



**COLLEGE OF MEDICINE AND HEALTH SCIENCE**

**SCHOOL OF PUBLIC HEALTH**

**INCIDENCE AND PREDICTORS OF MORTALITY AMONG NEONATES WITH  
RESPIRATORY DISTRESS SYNDROME ADMITTED TO NEONATAL  
INTENSIVE CARE UNITS OF PUBLIC HOSPITALS IN HAWASSA, ETHIOPIA.**

**BITSIT DEMEKE (BSc)**

**MAY, 2024**

**HAWASSA, ETHIOPIA**

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**BITSIT DEMEKE**

**ADVISORS**

**Main Advisor: YUSUF HAJI (ASSISTANT PROFESSOR)**

**Co-Advisor: AYANTU MELKE (MPH)**

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## DECLARATION

I declare that this Thesis entitled “**Incidence and predictors of mortality among neonates with respiratory distress syndrome admitted to neonatal intensive care unit of public hospitals in Hawassa, Ethiopia**” is my own work and all the sources I used have been indicated and acknowledged as complete reference.

**Name of investigator**

**Signature**

**Date**

**Bitsit Demeke**

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**HAWASSA UNIVERSITY**  
**SCHOOL OF GRADUATE STUDIES**  
**EXAMINERS' APPROVAL SHEET**

We, the undersigned, members of the board of Examiners of the final open defense by Bitsit Demeke have read and evaluated the thesis entitled “**Incidence and predictors of mortality among neonates with Respiratory Distress Syndrome admitted to neonatal intensive care units of public hospitals in Hawassa, Ethiopia, 2024**” submitted to Hawassa University, College of Health science and Medicine, School of public health. Therefore, we certify that the thesis has been accepted in partial fulfillment of the requirements of the master’s degree.

| <b>Advisors' Name</b>                 | <b>Signature</b> | <b>Date</b> |
|---------------------------------------|------------------|-------------|
| Yusuf Haji (Assist.prof)<br>_____     | _____            | _____       |
| Name of Internal Examiner I<br>_____  | _____            | _____       |
| Name of Internal Examiner II<br>_____ | _____            | _____       |
| Name of External Examiner<br>_____    | _____            | _____       |
| SGS approval<br>_____                 | _____            | _____       |

Final approval and acceptance of the thesis is contingent upon the submission of the final copy of the thesis to the School of Graduate Studies (SGS) through the School Graduate Committee (SGC) of the candidate’ s department.

**Stamp of SGS**

Date: \_\_\_\_\_

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## Acronyms and abbreviations

|               |   |
|---------------|---|
| <b>AIDS:</b>  | Acquired Immune Deficiency Syndrome               |
| <b>ANC:</b>   | Antenatal Care                                    |
| <b>AHR:</b>   | Adjusted hazard ratio                             |
| <b>APGAR:</b> | Activity, Pulse, Grimace, Appearance& respiration |
| <b>CPAP:</b>  | Continuous positive airway pressure               |
| <b>CT:</b>    | Computed tomography                               |
| <b>GA:</b>    | Gestational age                                   |
| <b>HFNC:</b>  | High-flow nasal cannula                           |
| <b>HIV:</b>   | Human Immune Virus                                |
| <b>LOS:</b>   | Length of stay                                    |
| <b>NICU;</b>  | Neonatal intensive care Unit                      |
| <b>NRDS:</b>  | Neonatal respiratory Distress Syndrome            |
| <b>MAS:</b>   | Meconium Aspiration Syndrome                      |
| <b>PNA:</b>   | Perinatal Asphyxia                                |
| <b>PROM:</b>  | Prolonged rupture of membranes                    |
| <b>PEEP:</b>  | Positive end-expiratory pressure                  |
| <b>RDS:</b>   | Respiratory Distress Syndrome                     |
| <b>WHO:</b>   | World health organization                         |

## **Abstract**

**Background:** Respiratory distress syndrome (RDS) is a major contributor to increased level of morbidity and mortality among neonates. It is one of the primary reasons for admission in to neonatal intensive care units. This syndrome is one of the main causes of respiratory failure, morbidity, and mortality in Ethiopia, which drives up the expense of neonatal treatment in the country. Ethiopia is one of the top five nations with the highest number of newborn mortalities with RDS being the significant factor.

**Objective:** This study is aimed to determine the incidence and predictors of mortality among neonates with respiratory distress syndrome admitted to the neonatal intensive care units of public hospitals in Hawassa, Ethiopia, 2024.

**Method:** A retrospective cohort study was conducted from April 1-30, 2024. A total of 858 neonates were sampled using simple random sampling. Data were collected from medical records by data extraction tool using KoBo toolbox and exported to STATA version 16 for analysis. Median time, Kaplan-Meier survival estimation curves, and log-rank tests were then computed. Bivariable and multivariable regression were fitted to identify the predictors of respiratory distress syndrome. Adjusted hazard ratio with a 95% confidence interval was subsequently calculated. Variables with reported p-values < 0.05 were considered statistically significant.

**Results:** A 858 (93.4%) were included in the study. The incidence rate of RDS mortality was 39.475 per 1000 neonate-days (95% CI: 35.33- 43.62) with 8809 neonate-days of observation. Perinatal Asphyxia (AHR: 1.79; 95% CI: 1.37- 2.34), birth weight less than 2500 gram (AHR: 1.70 (95% CI: 1.10-2.64) and hypothermia (AHR: 1.66; 95% CI: 1.27 -2.17) were statistically significant predictors of mortality of neonates with respiratory distress syndrome.

**Conclusion:** The incidence rate of mortality among neonates with RDS was 39.475. Perinatal Asphyxia, hypothermia and birth weight less than 2500 gram were significant predictors of mortality of neonates with respiratory distress syndrome. Hence, attention should be given to the care of neonates.

## **1. Introduction**

### **1.1 Background**

Respiratory Distress Syndrome(RDS) is a common breathing disorder in a newborn, which mainly occurs either due to inadequate surfactant production, or surfactant inactivation in the context of immature lungs (1). It presents with apnea, cyanosis, grunting, inspiratory stridor, nasal flaring, poor feeding, tachypnea, and retractions in the intercostal, subcostal, or suprasternal areas (2). It is a prevalent condition that commonly affects newborns, particularly those born prematurely. In rare cases, RDS can also affect full-term newborns (3). Preterm birth, low Apgar scores, low birth weight, multiple pregnancy, caesarian section delivery, gestational diabetes, perinatal asphyxia and sepsis are among the major risk factors of RDS (4).

RDS is a major cause of neonatal morbidity and mortality worldwide and still a major contributor to high neonatal death rates in low and middle-income countries (5). In addition, RDS, which has a sudden onset, acute illness, and quick progression, is responsible for the majority of neonates being sent to neonatal intensive care units (6).

RDS is also a significant condition among neonates in Ethiopia which requires admission to the NICU(7). It is a leading cause of death in the country because of its abrupt increase in prevalence and erratic contribution to neonatal mortality rates (4).

In particular, RDS is the primary cause of illness and mortality among newborns during the first few months of life (8).

The World Health Organization (WHO) recommends the use of antenatal corticosteroid therapy for high-risk women, Kangaroo mother care, Continuous positive airway pressure, tocolytics for preterm labor, and optimal oxygen therapy to reduce newborn morbidity and mortality. Additionally, the Federal Ministry of Health has focused on expanding high-quality neonatal care to reduce neonatal morbidity, such as RDS. Despite these efforts, RDS remains a major public health problem, causing increased suffering and mortality in low-income and middle-income countries, including Ethiopia (9).

## 1.2 Statement of the problem

Respiratory distress syndrome is a common reason for neonates to be admitted to the neonatal intensive care unit (NICU), accounting for 15% of term infants and 29% of late preterm infants admitted to the NICU who develop significant respiratory morbidity (7). RDS is a prevalent neonatal condition worldwide, with reported rates of 18.5% in France, 4.24% in Pakistan, and 20.5% in China (10). It is the leading etiology of neonatal respiratory failure, with the highest prevalence in Africa, the Middle East, and Asia (11).

Among the major causes of death that takes the lives of more than one million preterm neonates worldwide, respiratory distress syndrome is the leading one (11). Respiratory distress syndrome affects about 50% of premature newborns born between 26 and 28 weeks of pregnancy, whereas less than 30% of those born between 30 and 31 weeks of pregnancy have the illness (12). In resource limited settings, neonatal mortality contributed by preterm ranges from 30-40%, while RDS being the major contributor (13)

In Central and Southern Asia, neonatal mortality rate was 24 deaths per 1,000 live births. In Sub-Saharan Africa, it is much higher with 27 deaths per 1,000 live births (14). Approximately, 70% of the neonatal death occurs in resource limited settings, especially in East Africa (15). Respiratory distress syndrome still continues to be the most common predictor of neonatal death in the region (14).

The study conducted in Sudan in 2014 found that out of 177 newborns who were admitted to the NICU, 100 of them were due to NRDS (13). This indicates the importance of recognizing and managing NRDS in the care of newborns. A Rwandan study explained that there is a challenge in implementing hospital-based interventions for Neonatal respiratory distress in resource limited settings (10).

Ethiopia ranks among the top five countries with highest number of neonatal deaths (17). The neonatal mortality rate in Ethiopia was 30/1000 live births in 2019 and decreased to 27/1000 live births by 2020(1). A multicenter prospective observational study conducted in Ethiopia found that RDS was responsible for 45% of deaths in the country (18). The proportion of RDS was reported to be 40% of which 49.5% died in a study done in Debretabor, Ethiopia (19). Studies done in Addis Ababa and Gondar, Ethiopia revealed that the incidence of RDS was 8.1 and 11.5 per 100 person-

years, respectively (4)(7). The incidence of RDS was found to be 185(37.15%) in a retrospective study done in DebreMarkos, Ethiopia (20). An overall incidence rate of RDS mortality was 60.19 per 1000 livebirths was also reported in a study done in the Eastern Amhara region of Ethiopia(21). Additionally, a multi-centered institution based retrospective follow-up study conducted in West Oromia Referral Hospitals, Ethiopia found a proportion of 152 (37.44%) RDS mortality (1).

Several risk factors increase the likelihood of mortality among neonates with RDS, including prematurity, low first and fifth minute Apgar scores, caesarian section delivery, low birth weight, maternal chorioamnionitis, premature rupture of membranes, and perinatal asphyxia, as well as structural lung abnormalities identified in previous studies. Other common predictors of RDS death include meconium aspiration syndrome, sepsis, jaundice and neonatal hypothermia. The risk of RDS death also decreases with each advancing week of gestation and birth through spontaneous vaginal delivery (7).

Indeed, RDS is a major cause of morbidity and mortality in Ethiopia, resulting in higher neonatal care cost in the country. Despite the fact that a number of risk factors have been investigated, there are inconsistent findings about factors that predict RDS mortality, such as birth weight and sex, which call for further investigation. According to certain studies, male newborns are significantly more likely than female newborns to die from NRDS. This result is consistent with the idea that men can encounter more serious respiratory problems and symptoms. Other studies, on the other hand, show that there is no meaningful correlation between a neonate's sex and the death rate from RDS.

Low birth weight is another known risk factor for NRDS mortality. Compared to their counterparts, preterm neonates with birth weights under 2500 grams have a greater chance of dying. However, it's interesting to note that certain research suggests that NRDS mortality may not always be predicted by birth weight.

Thus, further research is necessary in light of the contradictory findings about the predictive value of sex and birth weight. Targeted interventions could be informed by knowledge of the underlying mechanisms and potential vulnerabilities specific to birth weight and sex.

Therefore, this study is aimed to determine the incidence and predictors of mortality among neonates with RDS who are admitted to the NICU of public hospitals in Hawassa, Ethiopia.

### **1.3 Significance of the study**

Findings on neonatal respiratory distress syndrome mortality and its predictors provide knowledge for health professionals in the early identification of high-risk neonates and timely intervention to enhance their survival.

The present study holds great importance as it aligns with the Ethiopian government's plan to achieve SDG 3, which is aimed at ending preventable deaths of newborns and children under 5 years of age. All countries are striving to reduce neonatal mortality to a minimum of 12 per 1,000 live births and under-5 mortality to a minimum of 25 per 1,000 live births. It is expected that the findings of this study will be instrumental in developing strategies and recommendations for reducing the occurrence, severity, and mortality associated with neonatal respiratory distress.

Studying the incidence and predictors of mortality among neonates with NRDS helps to identify the risk factors associated with the condition and to develop evidence-based recommendations for improved perinatal care. Identifying these risk factors can help healthcare providers take preventive measures to reduce the incidence of neonatal respiratory distress and improve the quality of care provided to neonates.

Experts will benefit from this study in devising protocols and policies related to NRD. The study's results will also provide valuable insights to the selected hospital about the incidence of NRD in their neonatology unit and the underlying factors that contribute to the development of respiratory distress. This study has the potential to contribute to nursing education and inspire further research in the field.

## **2. Literature review**

### **2.1 Incidence of mortality among neonates with respiratory distress syndrome**

Respiratory distress syndrome is known to be a frequent cause of neonatal respiratory failure and death worldwide. This condition affects 2.2% to 7.6% of all term deliveries worldwide, and 50%, 75%, and 90% of newborns born at 30 weeks, 28 weeks, and 26 weeks, respectively (4). Globally, respiratory distress syndrome is an urgent neonatal condition and still poses a serious health issue in developing countries (22).

According to different studies conducted, a varying rate of RDS was reported across the world. In the Middle East, according to a prospective cross-sectional study done in Syria, a frequency of 36.1% was reported(23). Similarly, a cross sectional study done on neonates admitted to Neonatal Intensive Care Unit in Nepal Medical College and Teaching Hospital revealed RDS prevalence of 34% (24). Another cross sectional study done in Saudi Arabia indicated RDS to be a major problem among the newborn reporting a prevalence of 54.7% (25). A higher prevalence rate of RDS which was 84.8% was reported in a cross sectional study done in Iraq, Misan (26).

However, a quantitative ultrasound fetal lung maturity analysis done in Northern Italy found 20.1% cases of RDS among 144 neonates (27). A retrospective a study done in Portugal revealed an incidence of 8.83% of RDS (28). In Africa, a retrospective study done in Cameroon revealed the prevalence rates of NRD to be 47.5% (29). Another retrospective descriptive cross-sectional study done in the neonatology unit of Charles de Gaulle in Ouagadougou, Burkina Faso found a frequency of 39.1% (30). In Ethiopia, according to an institution-based retrospective study done at black lion specialized hospital, the overall proportion of neonates with RDS admitted to the NICU was 42.9% (7). In an institution-based retrospective follow-up study done in Debretabor, Ethiopia, the proportion of RDS was reported to be 40% (19). Additionally, in a retrospective study conducted in DebreMarkos, Ethiopia, the incidence of RDS was found to be 185(37.15%) (20). According to an institutional-based cross-sectional study conducted in Gurage zone, Ethiopia, the prevalence of respiratory distress syndrome (RDS) was 45.1% (31).

Globally, RDS results in approximately 15% of all neonatal deaths. Although the rate of mortality has decreased in the developed countries, it is still a major cause of neonatal mortality in resource limited

settings. The data on the incidence of RDS mortality varies from region to region (32). While a retrospective cohort study done in Kragujevac, Serbia, reported 10% death of RDS cases, a prospective study done in Yemen, identified RDS as the most common underlying cause of death in the neonates (44%). Among the 250 neonates with respiratory disorder who were admitted to the neonatal care unit of Mukalla Maternity hospital Yemen, death occurred in 49.2% of cases (33,34). A prospective study done in Tanzania shows that the mortality rate from RDS during the first week of life was 31.3% (22).

In a cross sectional study conducted in Nepal, out of the total RDS cases, 12.8% of them died (24). According to another hospital-based prospective observational study done in Nepal, the survival rate of neonates with RDS varied with their gestational age. For those neonates with above 32 weeks of GA the survival rate was found to be 97%, 95% and 95% on day 10, 20 and 30 respectively. In contrast, for those with GA of below 32 weeks, survival rate was shown to be 80%, 66% and 61% on day 10, 20 and 30 respectively (35).

In an institution-based retrospective follow-up study done in East Amhara region, Ethiopia, the probability of survival of RDS among neonates was higher on the first day of admission and it subsequently decreased with increasing follow-up time(21). According to a hospital-based prospective descriptive cross-sectional study done in Gondar, Ethiopia, 32% of death was reported among neonates with RDS. Half (50%) of the death was recorded within 24 hours of birth and 32.7% death was recorded within 24 to 72 hours (13). In a prospective cohort study done in Uganda, it was found that respiratory distress syndrome has an impact on the survival of preterm neonates. Similar result was reported in a retrospective cross-sectional study done in Felege Hiwot Specialized Hospital. A cross-sectional study conducted in Jimma, Ethiopia, also revealed the survival status of neonates is greatly affected by the presence of RDS (6)(36) (37). According to a meta-analysis done in the East Africa continent: the pooled effect of respiratory distress syndrome on the survival of preterm neonates showed that there was a 3.2 times increased risk of death in preterm neonates with respiratory distress syndrome as compared to preterm neonates without respiratory distress syndrome. There was unacceptably increased level of preterm mortality in Eastern Africa. The main causes of death were found to be respiratory distress syndrome (38).

In a prospective, cross-sectional, observational study conducted in five hospitals in Ethiopia, respiratory distress syndrome accounts for 45% of cause of death (18). According to a retrospective study done in Debre Tabor general, the mortality rate of RDS was reported to be 49.5% (19). In a retrospective follow up study conducted in the Eastern Amhara region, the incidence rates of mortality among neonates with RDS within 7 days and more than 7 days were found to be 60.19 and 58 per 1000 person-days of observation, respectively (21). An institution-based retrospective follow up study done in Debre Markos, Ethiopia, reported 53.33% of death among preterm neonates due to RDS. Those preterm neonates with respiratory distress syndrome were 1.49 times more likely to die than those neonates without RDS (20). A high number of poor clinical outcome of RDS(62.8%) was also reported in a retrospective study conducted in Adama among preterm neonates (39).

## **2.2 Predictors of mortality among neonates with respiratory distress syndrome**

Identification of risk factors of mortality due to neonatal respiratory distress syndrome is necessary for the development of preventive and early treatment strategies. Several studies around the world found that multiple predictors of RDS mortality in neonates, including, male gender, preterm birth, caesarean section delivery, Apgar score < 7, sepsis, PROM, maternal DM, and home delivery (40).

### **2.2.1 Socio- demographic factors**

A retrospective cohort Study done in Serbia on neonates with RDS, reported the effect of male gender on RDS mortality increased significantly when it comes together with additional factors (33). In a review article on respiratory distress syndrome in infants, it is found that male premature infants with birth weights of about 1,500 gm were three times more likely to have severe respiratory distress syndrome than female infants(41). Data from a meta-analysis in over 500,000 preterm newborn infants highlighted a sex ratio of 1.56–1.84 in favor of males for respiratory distress (42). According to a facility based cross-sectional study done in Saudi Arabia, male gender was found to be an important risk factor for RDS(25). A significant association between male gender and NRDS was also reported by a prospective case–control study done in Cyprus (43). An institution based cross-sectional study done in Misan, Iraq found that among the different risk factors, sex of neonates did not appear to be significantly associated with the survival status of newborns who had respiratory distress syndrome (26). In addition, a retrospective study done in Iran showed no

relationship between RDS and sex. It was reported that neonatal mortality did not differ among the two genders (44). According to an institutional-based cross-sectional study done in Gurage zone, it was reported that Maternal age  $< 20$  years and  $\geq 35$  years old to be a significant factor in developing RDS (31).

### **2.2.2 Preterm birth**

The WHO defines preterm birth as all birth before 37 weeks of gestation. There are three classifications of preterm birth based on gestational age: extremely preterm (less than 28 weeks), very preterm (28 to less than 32 weeks), and moderate to late preterm (32 to 37 weeks) (45). Preterm birth is also known to be a major predictor of NRDS according to several studies. A retrospective cohort study conducted in black lion hospital, Ethiopia reported that preterm neonates had a threefold greater likelihood of NRDS than those who were term births (7). A retrospective study done in Cameroon also found a significant relationship between prematurity and the development of RDS (29). A hospital based cross-sectional done in Saudi Arabia also showed similar result regarding the relationship between prematurity and RDS (25). Another institution based cross-sectional study done in Misan, Iraq reported that the majority of total preterm neonates (86%) had RDS, indicating positive association between prematurity and respiratory distress syndrome (26).

### **2.2.3 Neonatal factors**

Several neonatal factors, including birth weight, sepsis, length of stay, PNA and Apgar score are known to be significant predictors of survival among neonates with respiratory distress syndrome. A retrospective cohort study conducted in black lion hospital, Ethiopia found the risk of RDS to be increased by threefold in neonates who had an Apgar score less than 7 (7). According to an institution based retrospective study conducted in Jeddah, Saudi Arabia, infants with RDS had significantly lower Apgar scores at one and five Minutes (40). In a prospective study done in Tanzania, an APGAR score less than seven at first and fifth minute is shown to affect the time to recovery from RDS. Similarly, an institution-based retrospective follow-up study conducted in Gondar, Ethiopia indicated that those neonates with RDS having an APGAR score of  $< 7$  at 5th minute are at higher risk of dying (4)(22). On the other hand a prospective cohort follow up study

conducted in Addis Ababa indicated that APGAR score has statistically insignificant association with RDS (46).

Neonatal sepsis was also found to be significantly associated with the risk of developing RDS according to a retrospective study done in Cameroon (29). Similarly, an institution-based cross-sectional study conducted in Gurage zone, Ethiopia showed that neonatal sepsis appear to be significantly linked with the risk of RDS (31). Similar result regarding the association between neonatal sepsis and the risk of RDS was also reported in a cross sectional study done in Nepal Medical College and Teaching Hospital (24). Additionally, a retrospective cross-sectional study conducted in Northern Ethiopia also found that neonatal sepsis is significantly associated with RDS (47). According to a prospective study done in Nepal, sepsis was observed in 28.7% of the neonates and was found to be a significant predictor of neonatal mortality from RDS(35). An institution-based retrospective follow-up study conducted in Gondar, Ethiopia found that the time to recover from RDS was delayed by 50% in Neonates with sepsis compared to their counterparts(4). The death rate among NRDS patients was mainly caused by neonatal sepsis, which confirms that neonatal infections are the leading cause of neonatal mortality in developing countries, as reported by the World Health Organization (29).

Being LBW is also reported to increase the hazard of RDS among neonates. A retrospective study done in Northern Italy concluded that low-birth weight is the main risk factor for RDS, with a higher odds ratio in term birth (48). It was also reported in a retrospective cohort study done in Thailand that majority of survival group with RDS (47.5%) had birth weight at 1,000-1,499 grams whereas those of the non-survival group (76.2%) had birth weight less than 1,000 grams (8). An institution-based retrospective follow-up study conducted in Gondar, Ethiopia reported that neonates admitted with very low birth weight and low birth weight had 83% and 50% delay in time to recover from RD respectively(4). Furthermore, a prospective study done in Tanzania showed that birth weight was independently associated with mortality. Higher mortality rate(40%) was reported among neonates with birth weight < 1500 g (22). On the other hand a review article on respiratory distress syndrome in infants indicated that the effect of birth weight on RDS survival depends on how the scope of was defined. When only the severe form of RDS was included while excluding the mild ones, no significant decrease was seen in the fatality rates(41). A retrospective descriptive cross-sectional study also revealed that NRDS was more common in newborns with normal birth weight (30). A

retrospective study done in Iran, reported no significant association between birth weight of neonates and respiratory distress syndrome (44). A prospective cross-sectional study done in Syria also showed no association between birth weight of neonates and respiratory distress syndrome (23). In addition, a hospital-based prospective descriptive cross-sectional study done in Gondar, Ethiopia also found similar result (13).

Length of stay also appeared to affect the survival status of neonates with RDS in some studies. A retrospective cohort study done in Thailand concluded that a prolonged length of stay increases the survival of preterm neonates with RDS. This study indicated that the length of stay could be 35 times more likely to predict survival of preterm infants with RDS (8). Meanwhile, a retrospective study done in Iran found a contradicting result which suggested that no significant relationship was found between LOS and survival among preterm infants with RDS (44).

Perinatal asphyxia is another risk factors that is known to predict the survival of neonates with RDS. According to a retrospective cohort study done in West Oromia region, Ethiopia, PNA is found to significant predictor and increases the hazard of death by 2.7 times (1). Similarly, a retrospective case-control study conducted in China identified PNA increase mortality among neonates with RDS and extends the length of hospital stay of RDS patients (49).

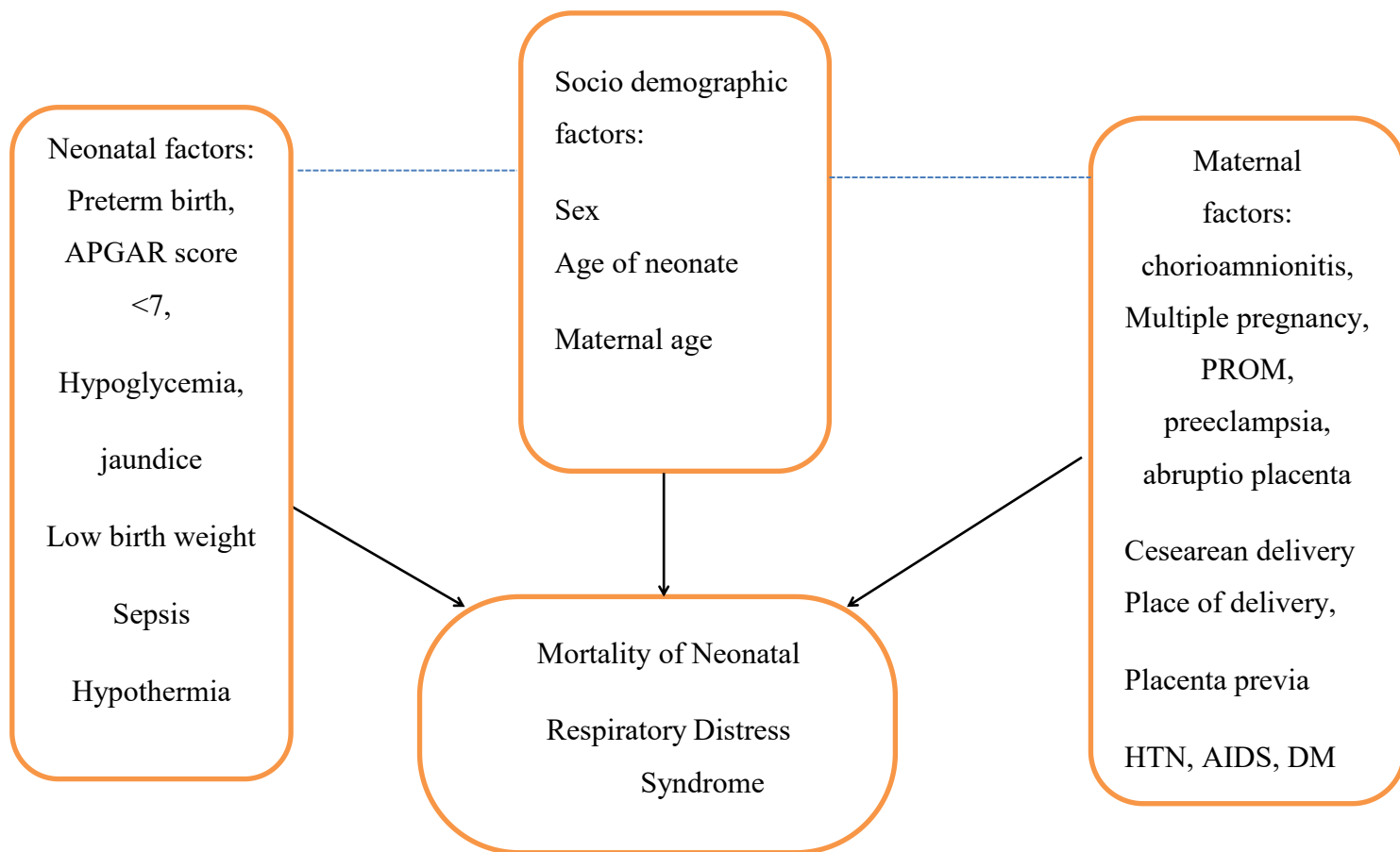
Neonatal hypothermia is also reported to affect the survival of neonates with RDS in different studies. A retrospective cohort study done in Gondar, Ethiopia, found out those neonates with RDS have delayed recovery than their counter parts (4). Additionally, a retrospective cohort study conducted in Eastern Amhara region also identified hypothermia as an important factor in the survival status of neonates with RDS (21). A multicenter prospective study done in china also found that hypothermia is associated with mortality and poor outcomes of neonates with RDS (50).

Meconium aspiration syndrome is another predictor that affects the outcome of among neonates with RDS. A prospective cohort study conducted in Qena University Hospital, Egypt showed that MAS is significantly associated with mortality rate of RDS (51).

#### **2.2.4 Maternal medical and obstetrics factors**

Various maternal and obstetrics factors such as maternal infection or chorioamnionitis, PROM, mode of delivery and multiple pregnancy are known to be associated with the survival of neonates with RDS. In a multi-centered institution based retrospective follow-up study done in West Oromia, Ethiopia, multiple pregnancy is found as a significant predictor of RDS and increased the hazard of death by two times among neonates admitted with RDS. It is associated with a greater risk of preterm birth, low birth weight, lung immaturities (1). In a retrospective case-control study conducted in China, PROM was also reported as a significant predictor of RDS (49). A retrospective cohort study revealed that Chorioamnionitis during the last pregnancy period or at the time of delivery is significantly associated with RDS mortality and increases the hazards of death by two times among neonates with RDS(1). A retrospective case control study conducted in China also showed that maternal infection can increase mortality among neonates with RDS(49). A retrospective study done in Eastern Amhara, Ethiopia found mode of delivery as a significant factor among neonates with RDS. It was reported that those neonates who are delivered with cesarean section were at an increased chance of dying than their counter parts (21). A retrospective cohort study done in Lombardy, Northern Italy also showed the risk of RDS was higher for those infants delivered through cesarean section (48). In a retrospective study done in East Amhara, Ethiopia also reported that abruptio placenta and preeclampsia were shown to be significant predictors of survival status among neonates with RDS. Abruptio placenta was found to increase the hazard of death among neonates with RDS by 2.09 times (21). In addition, preeclampsia was also found to increase the risk of severe RDS among neonates in a retrospective case control study done in Taiwan (52). A prospective study conducted in Tanzania, on 246 preterm neonates with RDS indicated that the place of delivery is also found to be associated with mortality in preterm neonates with RDS (22). A retrospective cohort study done in Black Lion specialized Hospital, Ethiopia reported that the risk of developing RDS for neonates delivered at home was almost three times higher than those delivered at a health institution (7).

### 2.3. Conceptual framework



**Figure 1; Conceptual framework to assess the incidence and predictors of mortality among neonates with respiratory distress syndrome admitted to neonatal intensive care units of public hospitals in Hawassa, Ethiopia,2024 (1,4,19).**

### **3. Objectives**

#### **3.1 General objective**

To assess the incidence and predictors of mortality among neonates with respiratory distress syndrome admitted to neonatal intensive care units of public hospitals in Hawassa, Ethiopia, 2024.

#### **3.2 Specific objective**

To assess the incidence of mortality among neonates with respiratory distress syndrome admitted to the neonatal intensive care units of public hospitals in Hawassa, Ethiopia, 2024.

To identify the predictors of mortality among neonates with respiratory distress syndrome admitted to the neonatal intensive care units of public hospitals in Hawassa, Ethiopia, 2024.

## 4. Method

### 4.1 Study setting

The study was conducted at Hawassa University Comprehensive Specialized Hospital and Adare general hospital in Hawassa city, the capital of Sidama region that is located 275 Km South of Addis Ababa. The estimated total population size in 2019 was 436,992 as projected from the central statistics authority of Ethiopia.

There are three public hospitals at Hawassa town. Hawassa University Comprehensive Specialized Hospital has a catchment population of 15-22 million people and one of the largest academic institutions in Ethiopia and located at the heart of Hawassa City. The Pediatrics department of the hospital has a well-organized neonatal intensive care unit, including personnel and equipment. It provides continuous life support and comprehensive care for extremely high-risk newborn infants and those with complex and critical illnesses.

Adare general hospital is not a teaching hospital but it also provides both preventive and curative services for more than 1,368,341 people. The neonatal ICU is one of the units in the hospital, which gives services under the pediatrics department. The hospital NICU gives all the services needed, including those with high-risk neonates.

### 4.2 Sample size determination

The sample size is determined by using single population proportion formula for the first objective taking mortality rate of 42.31% from a study done in East Amhara Region, Ethiopia(21).

$$n = Z_{\left(\frac{\alpha}{2}\right)}^2 * P(1-P)/(d)^2$$

Where; n= Sample size

Z=Standard normal deviation (1.96 for 95% CI)

d=precision level (0.05)

So the total sample size is calculated as **375**.

The sample size for the second objective is determined via the double population proportion formula using Epi-Info Version 7 by assuming a one-to-one ratio of exposed to non-exposed, 95% level of confidence, and a power of 80%.

$$n = \frac{\left\{ Z_{1-\frac{\alpha}{2}} \sqrt{2\bar{P}(1-\bar{P})} + Z_{1-\beta} \sqrt{P_1(1-P_1) + P_2(1-P_2)} \right\}^2}{(P_1 - P_2)^2}$$

Four significantly associated factors are considered to calculate the sample size; APGAR score, mode of delivery, type of pregnancy and birth weight. The largest sample size is 834. Taking 10 % incomplete patient's chart, the final sample size is taken as 918.

**Table 1; Sample size calculation to determine the incidence and predictors of mortality among neonates with respiratory distress syndrome admitted to neonatal intensive care units of public hospitals in Hawasaa, Ethiopia, 2024.**

| S.No | Significant variables | Confidence Level | Power | AHR  | Percentage of exposed | Percentage of unexposed | Required sample size(By Fleiss w CC) | Authors |
|------|-----------------------|------------------|-------|------|-----------------------|-------------------------|--------------------------------------|---------|
| 1    | APGAR score           | 95%              | 80%   | 2.2  | 64.1                  | 36.2                    | 228                                  | (19)    |
| 2    | Birth weight          | 95%              | 80%   | 1.48 | 43.1                  | 55.07                   | 834                                  | (21)    |
| 3    | Mode of delivery      | 95%              | 80%   | 1.59 | 35.06                 | 45.58                   | 622                                  | (21)    |
| 4    | Type of pregnancy     | 95%              | 80%   | 2.2  | 71.42                 | 32                      | 234                                  | (1)     |

### **4.3 Source population**

All neonates with RDS who were admitted to NICU within the last five years (from January 2019 to December 2023) were considered as the source population.

### **4.4 Study population**

All selected neonates with RDS who were admitted to NICU in public hospitals of Hawassa, Ethiopia within the last five years (from January 2019 to December 2023) were considered as the study population.

### **4.5 Inclusion/Exclusion criteria**

#### **4.5.1. Inclusion criteria**

All neonates who were admitted to NICU with the diagnosis of RDS in public hospitals of Hawassa, Ethiopia, from January 2019 to December 2023.

#### **4.5.2. Exclusion criteria**

Incomplete medical records of neonates with RDS (i.e., admission and discharge dates, gestational age, birth weight and outcome variable).

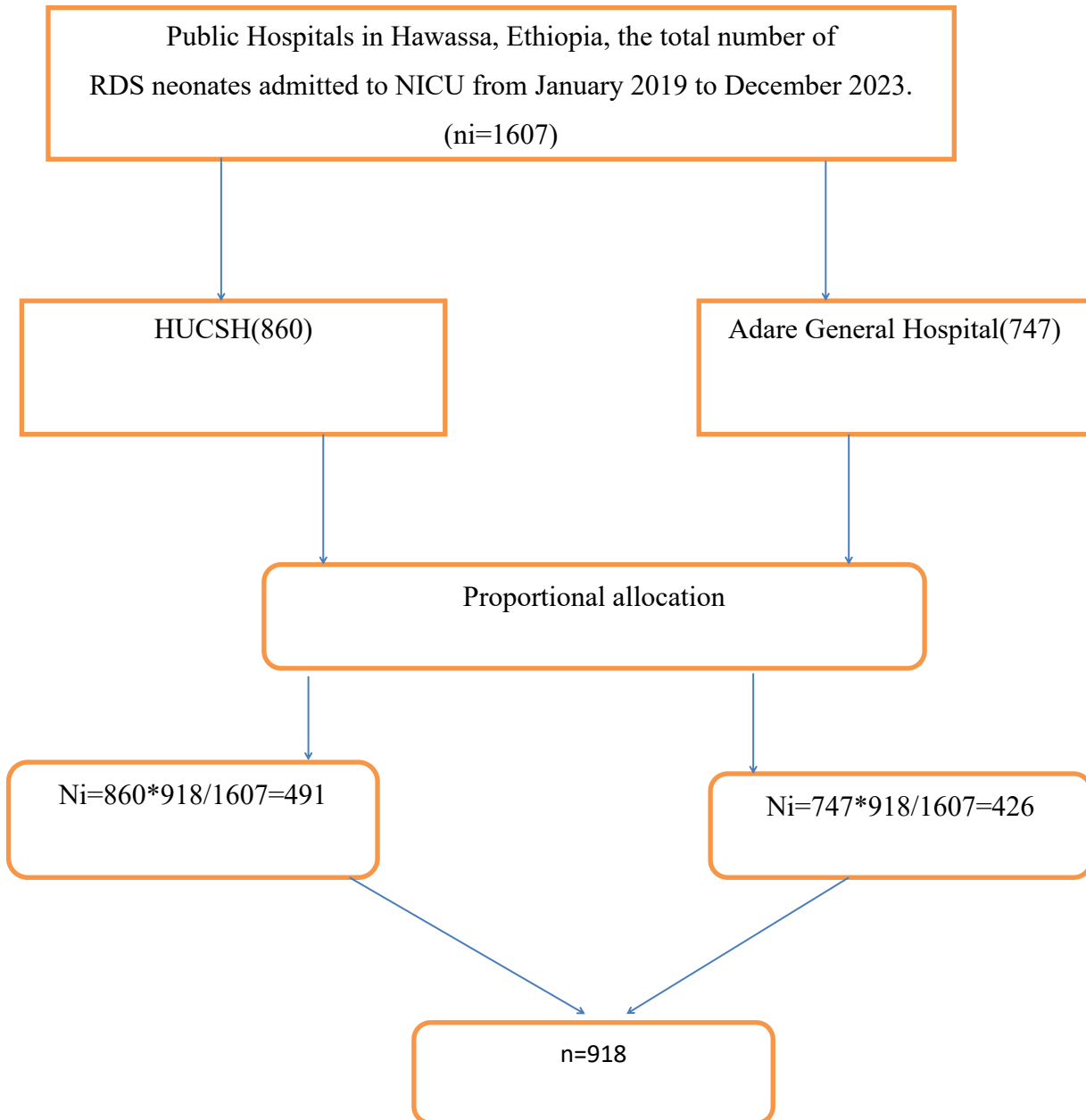
Patients with respiratory function affected by other serious diseases of the system (such as neonatal transient tachycardia (TTN) and congenital anomaly).

### **4.6 Study design and period**

A facility based retrospective cohort study was conducted among neonates admitted at NICU within the last five years (from January 2019 to December 2023).

### **4.7 Sampling technique**

The total number of neonates admitted to NICU with the diagnosis of RDS from January 2019 to December 2023, were selected and enlisted. The total sample size was proportionally allocated for each hospitals and finally, the required number of sample size was obtained using simple random sampling technique by computer generated numbers from each hospitals and all medical charts fulfilling the inclusion criteria were reviewed.



**Figure 2 Schematic presentation of the sampling procedure to determine the incidence and predictors of mortality among neonates with RDS admitted to the NICU from 2019-2023 in public hospitals of Hawassa, Ethiopia, 2024.**

#### **4.8 Data collection tools and procedure**

A structured data extraction tool that was adapted after reviewing different literatures (1,7,21) was used to collect the required data from the neonates' records. The tool consists of the following

sections: socio- demographic characteristics of neonates and mothers, maternal and neonatal medical-related factors, and obstetric and gynecology -related factors.

Data were collected by four Bachelor of Science (BSc) nurses. There was an additional supervisor, Master of Science (MSc) nurse, at each study sites who was responsible for supporting kobo toolbox utilization. The selected individual medical records were traced by using medical record number (MRN). All relevant data were extracted by review of charts and NICU registers. An electronic KoBo toolbox based instrument was used for data collection.

#### **4.9 Data quality control**

The data extraction tool was pre-tested at Adare General Hospital for different populations other than this study's focus group for consistency and access of relevant information on 5% of sample. A one-day orientation was given regarding the data collection tool and process by reviewing the complete medical records. During the data collection time, close supervision and monitoring was carried out by the principal investigator.

#### **4.10 Data processing, analysis and presentation**

Data was exported from the KoBo toolbox to STATA 16 statistical software for analysis. Data was cleaned, edited, and coded. Descriptive statistics were carried out to summarize and present the data. The incidence rate was calculated by dividing the total number of cases by person days of observation. Kaplan-Meier survival curves was used to estimate the mean survival time and the log-rank tests were used to compare survival curves. Proportional hazard assumption was tested both graphically and through the Schoenfeld residual test for all predictors, to ensure whether the proportional hazard assumption was met or not. Variables having a p-value less than or equal to 0.25 in the bivariate analysis were fitted to the multivariable regression model with a 95% confidence interval. A p-value less than 0.05 was considered statistically significant.

#### **4.11 Study variables**

**Dependent variable:** RDS mortality.

#### **Independent variables**

**Socio-demographic factors:** age of neonate, sex, maternal age.

**Gynecologic-obstetric related factors:** multiple pregnancy, PROM, preeclampsia, chorioamnionitis,

placenta previa, abruption placenta.

**Medical disorders in mother:** Hypertension (HTN), diabetes mellitus (DM) and human immune virus/ acquired immune deficiency syndrome (HIV)/ (AIDS).

**Neonatal medical related condition:** Apgar score, sepsis, jaundice, hypothermia, gestational age, birth weight, perinatal asphyxia (PNA), hypoglycemia and meconium aspiration syndrome.

#### **4.12 Operational definition**

**Censored:** Premature neonate still alive at the end of the study or discharged before end of study time including discharged to home, discharged against medical advice or referred out to other health institutions without knowing their outcome.

**Event:** Death of preterm neonate within 28 days of birth.

**Follow up time:** From time of admission until either an event or censorship occurs.

**Neonatal RDS;** The presence of two or more of the following signs: an abnormal respiratory rate or signs of labored breathing (expiratory grunting, nasal flaring, intercostal recessions, chest wall recessions), with or without cyanosis.

**Low APGAR Score-** A neonate with an Apgar score at first and fifth minute  $< 7$

**Medical disorders in the neonate:** Any recorded medical diagnosis for the preterm neonates on their medical records.

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

#### **4.13. Ethical consideration**

Ethical clearance was obtained from IRB of Hawassa University, College of health science. Letters of cooperation was written to each study facility from the Hawassa city administration and Hawassa University, College of medicine and health science, school of public health. The objective of the study was informed to the heads of the study health facilities. Subsequently permission was obtained from the clinical director and relevant department and unit heads of the hospital. Name or any other identifying information was not recorded on the checklist and all information that were taken from the records were kept strictly confidential and in a safe place.

#### **4.14 Dissemination of the result**

After completion of the study, the result will be presented to Hawassa University College of medicine and health science, school of public health.

In addition to this, the study findings will be presented and disseminated to the health facilities where the data was collected and to the Sidama region health bureau.

Additionally, it will be given for peer review for publication.

## 5. Result

### 5.1. Socio-demographic and obstetric characteristics of mothers of neonates

A total of 858 RDS neonate's medical records were reviewed giving 93.4% of response rate. In this study, 464(54.1%) were male neonates and 325 (37.9%) of the neonates resided in rural areas. The median length of hospital stay was 10, IQR (5, 14). Most 671 (78.2%) of the mothers aged between 21–34 years of age group. The median age of the mothers was 25 years, IQR (21, 30). In this study, 842(98.1%) of mothers had given birth at the health institutions. About 646 (75.3%) neonates of neonates were admitted within the first 7 days of birth (Table 2).

**Table 2; Socio-demographic characteristics of neonates with RDS admitted to NICU at public hospitals Hawassa, Ethiopia, 2024 (n=858).**

| Characteristics           |                    | Frequency(%) | Censored | Death | P value |
|---------------------------|--------------------|--------------|----------|-------|---------|
| Sex                       | Female             | 394 (45.9)   | 247      | 147   | 0.097   |
|                           | Male               | 464 (54.1)   | 265      | 199   |         |
| Residence                 | Urban              | 533 (62.1)   | 304      | 229   | 0.044   |
|                           | Rural              | 325 (37.9)   | 208      | 117   |         |
| Neonatal age at admission | <7 days            | 646 (75.3)   | 375      | 271   | 0.09    |
|                           | >=7 days           | 212(24.7)    | 137      | 75    |         |
| Maternal Age              | <=20               | 87(10.1)     | 47       | 40    | 0.243   |
|                           | 21–34              | 671 (78.2)   | 399      | 272   |         |
|                           | >34                | 100 (11.7)   | 66       | 34    |         |
| Gestational Age           | <37                | 470 (54.8)   | 269      | 201   | 0.109   |
|                           | >=37               | 388 (45.2)   | 243      | 145   |         |
| Place of delivery         | Health institution | 842 (98.1)   | 503      | 339   | 0.778   |
|                           | Home               | 16 (1.9)     | 9        | 7     |         |
| Length of hospital stay   | <=7 days           | 370(43.1)    | 140      | 230   | 0.992   |
|                           | >7days             | 488(56.87)   | 372      | 116   |         |

## 5.2. Obstetric and gynecological problems of the study participants

In this study, 514 (59.94%) of the mothers were multigravida and 344 (40.1%) were primigravida. Most 770(89.7%) of the mothers had ANC follow up and 125(14.6 %) had multiple pregnancy. More than half 510(59.4%) of study participants were delivered through spontaneous vaginal delivery. (table 3)

**Table 3; Obstetric and gynecological characteristics of mothers who had neonates with RDS admitted to NICU at of public hospitals in Hawassa, Ethiopia, from January 2019 to December 2023.**

| Characteristics   |              | Frequency(%) | Censored | Death | P value |
|-------------------|--------------|--------------|----------|-------|---------|
| ANC follow up     | Yes          | 770 (89.7)   | 459      | 311   | 0.911   |
|                   | No           | 88 (10.3)    | 53       | 35    |         |
| Gravidity         | Primigravida | 344 (40.1)   | 197      | 147   | 0.240   |
|                   | Multigravida | 514 (59.94)  | 315      | 199   |         |
| Parity            | Premipara    | 334 (38.9)   | 183      | 151   | 0.020   |
|                   | Multipara    | 524 (61.1)   | 329      | 195   |         |
| Mode of delivery  | SVD          | 510 (59.4)   | 312      | 198   | 0.277   |
|                   | CS           | 348(40.6)    | 200      | 148   |         |
| Type of pregnancy | Single       | 733 ( 85.4)  | 434      | 299   | 0.501   |
|                   | Multiple     | 125 (14.6)   | 78       | 47    |         |
| PROM              | Yes          | 105 (12.2)   | 63       | 42    | 0.942   |
|                   | No           | 753 (87.8)   | 449      | 304   |         |
| Preeclampsia      | Yes          | 146 (17.0)   | 79       | 67    | 0.132   |
|                   | No           | 712 (83.0)   | 433      | 279   |         |
| Abruptio placenta | Yes          | 55 (6.4)     | 30       | 25    | 0.423   |
|                   | No           | 803 (93.6)   | 482      | 321   |         |
| Placenta previa   | Yes          | 16(1.9)      | 8        | 8     | 0.426   |
|                   | No           | 842(98.1)    | 504      | 338   |         |
| Breast feeding    | Yes          | 336 (39.2)   | 186      | 150   | 0.039   |
|                   | No           | 522 (60.8)   | 326      | 196   |         |
| Chorioamnionitis  | Yes          | 93 (10.8)    | 56       | 37    | 0.910   |
|                   | No           | 765 (89.2)   | 456      | 309   |         |

<sup>a</sup>Antenatal Care; <sup>b</sup>Premature Rupture of Membrane

### 5.3. Maternal Medical Diagnosis of the Study Participants

In this study, 58 (6.8%) mothers had HTN, 74 (8.6%) had diabetes, and 21 (2.4%) had HIV/AIDS (table 4).

**Table 4 Maternal medical diagnosis in NICU at public hospitals Hawassa, Ethiopia, from January 2019 to December 2023(n=858).**

| Characteristics |     | Frequency(%) | Censored | Death | P value |
|-----------------|-----|--------------|----------|-------|---------|
| HTN             | Yes | 58 (6.8)     | 33       | 25    | 0.655   |
|                 | No  | 800 (93.2)   | 479      | 321   |         |
| DM              | Yes | 74 (8.6)     | 48       | 26    | 0.341   |
|                 | No  | 784 (91.4)   | 464      | 320   |         |
| HIV/AIDS        | Yes | 21 (2.4)     | 8        | 13    | 0.041   |
|                 | No  | 837 (97.6)   | 504      | 333   |         |

<sup>a</sup>Hypertension; <sup>b</sup>Diabetes Mellitus; <sup>c</sup>Human Immune Virus/Acquired Immune Deficiency Syndrome

### 5.4. Neonatal medical -related factors

Among the neonatal medical problems identified during the study, sepsis was 310 (36.1%), hypothermia was 533 (62.1%) and PNA was 215( 25.1%). In this study, nearly two-third of the neonates had 1st and 5th minute Apgar scores of <7, respectively. Among the neonates about 473 (55.1%) weighed <2500 gram and 385 (44.9%) weighed above 2500 gram. (table 5 )

**Table 5 Neonatal medical -related factors among neonates admitted to NICU at public hospitals Hawassa, Ethiopia, from January 2019 to December 2023 (n=858).**

| Characteristics |     | Frequency(%) | Censored | Death | P value |
|-----------------|-----|--------------|----------|-------|---------|
| PNA             | Yes | 215 (25.1)   | 104      | 111   | <0.001  |
|                 | No  | 643 (74.9)   | 408      | 235   |         |
| Sepsis          | Yes | 344 (40.1)   | 174      | 136   | 0.111   |
|                 | No  | 514 (59.94)  | 338      | 210   |         |
| Jaundice        | Yes | 334 (38.9)   | 58       | 52    | 0.112   |
|                 | No  | 524 (61.1)   | 454      | 294   |         |

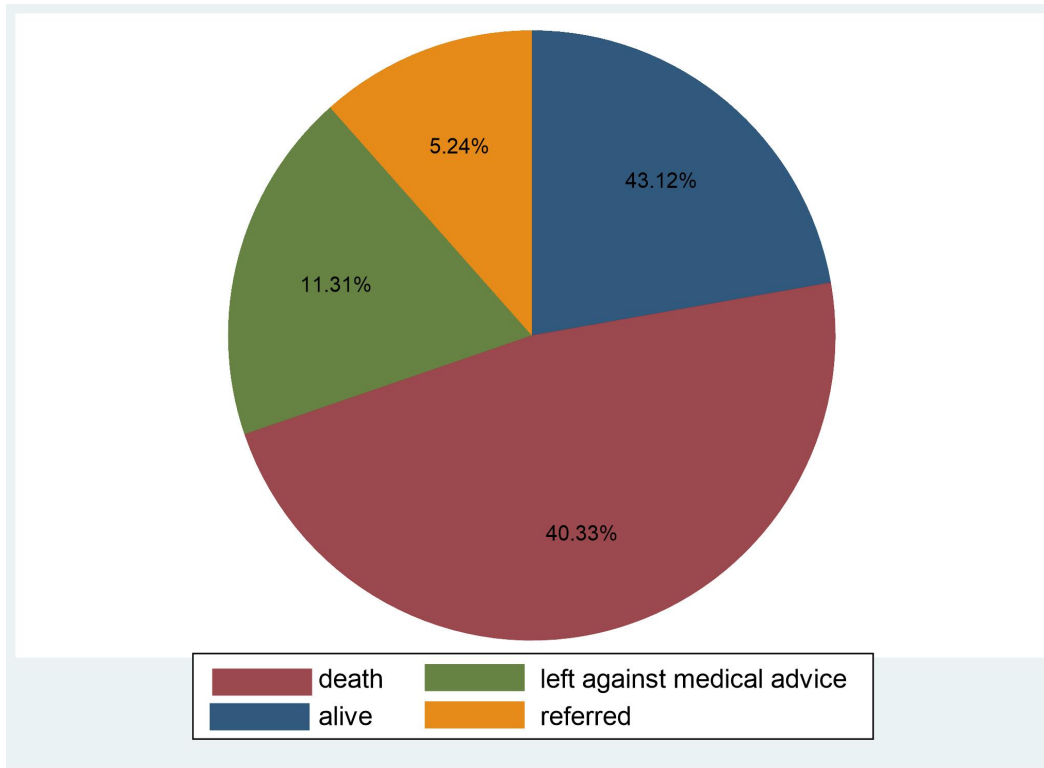
|                                 |            |             |     |     |        |
|---------------------------------|------------|-------------|-----|-----|--------|
| MAS                             | Yes        | 510 (59.4)  | 48  | 38  | 0.433  |
|                                 | No         | 348(40.6)   | 464 | 307 |        |
| Hypothermia                     | Yes        | 733 ( 85.4) | 287 | 246 | <0.001 |
|                                 | No         | 125 (14.6)  | 225 | 100 |        |
| Hypoglycemia                    | Yes        | 105 (12.2)  | 49  | 40  | 0.348  |
|                                 | No         | 753 (87.8)  | 463 | 306 |        |
| Birth weight in gram            | <2500 gram | 146 (17.0)  | 298 | 217 | 0.028  |
|                                 | >2500 gram | 712 (83.0)  | 214 | 129 |        |
| 1 <sup>st</sup> min APGAR score | <7         | 55 (6.4)    | 307 | 233 | 0.185  |
|                                 | >7         | 803 (93.6)  | 205 | 113 |        |
| 5 <sup>th</sup> min APGAR score | <7         | 16(1.9)     | 327 | 246 | 0.027  |
|                                 | >7         | 842(98.1)   | 185 | 100 |        |

<sup>a</sup>Perinatal Asphyxia; <sup>b</sup>Meconium Aspiration Syndrome; <sup>c</sup>Activity, pulse, Grimace, Appearance, Respiration

### 5.5. Survival Status of RDS neonate admitted at NICU

Total neonates that were admitted to NICU had been observed for a total of 8809 neonate days. The overall mortality rate among the RDS neonates was 346 (40.3%) (95% CI 37.00, 43.7) and 512 censored RDS neonates, of whom 370(43.42%) were discharged with improvement, 97 (11.31%) were discharged against medical treatment, and 45 (5.24%) were referred to other health institutions (figure 3).

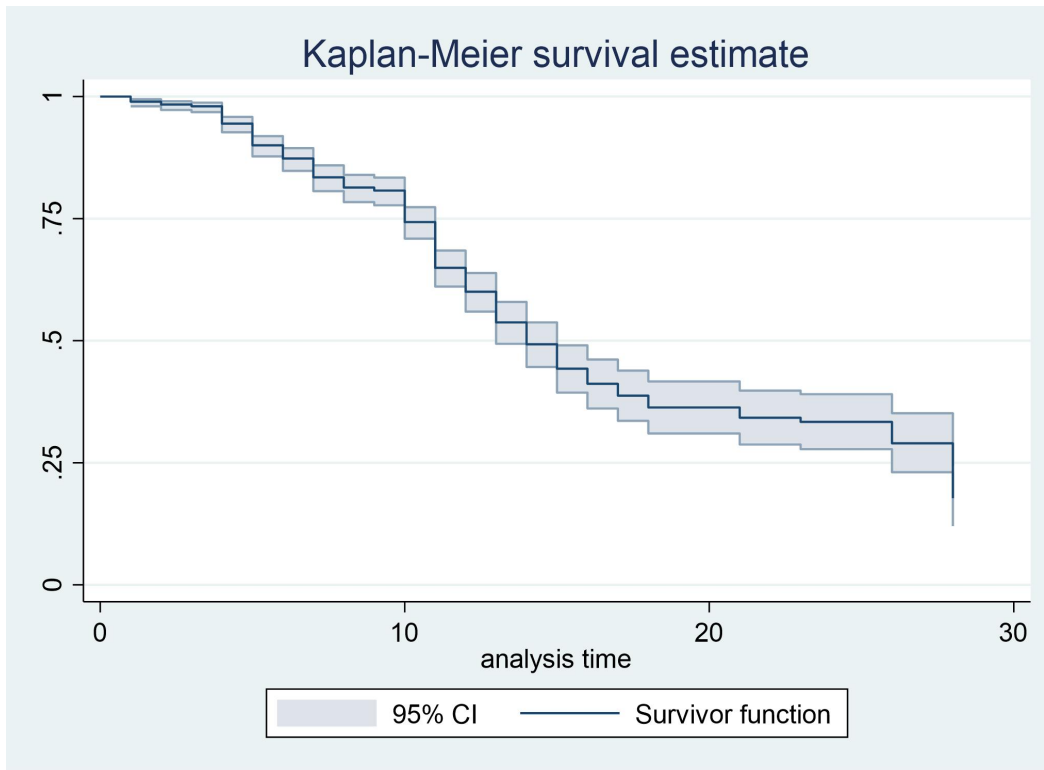
The overall mean hospital stay was 10.27 days (95% CI: 9.92, 10.61), with a minimum and maximum follow-up time of 1 and 28 days, respectively. The overall cumulative incidence rate of mortality was 39.475 per 1000 person-days (95% CI: 35.33, 43.62) with 8809 person-days of observation.



**Figure 3 Outcome of RDS neonates admitted to NICU of public hospitals, Hawassa, Ethiopia, from January 2019 to December 2023.**

### **5.6. Kaplan-Meier survival rate of RDS**

According to the overall Kaplan-Meier estimate, there was a high chance of survival for RDS infants on the first day of admission, and this probability progressively decreased with longer follow-up periods. On the first day of the hospital stay, there was a maximum observed survival probability of 97.97% (95% CI: 0.96, 0.98). At half of the study follow-up day, the survival probability was also found to be 46.94 % (95% CI: 0.42, 0.51 and at the end of the study, the cumulative survival probability was found to be 12.46% (95% CI: 0.06, 0.19). The overall median survival time of neonates admitted to the NICU in the study was 14 days (**figure 4**).

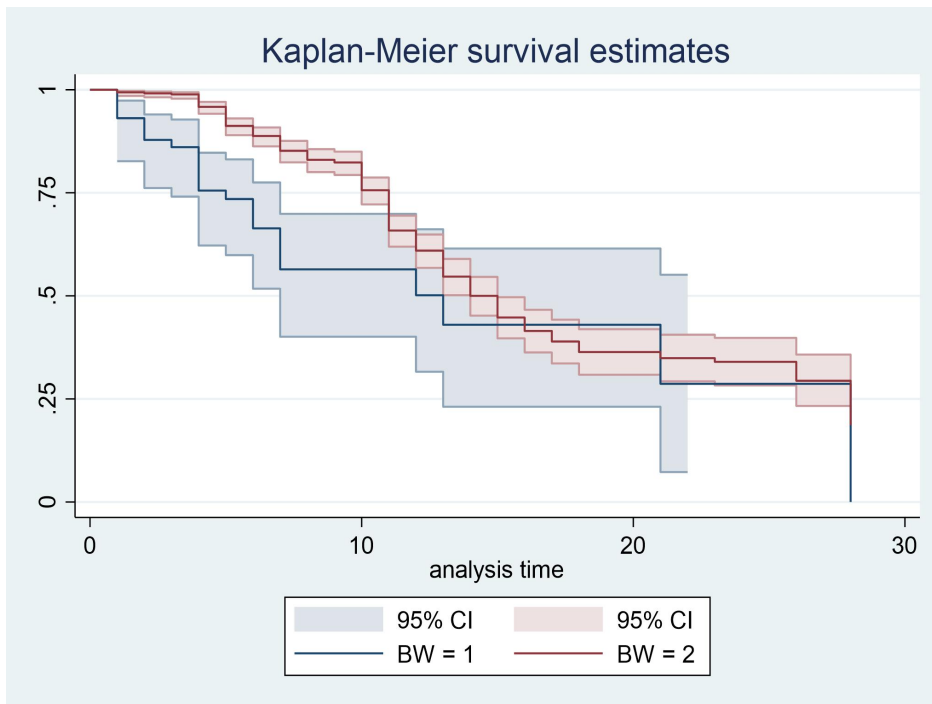


**Figure 4 Overall Kaplan-Meier survival estimate of RDS neonates admitted to NICU at public hospitals Hawassa, Ethiopia, 2024.**

### 5.7. Survival function and comparison of survivorship functions for different categorical Variables

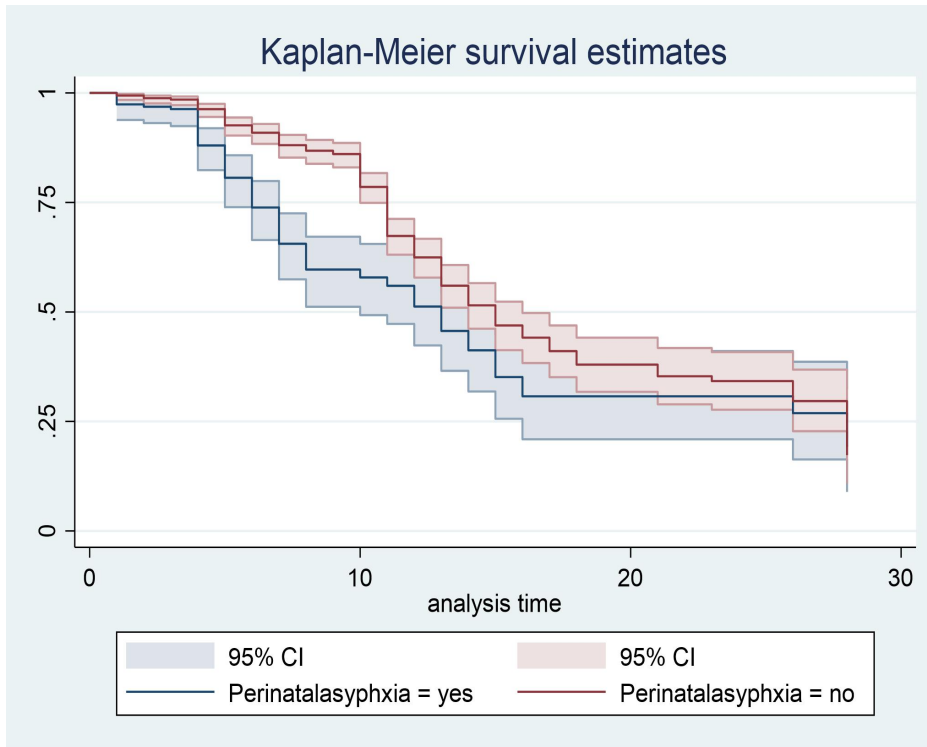
The Kaplan-Meier estimator survival curve provides the survivor function estimate across several sets of covariates to facilitate comparisons. As was shown below, distinct graphs containing the estimates of the Kaplan-Meier survivor functions were created for various categorical covariates. When two survival functions lie above one other, it often indicates that the group described by the upper curve has a higher survival rate or has had a more favorable experience with survival than the group indicated by the lower curve. However, whether or whether the observed difference shown on the plot is significant is the statistical question. The log rank test can demonstrate this to determine whether survival curves for various categorical explanatory variables are equal. There was a Cochran-Mantel-Haenszel log rank test (table 7). The test statistics, which are derived from the log-rank, demonstrated that the null hypothesis—which states that there is a difference in the distribution of survival times among categorical variables—is statistically different from the other.

In this study, birth weight <2500 has a lower survival time (with a median birth weight of 2200 grams, 95% CI: 2100-2300) as compared to birth weight > 2500 grams. At 28 days of hospital stay, the overall survival probability of birth weights <2500 and >2500 is found to be 11.93 % and 13.09 %, respectively. This difference was statistically significant (p-value = 0.003).



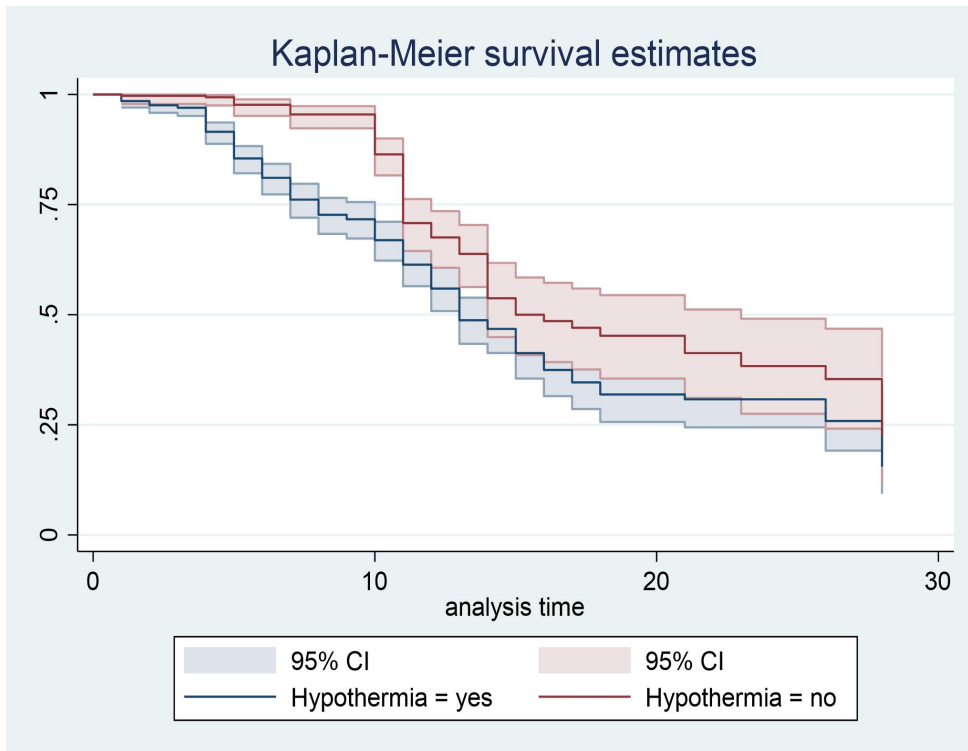
**Figure 5 Kaplan-Meier survival estimate among RDS neonates admitted to NICU at public hospitals in Hawassa, Ethiopia, with the category of Birth weight.**

Neonates diagnosed with PNA had a lower survival time as compared to those who didn't have PNA, with an overall survival probability of 22.25% and 12.44%, respectively, at the end of the follow-up period (p<0.001).



**Figure 6 Kaplan-Meier survival estimate among RDS neonates admitted to NICU at public hospitals in Hawassa, Ethiopia, 2024, with the category of Perinatal Asphyxia.**

Neonates diagnosed with hypothermia had a lower survival probability as compared to those who didn't have hypothermia, which are found to be 10.72% and 16.22%, respectively, at the end of the follow-up period ( $p < 0.001$ ).



**Figure 7 Kaplan-Meier survival estimate among RDS neonates admitted to NICU at public hospitals in Hawassa, Ethiopia, 2024 with the category of Hypothermia.**

Finally, the log-rank test was conducted to check for the existence of any significant differences in survival among the numerous levels of the categorical predictors considered in the study.

Accordingly, the Kaplan-Meier analysis indicated significant evidence of differences in survival times in the categories.

The table below describes how to evaluate whether or not overall Kaplan Meier curves for two or more categories of covariates are statistically equivalent using the log-rank test (table 7).

**Table 7 Median survival time and log-rank test for equality of survivor function among RDS neonate admitted to NICU at public hospitals Hawassa, Ethiopia, from January 2019 to December 2023 (n=858).**

| Variables           | Category     | Median survival 95% CI | Log rank test         | P value  |
|---------------------|--------------|------------------------|-----------------------|----------|
| Maternal age        | <20          | 7 (6,21)               | X <sup>2</sup> =17.63 | p< 0.001 |
|                     | 20-34        | 15( 14,16)             |                       |          |
|                     | >34          | 14( 12,15)             |                       |          |
| Gestational age     | <37          | 14(13,15)              | X <sup>2</sup> = 9.4  | p<0.05   |
|                     | >37          | 15(13,16)              |                       |          |
| Gravidity           | Primigravida | 13 (11,15)             | X <sup>2</sup> = 7.23 | p<0.05   |
|                     | Multigravida | 15 (13 ,16)            |                       |          |
| Preeclampsia        | Yes          | 12(11,17)              | X <sup>2</sup> =6.60  | p<0.05   |
|                     | No           | 14( 14,15)             |                       |          |
| Mode of delivery    | SVD          | 17(15,21)              | X <sup>2</sup> =14.45 | p<0.001  |
|                     | CS           | 13(12,14)              |                       |          |
| Breast feeding      | Yes          | 14(12, 15)             | X <sup>2</sup> =17.69 | p<0.001  |
|                     | No           | 16(14,17)              |                       |          |
| Hypertension        | Yes          | 13(7,14)               | X <sup>2</sup> =13.86 | p<0.001  |
|                     | No           | 15(14,15)              |                       |          |
| Perinatal Asyphyxia | Yes          | 13(10,15)              | X <sup>2</sup> =14.84 | p<0.001  |
|                     | No           | 15(14,16)              |                       |          |
| Sepsis              | Yes          | 14(12,15)              | X <sup>2</sup> = 8.94 | p<0.05   |
|                     | No           | 15(13,17)              |                       |          |
| Hypothermia         | Yes          | 13(13, 15)             | X <sup>2</sup> =19.55 | p<0.001  |
|                     | No           | 15(14,23)              |                       |          |
| Birth weight        | <2500 gram   | 14(13,15)              | X <sup>2</sup> =9.32  | p<0.05   |
|                     | >2500 gram   | 15(14,16)              |                       |          |

### 5.8. Cox proportional hazard model for different predictor variables

A Cox proportional hazard model was used to identify predictors of mortality in RDS neonates. In bivariable Cox proportional hazard regression, maternal factors like Gravidity, mode of delivery, preeclampsia, HTN, maternal age, and neonatal medical-related factors like birth weight, PNA, hypothermia and sepsis were significant predictors of mortality in RDS neonates at (p value<0.25).

After assessing multi-collinearity, those significant predictors in bivariable analysis were analyzed in a multivariable Cox proportional model. In a multivariable proportional hazard model, perinatal asphyxia, hypothermia, and low birth weight were potential independent predictors of RDS neonatal mortality at (p-value <0.05).

Those RDS neonates whose birth weight was less than 2500 were 1.70 times more probable to die as compared to those neonates whose birth weight was greater than 2500 (AHR: 1.70; 95% CI: 1.10-2.64).

Respiratory distress syndrome neonates who had hypothermia at the time of admission were also 1.66 times more likely to die than those neonates without hypothermia (AHR: 1.66 ; 95% CI: 1.27-2.17).

Respiratory distress syndrome neonates with PNA at base admission had a 1.79 times higher probability of dying as compared to those neonates without PNA (AHR: 1.79; 95% CI: 1.37- 2.34). (Table 8).

**Table 8 Bivariable and multivariable Cox proportional hazard analysis of study participants, Hawassa, Ethiopia, from January 2019 to December 2023.**

| Characteristics | Category     | Censored | Death | CHR(95%CI)       | AHR(95% CI)       |
|-----------------|--------------|----------|-------|------------------|-------------------|
| Maternal age    | <20          | 47       | 40    | 2.06 (1.29-3.27) | 1.095 (0.64-1.89) |
|                 | 20-34        | 399      | 272   | 1.05(.74-1.52)   | 0.78 (0.54-1.14)  |
|                 | >34          | 66       | 34    | 1                | 1                 |
| Gestational age | <37          | 269      | 201   | 1.38 (1.11-1.71) | 1.09 (0.85-1.40)  |
|                 | >37          | 243      | 145   | 1                | 1                 |
| Gravidity       | primigravida | 197      | 147   | 1.32 (1.07-1.64) | 0.91 (0.70-1.17)  |
|                 | multigravida | 315      | 199   | 1                | 1                 |
| Preeclampsia    | Yes          | 79       | 67    | 1.40 (1.07-1.83) | 1.19(0.86-1.66)   |
|                 | No           | 433      | 279   | 1                | 1                 |
| Hypertension    | Yes          | 33       | 25    | 1.01 (0.82-1.27) | 1.23(0.98-1.55)   |

|                    |            |     |     |                  |                     |
|--------------------|------------|-----|-----|------------------|---------------------|
|                    | No         | 479 | 321 | 1                | 1                   |
| Perinatal Asphyxia | Yes        | 104 | 111 | 2.01 (1.60-2.52) | 1.79(1.37-2.34)**   |
|                    | No         | 408 | 235 | 1                | 1                   |
| Sepsis             | Yes        | 174 | 136 | 1.37 (1.10-1.70) | 1.04 (0.80-1.34)    |
|                    | No         | 338 | 210 | 1                | 1                   |
| Hypothermia        | Yes        | 286 | 246 | 1.65 (1.30-2.08) | 1.66(1.27 - 2.17 ** |
|                    | No         | 225 | 100 | 1                | 1                   |
| Birth weight       | <2500 gram | 298 | 217 | 2.08 (1.38-3.13) | 1.70(1.10-2.64)**   |
|                    | >2500 gram | 214 | 129 | 1                | 1                   |

\*p-value <0.05, ( Schoenfeld residual Global test =0.95)

## 6. Discussion

This study aimed to assess the incidence and predictors of mortality among neonates with respiratory distress syndrome admitted to neonatal intensive care units of public hospital in Hawassa, Ethiopia.

The result of this study has demonstrated an overall incidence of RDS mortality 39.2 per 1000 neonate days. The finding of this study is lower than the previous studies conducted in the East Amhara region of Ethiopia and West Oromia which reported an overall incidence rate of 60.19 and 59.87 respectively (21)(1). This marked variation might be attributed to difference in sample sizes and study subjects. The studies done in East Amhara region of Ethiopia and West Oromia used smaller sample size while the current study was conducted on a larger sample size. On the contrary, the result of this study is higher than the study done in Northern Thailand(7.68) per 1000 person days(46). This wide variation might be due to the differences in the socio demographic characteristics and study settings, where more advanced maternal newborn care services are offered in Northern Thailand.

Based on the study finding, the overall mortality rate of neonates with RDS was 40.32% (95% CI; 0.370, 0.437). This finding is in line with studies conducted in Eastern Amhara region (42.31%),and Bangladesh (36.5%) (21) (53). The finding of this study is lower than the study done in Debre Tabor, Ethiopia (49.5%) and Kenya (72.3%) (12,19). The observed discrepancy might be due to the difference in the study population and sample size. The study in Debre Tabor, Ethiopia included only preterm infants which is the major risk factor of RDS while the current study includes neonates of all gestational age. On the other hand, the study done in Kenya uses a much lower sample size and included only preterm and low birth weight babies, which are known to increase the risk of newborn death.

However, this finding was higher than studies conducted in Jeddah, Saudi Arabia (5.1%), and Thailand (17.4%) and China (3.90%) (8,40,49). The possible difference might be the difference in study units, data collection method and study variables.

The study done in Jeddah, Saudi Arabia doesn't include important variables such as Hypothermia, hypoglycemia and PNA. In addition, the study conducted in Saudi Arabia included only term neonates while the current study used neonates of all gestational age.

The difference observed between the current study and the study done in Thailand might be attributed to data collection method. The study done in Thailand used data that was collected by the research team while data collectors were employed in the current study which helps to reduce bias.

Additionally, variable like PROM which is an important predictor of RDS death is not taken in to consideration in the study conducted in Thailand.

The possible reason for the inconsistent results with the Chinese study might be due to the difference in the study population. While newborns of all gestational ages were included in this study, the research conducted in China exclusively employed term neonates, which may have contributed to the lower death rate. In addition, the observed divergence from the current study may also be explained by China's advanced medical treatment technologies.

The current study shows that birth weight, perinatal asphyxia and hypothermia as significant predictors for neonates admitted with RDS in the neonatal intensive care unit. In this study, RDS neonates with perinatal asphyxia at admission had 1.79 times higher risk of dying as compared to RDS neonates without perinatal asphyxia. This finding was supported by studies in West Oromia (1), Cameroon(29), and Serbia(33). The possible reason is asphyxia from birth can cause hypoxia, which can harm type II epithelial cells in the alveoli and decrease surfactant synthesis, increasing the prevalence and mortality of RDS. This condition also leads to progressive hypercapnia resulting in central nervous and other end organ damage. Furthermore, the rationale is due to the subsequent two factors: Hypoxia lowers pulmonary surfactant activity and may even cause its inactivation, and acute lung injury from severe birth asphyxia decreases pulmonary surfactant secretion and synthesis(49). Having neonatal hypothermia was found to be a significant predictor of mortality among neonates with respiratory distress syndrome admitted to the NICU. Those who had neonatal hypothermia were 1.66 times more likely to die as compared to those who did not have hypothermia. This finding is supported by studies conducted in East Amhara Region and Gondar(4,41). The possible explanation was that, hypothermia causes higher oxygen consumption, which in turn causes hypoxemia, pulmonary vasoconstriction, a decrease in pulmonary surfactant release, and less effort from the respiratory muscles. Therefore, the cold stress may potentially cause tissue hypoxia and brain impairment in newborns with respiratory insufficiency (e.g respiratory distress syndrome). Persistent hypothermia also raises the risk of hypoglycemia and metabolic acidosis, all of which aggravate respiratory distress syndrome, postpone recovery and increase the risk of death(54).

In agreement with studies done in Serbia(33), Bangladesh(53) , Thailand(8), and West Oromia (1), low birth weight was significantly associated with increased mortality among neonates with RDS. Those neonates with birth weight <2500 gram were at higher risk to die compared to those with birth weight >2500 gram. This conclusion is based on the fact that low birth weight is a strong predictor of physiological and anatomical immaturity in infants, including lung immaturity-related surfactant deficiency. Low birth weight infants have slower growth, lack of subcutaneous tissue, large surface area to body mass ratio, fragile capillaries in their brain and weak organ development resulting in underdeveloped lungs and fewer alveoli. Due to this complications and mortality may rise. Thus, newborns with RDS may be predicted to survive based on their birth weight(36).

## **7. Conclusion**

The high incidence rate of neonatal RDS mortality in this study remains a public health concern. The survival probability is higher on the first day of admission and decreases with longer follow up period. PNA, hypothermia, and birth weight were the main predictors of the incidence of RDS death in newborns.

## **8. Recommendations**

For health providers working in NICU: It is preferred to concentrate on PNA, hypothermia, and low birth weight prevention, early diagnosis, and appropriate care.

For hospitals: In order to lower the death rate from RDS, hospitals should pay close attention to the identified predictors.

For researchers; further research (prospective study) is needed to explore other predictors including socioeconomic, maternal nutritional status and environmental factors.

Future research should also explore the impact of health service factors such as access to specialized neonatal care units, protocols for surfactant administration, and health care provider training on reducing mortality rates associated with NRDS.

## **9. Limitation and strength of the study**

### **Strength;**

This study was conducted on a large sample size.

### **Limitation;**

Important factors such maternal educational status, maternal nutritional health, birth interval, and family income were overlooked in the study since it relied on secondary data.

The inclusion of solely hospitalized and admitted newborns (high-risk neonates) may have led to an overestimation of the fatality rate and its contributing factors.

There is a potential to miss neonatal deaths particularly those registries considered as incomplete which would underestimate the overall mortality.

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## 8. Annex

### Data Extraction Checklist

#### 1.1 Information sheet

**Title of the research project;** Incidence and predictors of mortality among neonates with respiratory distress syndrome admitted to neonatal intensive care units of public hospitals in Hawassa, Ethiopia, 2024.

**Name of the investigator;** Bitsit Demeke(BSc in Public health)

**Name of the organization;** Hawassa University, College of health science and medicine, school of public health.

**Introduction;** - This information sheet has been prepared for the Administrative Offices of Selected Public hospitals of Hawassa, Ethiopia. The purpose of this form is to clarify the goal of the research, data collection procedures, and permission to conduct the research.

**Procedure;** - To achieve the research goal, the information necessary for the research was taken from the medical records of admitted pediatric patients.

**Risk or Discomfort;** - The study was conducted by taking into account appropriate information from medical records and does not harm patients. No name or other identifying information was included in the questionnaire and all information was obtained from patient records and was kept strictly confidential. The information retrieved was only be used for study purposes.

**Benefit;** the research has no direct benefit to anyone whose medical record was included in this research. But the indirect benefit of the research to the participant and other program customers is clear. When program planners create predicted plans, clients in the program have the benefit of receiving appropriate care and treatment services. Generally, research has excellent direct benefits for healthcare planners and managers.

**Confidentiality;**- To ensure confidentiality, the data on the chart was collected without the names of the patients, and the information collected from this research project was kept confidential and kept in a selected room. In addition, it wasnot be exposed to anyone except the main investigator.

**Person to contact;** Bitsit Demeke(BSc in public health), Hawassa university, College of health science and medicine, School of public health.

Cell phone; +251916622659 E-mails; [enujcs@gmail.com](mailto:enujcs@gmail.com)

## 1.2 Data collection tool

Structured data extraction was designed based on the study objectives and the checklist was also include Socio-demographic characteristics of the neonate and the mother, Obstetric and Gynecological-related factors, maternal medical-related factors and Neonatal Medical -related factors of RDS neonates admitted to NICU at public hospitals of Hawassa, Ethiopia.

**Table 9; Data abstraction checklist to assess the incidence and predictors of mortality among neonates with respiratory distress syndrome admitted to neonatal intensive care units of public hospitals in Hawassa, Ethiopia, 2024.**

### Part 1: Socio-demographic characteristics of both the neonate and the mother

| Serial No | Questions                       | Choice of answer     |
|-----------|---------------------------------|----------------------|
|           | <b>Question for the mother</b>  |                      |
| 101       | Age                             | _____ Years.         |
| 102       | Place of residence              | 1. Urban<br>2. Rural |
|           | <b>Question for the neonate</b> |                      |
|           | Identification no (MRN)         | _____                |
| 103       | Sex                             | 1. 1. Male           |

|   |   |               |  |
|---|---|---------------|--|
|   |   |               | 2. 2. Female   |
| 104   | Age in day  |               | _____ days.  |
| 105   | Birth weight in gram                                    |               | _____ grams.   |
| 106   | Gestational age at birth in a week                      |               | _____ weeks.   |
| 107   | Date of admission                                       |               | _____ days   |
| 108   | Date of discharge                                       |               | _____ days   |
| 109   | Patient status  |               | 1. Died<br>2. Alive<br>3. Referred<br>4. Left against medical advice |
| 110   | Length of hospital stay                                 |               | _____  |
| <b>Part 2: Obstetric and Gynecological related factor</b> |   |               |  |
| 201   | Number of gravidities                                   |               | _____  |
| 202   | Number of parity  |               | _____  |
| 203   | Does the mother had ANC follow up                       |               | 1. Yes<br>2. No  |
| 204   | Has she been diagnosis for obstetrics And gynecological | 1.yes<br>2.No | If 'no' go to Q# 206   |

|   |   |   |                      |
|---|---|---|----------------------|
|   | problem?  |   |                      |
| 205   | Which among the following do you have Diagnosed?                            | <ol style="list-style-type: none"> <li>1.PROM</li> <li>2.Preeclampsia</li> <li>3. Abruption placenta</li> <li>4.placenta Previa</li> <li>5. chorioamnionitis</li> </ol> |                      |
| 206   | What was her Current mode of delivery?                                      | <ol style="list-style-type: none"> <li>1.Spontaneous vaginal Delivery</li> <li>2.Caesarian sections</li> </ol>  |                      |
| 207   | Place of delivery   | <ol style="list-style-type: none"> <li>1. Health institution</li> <li>2. Home</li> </ol>  |                      |
| 208   | Was the current pregnancy multiple (twin)?                                  | <ol style="list-style-type: none"> <li>1.Yes</li> <li>2. No</li> </ol>  |                      |
| 209   | Does the neonates breastfeed?   | <ol style="list-style-type: none"> <li>1. yes</li> <li>2. No</li> </ol>   |                      |
| <b>Part 3: Maternal medical related factors</b> |   |   |                      |
| 301   | Is she suffering from any medical conditions?                               | <ol style="list-style-type: none"> <li>1.Yes</li> <li>2.No</li> </ol>   | If 'no' go to Q# 401 |
| 302   | If the answer yes for question # 301, Which among the following do you have | <ol style="list-style-type: none"> <li>1.DM</li> <li>2.HTN</li> <li>3.HIV/AIDS</li> </ol>   |                      |

|   |  |               |                      |
|---|--|---------------|----------------------|
|   | Diagnosed?   |               |                      |
| <b>Part 4: Medical Neonatal related factors</b> |  |               |                      |
| 401   | Had the neonate diagnosed with any Other medical conditions? | 1.yes<br>2.No | If 'no' go to Q# 408 |
| 402   | Does the Neonates have Perinatal Asphyxia                    | 1.yes<br>2.No |                      |
| 403   | Does the neonate have Sepsis?                                | 1.yes<br>2.No |                      |
| 404   | Does the neonate have jaundice                               | 1.yes<br>2.No |                      |
| 407   | Does the neonate have hypoglycemia                           | 1.yes<br>2.No |                      |
| 408   | Does the neonate have MAS                                    | 1.Yes<br>2.No |                      |
| 409   | Temperature at admission                                     | _____         |                      |

**Name of data collector** \_\_\_\_\_ **signature** \_\_\_\_\_ **Date** \_\_\_\_\_.