source of referral | Inborn | 21 | 1.74 (1.13, 2.67) | 9.56 | 0.001 |
| | Out born | 116 | 8.73 (7.23,10.5) | | |
| Initiation BF within 1 hour | Yes | 16 | 2.67(1.64, 4.36) | 9.52 | 0.022 |
| | No | 121 | 6.24 (5.22, 7.46) | | |

SVD spontaneous vaginal delivery, C/S: cesarean sectioning, IAD: instrumental assisted delivery BF: breast feeding

## 5.5. Proportional Hazard Assumption test

For each explanatory variables proportional hazard assumption was performed separately and simultaneously. The test showed that the p-value for each predictor and the whole predictors simultaneously were greater than 0.05 which showed that there were no time-varying variables in the model and the proportional hazard assumption was fitted(p-value-0.1947) (Appendix 2).

## 5.6. Bivariable and multivariable proportional hazard regression model for different predictors

Based on log likelihood ratio test and Akaike information criteria, Weibull proportional hazard model was fitted (Table 6). Weibull proportional hazard regression model was fitted and used to identify predictors of mortality in neonates with respiratory distress. In bivariable Weibull proportional hazard regression: onset of labor, maternal age, number of parities, history of bag and mask recitation at birth, age of neonate at admission and respiratory support at admission were non-significant at p> 0.15 but, residence, ANC follow-up, types of pregnancy, history of bad obstetric diagnosis, history of maternal medical problem, mode of delivery, initiation of breast feed within one hour, sex of the neonate, cry immediately at birth, birth weight, place of delivery, gestational age, APGAR score at five minute, and source of referral were significant predictors of mortality among neonates with respiratory distress with p-value<0.15.

Table 5: Cox and parametric proportional Hazard model fitting among neonates admitted with respiratory distress in FHCSH, Bahir Dar, Northwest Ethiopia, 2022 (n=475)

| Model | Loglikelihood | AIC | BIC |
|---|---|---|---|
| Cox | -644.4 | 1316.9 | 1375.2 |
| Weibull | -260.1 | 552.1 | 618.1 |
| Exponential | -262.5 | 555.1 | 618.5 |
| Gompertz | -262.4 | 556.8 | 623.4 |

In a multivariable Weibull proportional hazard model after controlling the confounding: source of referral, birth weight, sex of the neonate, gestational age, APGAR score at five-minute, history of bad obstetric diagnosis in the index pregnancy and not crying immediately at birth have remained statistically significant predictors of mortality among neonates admitted with respiratory distress at (p-value<0.05).

Being male sex had 1.64 times the higher hazard of death than female neonates (AHR: 1.64, 95%, CI: 1.08, 2.5). The hazard of death in neonates with birth wight <2500 grams was 1.9 times higher compared to neonates with admission weight ≥2500 (AHR: 1.9, 95%, CI: 1.06, 3.27). Neonates who did not cried immediately at birth had a 2.7-times higher hazard of death when compared to neonates who had cried immediately at birth (AHR: 2.7, 95%, CI: 1.56, 4.5). Neonates who were born at an earlier gestational age had a 2.42 times greater likelihood of dying as compared to those neonates born at a normal gestational age (≥37 weeks) (AHR: 2.42 95%, CI: 1.33, 4.4). Neonates who had lower APGAR scores at five minutes (<3 and 3-6) had a 3.48- and 2.7-times higher hazard of death than neonates who had APGAR score of ≥7 (AHR: 3.48 and 2.7, 95%, CI: 1.8, 6.72, and 1.56, 4.69) respectively. Neonates who were referred had a 1.82 times higher hazard of death than neonates born inside the hospital (AHR: 1.82; 95%, CI: 1.1, 3.01). The risk of death was 1.94 times higher in those born to mothers with obstetric complications (AHR: 1.94; 95%, CI: 1.2; 3.13) (Table 6).

Table 6: Bivariable and Multivariable Weibull proportional hazard regression of neonates admitted with respiratory distress at FHCSH, Bahir Dar, Northwest Ethiopia, 2022 (n=475)

| Variables | Category | Survival status | | Admission to death | | P-value |
|---|---|---|---|---|---|---|
| | | Death | Censored | CHR (95%CI) | AHR (95%CI) | |
| Residence | Rural | 97 | 133 | 3.18(2.19,4.59) | 0.97 (0.64,1.46) | 0.889 |
| | Urban | 40 | 205 | 1 | 1 | |
| ANC follow up | Yes | 101 | 318 | 1 | 1 | |
| | No | 36 | 20 | 4.19(2.85,6.16) | 0.91(0.57, 1.43) | 0.694 |
| Types of pregnancy | Single | 96 | 315 | 1 | 1 | |
| | Twin | 41 | 23 | 4.43(3.06,6.39) | 1.12(0.7,1.8) | 0.622 |
| Place of birth | Home | 24 | 4 | 10.66(6.34,17.9) | 1.28(0.69,2.37) | 0.421 |
| | HC | 77 | 89 | 4.57(3.07,6.79) | 1.3(0.83, 2.04) | 0.241 |
| | Hospital | 36 | 245 | 1 | 1 | |
| Mode of delivery | SVD | 54 | 219 | 1 | 1 | |
| | CS | 65 | 80 | 2.79(1.94, 4.01) | 0.89(0.58,1.37) | 0.621 |
| | IAD | 18 | 39 | 1.72(1.00,2.93) | 1.11(0.63, 1.96) | 0.699 |
| Obstetric diagnosis | Yes | 99 | 55 | 5.82(4.10,8.26) | 1.94(1.2,3.13) | 0.006 |
| | No | 38 | 283 | 1 | 1 | |
| Source of referral | Inborn | 21 | 197 | 1 | 1 | |
| | Out born | 116 | 141 | 7.73(5.31,11.25) | 1.82(1.1,3.01) | 0.02* |
| Maternal medical problem | Yes | 68 | 42 | 4.32(3.08, 6.04) | 1.06(0.71,1.57) | 0.770 |
| | No | 69 | 296 | 1 | 1 | |
| BF Initiation within 1 hour | Yes | 16 | 80 | 1 | 1 | |
| | No | 121 | 258 | 2.30(1.36, 3.88) | 1.14(0.66,1.98) | 0.626 |
| Sex | Male | 100 | 151 | 3.11(2.13,4.54) | 1.64(1.08,2.5) | 0.02* |
| | Female | 37 | 187 | 1 | 1 | |
| Birth weight | <2500 | 112 | 90 | 8.64(5.59,13.34) | 1.90(1.06,3.27) | 0.03* |
| | ≥2500 | 25 | 248 | 1 | 1 | |
| APGAR score at 5 min | <3 | 25 | 13 | 7.36(4.51,12.02) | 3.48(1.8,6.72) | <0.001* |
| | 3-6 | 67 | 38 | 6.63(4.54,9.68) | 2.7(1.56,4.69) | <0.001* |
| | ≥7 | 45 | 287 | 1 | 1 | |
| Gestational age | <37 | 111 | 64 | 11.1(7.2, 16.9) | 2.42(1.33, 4.4) | 0.004* |
| | ≥37 | 26 | 274 | 1 | 1 | |
| Cry at birth | Yes | 26 | 294 | 1 | 1 | |
| | No | 111 | 44 | 14.3(9.36,22) | 2.7(1.56,4.5) | <0.001* |

- HC: Health Center, IAD: Instrumental assisted delivery

# 6. DISCUSSION

This study was conducted to determine the time to death and predictors among neonates admitted with respiratory distress. The mean time to death was 5.34 days. In this study of all deaths, about 41% of the neonates died in the first day, nearly 78% died in the first 3 days, and almost 90% of the neonatal deaths occurred in the first week of life. This is supported by studies in Cameron (36) , Kenya (49) and Iran (32). In Cameroon, 90% of deaths occurred within 7 days and in Kenya, 61% in the first week of life. This implies that neonates with respiratory distress mortality occurred in the first few days and almost all deaths occurred in the first week. It also supported by study in Iran, when neonates' duration with in NICU was prolonged by one more day, the mortality decreased by 18.5 percent, and the reverse is that the first few days of neonatal age were associated with a higher risk of neonatal mortality (32).

This study demonstrated a higher neonatal mortality rate (28.8%, 95%, CI: 20.8, 33.1) among neonates admitted to the NICU with respiratory distress. This finding is consistent with studies conducted on 21.5 in India (21), 24.5 in Cameroon (36), and 26.2 in Egypt (52). This explains why cohorts of neonates with respiratory distress have a higher risk of death than neonates admitted without respiratory distress (11). But this finding is lower than studies done on 36 in Sudan (35), 49.2 in Yemen (40) per 100 live births. The possible reasons for the discrepancy could be related to the types of data used or geographic differences. The data in this study came from secondary sources, whereas studies in Sudan and Yemen used primary data. In contrast, this is higher than studies conducted in 4.6 in Nepal (51), and 19.3 in India (29). The possible reasons for both studies could be different in design, sample size, and socio-demographic. The other reason for the discrepancy could be a difference in the availability of neonatal intensive unit equipment like mechanical ventilation (60).

The overall death incidence rate in this study was 54 (95% CI 45.67, 63.84) per 1000 neonatal days from diagnosis with respiratory distress to death. This implies that when we followed 1000 neonates with respiratory distress for one day, 54 neonates died.

In this study, neonates who did not cry at birth had a greater hazard of death compared with those who did cry at birth. Healthy neonates are expected to cry at birth, and it is a measure of breathing effort (61). Neonates who did not cry vigorously at birth could have had irregular or slow birth, and the cumulative Apgar could be lower. Findings from different studies that also show a higher risk of death among neonates with lower Apgar scores could support this explanation (36).

Neonates who were born at an earlier gestational age in this study had a greater likelihood of dying as compared to those neonates born after 37 weeks of gestation. This finding is supported by studies conducted in Cameroon (36) and Iraq (11) that showed prematurity had a higher risk of neonatal mortality with respiratory distress. Prematurity goes along with structural and functional immaturity of the lungs (deficiency in surfactant) (62). It is scientifically proven that due to a lack of surfactant production in the fetal lung, hyaline membrane disease occurs among newborns delivered before the gestational age of 34 weeks and eventually causes inefficient gas exchange. respiratory collapse and death (63).

Regarding sex of the neonate that male sex had a greater risk of death than female. This is supported by studies conducted in India, Pakistan, and Cameroon, wherein male sex is a non-modified predictor of mortality in neonates with RD (34, 35, 54). The association of neonates with respiratory distress with male gender is explained by the antagonism of pulmonary maturation by the higher concentration of androgens (64). While testosterone secreted by the fetal testes has primarily inhibitory effects and delays the surge of surfactant production, estrogens produced by the placenta have positive effects on fetal surfactant production as well as alveologenesis during the neonatal and pubertal periods (65).

The hazard of death in neonates with birth weight less than 2500 grams was higher compared to neonates with admission weight of ≥2500. There are similar findings in India  and this finding is supported by the fact that low birth weight neonates are severely harmed and are more likely to die as a result of their susceptibility to the development of potentially fatal conditions like hypothermia and hypoglycemia (15). According to the findings, a birth weight of 2000 g is associated with a greater need for mechanical ventilation (15). This finding is supported by a study done in Vietnam where birth weights of less than 2500 g were highly exposed to respiratory failure (66).

Neonates who had lower APGAR scores at five minutes had a higher hazard of death than neonates who had an APGAR score of ≥7. The finding is supported by studies conducted in India  (61), Colombia (50) and Cameroon (36). Since the APGAR score is the main component in the diagnosis of respiratory distress in neonates, Findings from different studies that also show a higher risk of death among neonates with lower Apgar scores could support this explanation (36, 67). An APGAR score of 0–3 correlates with neonatal mortality in large populations (68).

Based on this finding, referred neonates had a higher risk of death than neonates born in this hospital. The finding is supported by a study done in Nigeria (22). Lack of emergency care on the way to higher centers, poor stabilization before referral, and inadequate care during transport increase neonatal mortality(69). Distance to specialty care is an important risk factor for early neonatal mortality. Proximity to health services and a higher level of care are associated with lower early neonatal mortality rates(70, 71). The possible indication behind this explanation is that respiratory problems need immediate management, and delay in management increases the risk of mortality.

According to this study, neonates born to mothers who experienced obstetric problems during the index pregnancy were at an increased risk of dying as compared to those born without complications. This is supported by findings from Egypt (52) and India (55). Scientifically, it is proven that obstetric complications like chorioamnionitis and PROM can cause injury to the fetal lungs and alveolar type II cells directly, resulting in decreased synthesis and release of surfactant (72).

The last predictor in this finding, neonates born to mothers who experienced obstetric problems during the index pregnancy were at an increased risk of dying as compared to those born without complications. This is supported by findings from Egypt (52) and India (55). Scientifically, it is proven that obstetric complications like chorioamnionitis and PROM can cause injury to the fetal lungs and alveolar type II cells directly, resulting in decreased synthesis and release of surfactant (72).

# 7. STRENGTH AND LIMITATIONS OF THE STUDY

## 7.1. Limitation

This study was based on secondary data due to its retrospective nature, the analysis of predictors of time to death was limited by the information obtained from the neonates' charts. As a result, data on demographic characteristics and other clinically related factors were not available in the neonates' record, and these variables were not included in the study. The other limitation, since the study conducted in a single institution it might not represent neonates in the other institutions.

# 8. CONCLUSION AND RECOMMENDATIONS

## 8.1. Conclusion

The first few days of life in neonates with respiratory distress had higher risk of mortality. The mean time to death among neonates with respiratory distress was 5.34 days., birth weight, gestational age, APGAR score at five-minute, sex of neonate, history of bad obstetric complications, not crying immediately at birth and Source of referral at birth were predictors of mortality among neonates admitted with respiratory distress.

## 8.2. Recommendations

For Health professionals: the first day is the critical time of neonates with respiratory distress, so it's better to manage immediately in order to increase the survival of neonates. As soon as the diagnosis is set, it is better to transfer to a neonatal intensive care unit for better management. Neonates' diagnosis with respiratory distress requires immediate attention, particularly those born with a lower APGAR score, male neonates, low birth weight, preterm, and mothers with obstetric complications. It is better to give appropriate care before referral for neonates with respiratory distress, and it is essential to strengthen the service provision capacity of the health institutions and health service providers during the referral systems

For researchers: because this is secondary data analysis, future researchers would be better off using a prospective cohort study design to obtain more information by incorporating additional predictors not included in this study. It is better to use multicenter setting to overcome limitations of single institutions.

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## ANNEX

**Data extraction checklist**

This tool is prepared for the collection of socio-demographic characteristics of the neonates, factors of RD and other related factors that is important for the assessment of time to death and predictors of mortality among neonates admitted with respiratory distress at FHCSH, northwest Ethiopia, 2022. All this information was retrieved from individual cards without mentioning the name of the neonate. This information was collected by Two BSc Nurses working in FHCSH.

**Contact information:** Selamsew Kindie cell phone +251931499744

Data collection date............................................Month.................................Year........................

Name data collector..........................................Signature ..............................................................

Name of supervisor............................................Signature ............................................................

Code no ...........................................................................................................................................

| Question Number | Questions | Possible answers | Remark |
|---|---|---|---|
| **Questions for the mother** | | | |
| **1. Socio-demographic predictors** | | | |
| 101. | Age of Mother | ……Years | |
| 102. | Place of residence | 1. Ruler<br>2. Urban | |
| **2. Obstetric related predictors** | | | |
| 201 | Number of Gravidity | ………in number | |
| 202 | Number of Parity | …………in number | |
| 203 | Does the mother have ANC follow-up? | 1. Yes<br>2. No | |
| 204 | If yes to Q203 how many times | ……… in number | |
| 205 | Types of pregnancy | 1. Singleton<br>2. Twin<br>3. Other specify…… | |
| 206 | Place of delivery | 1. Home<br>2. Health center<br>3. Hospital | |

| | | | |
|---|---|---|---|
| 207 | Onset of labor | 1. Elective cesarean section<br>2. Spontaneous onset<br>3. Induced | |
| 208 | What was her Current mode of delivery? | 1. Spontaneous vaginal delivery<br>2. Cesarean section<br>3. Instrumental | |
| 209 | Do the neonates breastfeed? | 1. Yes<br>2. No | To Q301 |
| 210 | If yes, when was the breastfeeding initiated | ………in hours | |
| **3. Mothers' medical predictors** | | | |
| 301 | Has she been diagnosed with any medical problems? | 1. Yes<br>2. No. | To Q NO 401 |
| 302 | If yes for question no 201, what was the diagnosis | ………………………………<br>………………………………<br>………………………. | |
| **II. Questions for the neonate** | | | |
| **4. Socio-demographic / Identifications** | | | |
| 401 | age of admission | ……… in days | |
| 402 | Age in day | ………..in days | |
| 403. | Sex | 1. Male<br>2. Female | |
| 404 | Gestational age at birth | ………..weeks | |
| 405 | Birth weight | ………...gm | |
| 406 | History of bag and mask resuscitation at birth | 1. Yes<br>2. No | |
| 407 | APGAR score of | 1.1$^{st}$minute…<br>2.5$^{th}$ minute… | |
| 408 | Neonate cry at birth | 1. Yes<br>2. No | |
| 409 | Was neonate on respiratory support on admission | 1. Yes<br>2. No | To Q411 |
| 410 | If yes Q410 what types of support | 1. Internasal oxygen<br>2. continues positive airway pressure /CPAP<br>3. other | |
| 411 | Treatment given at birth | ………………………. | |

| | | | |
|---|---|---|---|
| 412 | Diagnosis of the neonates (specify any diagnosis) | ………………………………<br>………………………………<br>………………………………<br>…………………………… | |
| | **6. Neonatal outcome** | | |
| 413 | Neonatal outcome | 1. Improved and discharge<br>2. Referred to other hospital<br>3. Self discharge or againest medical advice /unknown outcom<br>4. Death | |
| 414 | Event | 1. Death<br>2.Censored | |
| 414 | Event | | |
| 415 | Age at when outcome occurred | ……….. | |
| 416 | Time to event (diagnosis to event) | | |

**Appendix 2**: Test of proportional hazard assumption among neonates admitted with respiratory distress

| Variables | rho | $X^2$ | df | p-value |
|---|---|---|---|---|
| Residence | 0.08506 | 1.01 | 1 | 0.3147 |
| ANC follow up | 0.02318 | 0.08 | 1 | 0.7709 |
| Types of pregnancy | -0.09409 | 1.48 | 1 | 0.2244 |
| History of bad obstetric diagnosis | -0.08701 | 1.43 | 1 | 0.2324 |
| Mode of delivery | -0.05669 | 0.49 | 1 | 0.4857 |
| Initiation of breastfeed within 1 hour | 0.06935 | 0.67 | 1 | 0.4115 |
| History of maternal medical problems | -0.14002 | 3.13 | 1 | 0.0768 |
| Sex | 0.09534 | 1.49 | 1 | 0.2229 |
| Cry immediately at birth | 0.01173 | 0.02 | 1 | 0.8773 |
| Birth weight | 0.06567 | 0.69 | 1 | 0.4064 |
| Place of delivery | -0.13031 | 3.07 | 1 | 0.0796 |
| Gestational Age | 0.12609 | 2.83 | 1 | 0.0923 |
| Source of referral | 0.03792 | 0.21 | 1 | 0.6479 |
| APGAR score at 1 min | -0.05394 | 0.50 | 1 | 0.4814 |
| Global test | | 18.27 | 14 | 0.1947 |

**Appendix 3: Life Table**

Life table of time to death and predictors of mortality among neonates admitted with respiratory distress at FHCSH, Bahir Dar, Northwest Ethiopia ,2022

| Time (Days) | N. at risk | Event | Cu. Failure | St. Error | 95 % CI | |
|---|---|---|---|---|---|---|
| 1 | 475 | 56 | 0.1179 | 0.0148 | 0.0920 | 0.1504 |
| 2 | 414 | 33 | 0.1882 | 0.0180 | 0.1558 | 0.2265 |
| 3 | 371 | 18 | 0.2276 | 0.0194 | 0.1923 | 0.2683 |
| 4 | 309 | 5 | 0.2401 | 0.0198 | 0.2038 | 0.2816 |
| 5 | 251 | 4 | 0.2522 | 0.0204 | 0.2147 | 0.2949 |
| 6 | 205 | 6 | 0.2741 | 0.0217 | 0.2342 | 0.3193 |
| 7 | 150 | 1 | 0.2789 | 0.0221 | 0.2383 | 0.3249 |
| 8 | 103 | 3 | 0.2299 | 0.0245 | 0.2548 | 0.3510 |
| 9 | 73 | 2 | 0.3191 | 0.0274 | 0.2689 | 0.3761 |
| 10 | 60 | 3 | 0.3532 | 0.0323 | 0.2939 | 0.4204 |
| 11 | 32 | 2 | 0.3936 | 0.0410 | 0.3187 | 0.4790 |
| 12 | 26 | 3 | 0.4636 | 0.0525 | 0.3672 | 0.5716 |
| ≥13 | 15 | 1 | 0.4993 | 0.0600 | 0.3890 | 0.6214 |