2022-09-29

Magnitude of Respiratory Distress Syndrome Related Death and Associated Factors Among Pre Term Neonates Admitted at Tibebe Ghion Specialized Hospital, Bahirdar, Amhara National Regional State, North West Ethiopia

Kidane, Meheret

BAHIR DAR UNIVERSITY, COLLEGE OF MEDICINE AND HEALTH SCIENCES, SCHOOL OF MEDICINE, DEPARTMENT OF Pediatrics and Child Health

Magnitude of Respiratory Distress Syndrome Related Death and Associated Factors Among Pre Term Neonates Admitted at Tibebe Ghion Specialized Hospital, Bahirdar, Amhara National Regional State, North West Ethiopia

By

Dr. Kidane Meheret (Pediatrics Resident, Md)

SEPTEMBER 2022

BAHIRDAR, ETHIOPIA

BAHIR DAR UNIVERSITY, COLLEGE OF MEDICINE AND HEALTH SCIENCES, SCHOOL OF MEDICINE, DEPARTMENT OF PEDIATRICS AND CHILD HEALTH

MAGNITUDE OF RESPIRATORY DISTRESS SYNDROME RELATED DEATH AND ASSOCIATED FACTORS AMONG PRE TERM NEONATES ADMITTED AT TIBEBE GHION SPECIALIZED HOSPITAL, BAHIRDAR, AMHARA NATIONAL REGIONAL STATE, NORTH WEST ETHIOPIA

A RESEARCH THESIS TO BE SUBMITTED TO BAHIR DAR

Acknowledgement

BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DEPARTMENT OF PEDIATRICS AND CHILD HEALTH

I herewith certify that I have supervised, read, and evaluated this thesis titled "**Magnitude of Respiratory Distress Syndrome-Related Death and Associated Factors Among Pre-Term Neonates Admitted at Tibebeghion Specialized Hospital, Bahirdar, Amhara National Regional State, North West Ethiopia**" by Kidane Mihret Desta, prepared under my guidance. I recommend the thesis for final submission.

Approved by

Dr. Workie Shita		09/03/15
Advisor's name	Signature	Date
Mr.Gizachew Worku		09/03/15
Advisor's name	Signature	Date
Dr.Senay Zerihun		09/03/15
Department Head	Signature	Date

Acknowledgment

First of all, I would like to thank and appreciate my advisors Dr. Workie Shita and Mr. Gizachew Worku for their unlimited assistance in every aspect of the research starting from the selection of the topic and in other steps of the research process. I would also like to thank Bahirdar University College of medicine and health science, Department of pediatrics and child health providing such an opportunity to do health related research. I also like to thank pediatrics residents and the staff at Tibebe Ghion Comprehensive Specialized Hospital for their commitment to supporting my academic endeavors.

ABSTRACT

BACK GROUND

Respiratory distress syndrome, formerly known as hyaline membrane disease, is a common problem in preterm infants. This disorder is caused primarily by deficiency of pulmonary surfactant in an immature lung. Characteristically, tachypnea, prominent (often audible) expiratory grunting, intercostal and subcostal retractions, nasal flaring, and cyanosis are noted. Respiratory distress syndrome is a major cause of morbidity and mortality in preterm infants.

OBJECTIVES

To assess magnitude of respiratory distress related death and associated factors of respiratory distress syndrome among pre term neonates admitted at Tibebe ghion specialized hospital North West Ethiopia from January to August 2022.

METHODS

A hospital-based prospective followup study was conducted among preterm newborns admitted to Tibebe Ghion comprehensive specialized hospital with the diagnosis of respiratory distress syndrome from January 1, to August 30, 2022. The collected data was coded and checked for completeness, and entered into SPSS version 25.0 for analysis. Descriptive statistics like frequency, mean, and median were used to describe the data. A binary logistic regression method was fitted to identify associated factors. The odds ratio, with a 95% confidence interval, was estimated to determine the strength of association. Variables with Odds ratio having p value <0.05 in multivariable analysis were considered to be as an independent associated factor for the outcome of respiratory distress syndrome.

RESULT

In the current study, about (42.6%) of neonates were died due to preterm respiratory distress syndrome within 96 hours of age after delivery. Preterm neonates delivered to preclamptic mothers and those from Preterm premature rupture of membrane mothers were the associated

factors for respiratory distress related death with (AOR = 0.488; 95% CI: 0.256, 0.929) and (AOR=3.54; 95% CI:1.167, 10.739).

CONCLUSION AND RECOMMENDATION

From the present study it can be concluded that the death rate of preterm neonatal respiratory distress syndrome was high. Preterm neonate born to preeclamptic mothers and preterm premature rupture of membrane mothers were associated factors that decrease and increase respiratory distress syndrome related death respectively. To decrease the death related to preterm neonatal respiratory distress syndrome, the hospital where the study was conducted should give emphasis on treatment strategies of respiratory distress syndrome, including antenatal corticosteroids, surfactants, and advanced respiratory care of the neonate.

Keywords: Respiratory Distress Syndrome, preterm, neonatal mortality, associated factors Bahirdar.

Table of Contents **Pages**

Abbreviations

BPD	Broncho Pulmonary Dysplasia
CS	Cesarean Section
DM	Diabetes Mellitus
GA	Gestational Age
HMD	Hyaline Membrane Disease
MAS	Meconium Aspiration syndrome
NICU	Neonatal Intensive Care Unit
NRDS	Neonatal Respiratory Syndrome
PROM	Premature Rupture of Membrane
RDS	Respiratory Distress Syndrome
SD	Standard Deviation
SVD	Spontaneous Vaginal Delivery
TTN	Transient Tachypenia of the New born

List of Tables

List of Figures

1. INTRODUCTION

1.1. Background of the study

Respiratory distress syndrome (RDS), formerly known as hyaline membrane disease, is a common problem in preterm infants. This disorder is caused primarily by deficiency of pulmonary surfactant in an immature lung [1].

It is essential to review fetal lung development and surfactant production to understand the etiology of RDS. The normal process of fetal lung development occurs in stages, known as embryonic, pseudo glandular, canalicular, saccular, and alveolar stages [2].

During the embryonic period, the lung bud first appears at 26 days as a ventral protrusion of the fetal esophagus and divides throughout the surrounding mesenchyme, initially forming the main stem bronchi by 37 days. The main stem bronchi branch further leading to the development of sub-segmental bronchi by 48 days. Pulmonary vasculature develops along with the developing lung and the pulmonary artery forms as a branch of the sixth aortic arch by 37 days. The pseudo glandular stage starts around the fifth week of gestation and ends at the 16th week, and is the stage at which neuro epithelial cells, cartilage, ciliated cells, goblet cells, and basal cells develop in the proximal pulmonary epithelium and the airways branch 15 to 20 times by the 18th week of gestation[3].The canalicular stage, beginning the 16th week and ending around the 25^{th} week, marks the beginning of the development of the pulmonary acinus, the formation of a blood-air barrier, and surfactant production via type 2 cells, culminating in a lung potentially viable for gas exchange. At 20 weeks, lamellar bodies begin to form in the cytoplasm of the glycogen-laden cuboidal epithelium of the bronchioles, and these cells differentiate into type 2 cells, which are capable of producing surfactant. During the saccular stage, from around the 24^{th} week to the 32^{nd} week of gestation, the terminal saccule forms, developing the respiratory bronchioles, allows for gas exchange. It is at this stage that the premature infant is potentially viable in extra uterine life.

At 32 weeks, the alveolar stage begins, and alveoli start to form as the respiratory bronchioles develop septations, increasing the surface area for gas exchange [4].

Signs of RDS usually appear within minutes of birth, although they may not be recognized for several hours in larger premature infants, until rapid, shallow respirations become more obvious. Some patients require resuscitation at birth because of intrapartum asphyxia or initial severe respiratory distress (especially with birth weight <1,000 g).Characteristically, tachypnea, prominent (often audible) expiratory grunting, intercostal and subcostal retractions, nasal flaring, and cyanosis are noted. RDS is a major cause of morbidity and mortality in preterm infants [5].

Neonatal respiratory distress syndrome (NRDS) is a breathing disorder arising at, or shortly after birth (<24 hours); it increases in severity during the first 48 to 72 hours of life [6]. Though full term new-borns with a gestational age [GA] between 37 and 42 weeks can be affected, approximately four out of five cases occur in those born prematurely (<37 weeks) [7].

Severity and incidence of NRDS are inversely related to GA with 92% of neonates born at 24–25 weeks affected, 88% at 26–27 weeks, 76% at 28–29 weeks and 57% at 30–31 weeks [8].

Treatment modalities, including antenatal corticosteroids, surfactants, and advanced respiratory care of the neonate, have improved the outcomes for patients affected by RDS, it continues to be a leading cause of morbidity and mortality in the preterm infant[9].

1.2 Statement of the problem

RDS occurs in about 24,000 infants born in the United States annually. It is also the most common complication of prematurity leading to significant morbidity in late preterm neonates and even mortality in very low birth weight infants. The most important risk factors are prematurity and low birth weight.The more premature the baby, the higher the risk and the more severe the RDS. Other risk factors include white race, male gender, late preterm delivery, maternal diabetes,white race, having a sibling born with RDS ,hypothermia, infection, perinatal hypoxia and ischemia, and delivery in the absence of labor [10].

The incidence of RDS increases with decreasing gestational age at birth. In one study of babies born between 2003 and 2007 at various National Institute of Child Health and Human

Development (NICHD) Neonatal Research Network centers, 98% of babies born at 24 weeks had RDS, while at 34 weeks, the incidence was 5%, and at 37 weeks was less than 1% [11].

In countries with poverty, mortality rates run roughly 10 times higher than in wealthier countries. But even in developed countries, the mortality rate reaches as high as 60% [12].In the U.S., respiratory distress syndrome is among the most common causes of death in the first month of life[13].

Between 2003 and 2013, the number of deaths due to NRDS dropped from 20.5 per 100,000 live births to 13.4. NRDS accounted for 2.3% of all infant deaths in the U.S. in2013 [14].

NRDS is also a threat for different reasons. About 1.9% of premature babies who had NRDS later developed cerebral palsy, compared with 0.5% of premature babies who did not have NRDS [15].In another study it was reported that premature infants had a higher risk of childhood epilepsy[16]. Moreover, the treatments for NRDS have risks of their own. Mechanical ventilation, for instance, which helps keep infants alive, also puts them at risk for broncho pulmonary dysplasia (BPD). An estimated 5,000 to 10,000 new borns develop BPD or other form of chronic lung disease [14, 17].

Prognosis of infants managed with antenatal steroids, respiratory support, and exogenous surfactant therapy is excellent. Mortality is less than 10%, with some studies showing survival rates of up to 98% with advanced care. Increased survival in developed countries is in stark comparison to babies who received no intervention in low-income countries, where the mortality rate for premature infants with RDS is significantly higher, at times close to 100%. With adequate ventilatory support alone, surfactant production eventually begins, and once surfactant production begins along with the onset of diuresis, RDS improves within 4 or 5 days. Untreated disease leading to severe hypoxemia in the first days of life can result in multiple organ failure and death [18].

Though RDS is common neonatal problem especially in preterm newborns there are limited studies. An institution-based retrospective follow-up study was conducted with 571 neonates from January 2013 to March 2018 on incidence of respiratory distress and its predictors among neonates admitted to the neonatal intensive care unit, Black Lion Specialized Hospital, Addis Ababa, Ethiopia. The result indicated that the proportion of neonates with respiratory distress and incidence rate were, respectively 42.9%, and 8.1/100. Significant predictors of respiratory distress

in neonates included being male, born via caesarean section, home delivery, maternal diabetes mellitus, preterm birth, and having an Apgar score of less than 7[19].

One retrospective follow up study done among 535 preterm neonates admitted at neonatal intensive care unit from January 1, 2014 to December 30, 2017 on the burden of hyaline membrane disease, mortality and its determinant factors among preterm neonates admitted at Debre Tabor General Hospital, North Central Ethiopia. The result revealed that the proportion of hyaline membrane disease was 40% of which 49.5% died. Preterm neonate born with Gestational age of less than 34 weeks of age, 5th minute Apgar score less than 7, and new born with birth weight of less than 1500 gram were predictors of hyaline membrane disease.Studies conducted worldwide and in Ethiopia clearly showed thatHyaline Membrane Disease (HMD) is a leading cause of morbidity and mortality in preterm new born babies[20].

As far as my personal information is concerned there is no similar study conducted in Bahir Dar city. Moreover, many of the studies conducted in Ethiopia were retrospective type which depends on secondary data. Therefore, the present study was focused on investigating magnitude of RDS related death and associated factors of neonatal RDS admitted at Tibebe Ghion Specialized Hospital using institutional based prospective follow up study type.Preterm neonatal RDS is the leading cause of death in preterm neonates especially in developing countries might be lacking of adequate treatment strategies. Most neonates end up in death and some others develop both physical and neurologic impacts. Despite this impact, magnitude of RDS related death and possible associated factors were not studied much. In Ethiopia there are only limited studies about preterm neonatal RDS and factors associated with it. So this paper will help much to predict and prevent the problem.

1.3. Objectives of the study

1.3.1 General objective

To assess magnitude of RDS related death and associated factors of respiratory distress syndrome among preterm neonates admitted at Tibebe ghion specialized hospital, 2022.

1.3.2 Specific objectives

1. To determine magnitude of respiratory distress syndrome related death among preterm neonates admitted at Tibebe Ghion specialized hospital, 2022.
2. To identify factors associated with respiratory distress syndrome related death among preterm neonates admitted at Tibebe Ghion specialized hospital, 2022.

1.4 Justification of the study

In daily clinical practice, it is common to see deaths related to RDS in preterm neonates, so assessing the magnitude of RDS-related deaths and its associated factors and working on possible intervention has paramount importance.

The findings of this study could be helpful in planning to reduce RDS related deaths, taking action on factors that increase the death rate, and promoting the factors that decrease the death rate for hospital management and health professionals.

It will help the researchers as a base line study and to identify the gaps for future study.

2. LITERATURE REVIEW

2.1 Magnitude of respiratory distress syndrome related death among preterm neonates

Based on study done on respiratory distress in newborn which was conducted at AVBRH, Wardha, Maharashtra, India to study morbidity and mortality of respiratory distress in neonates who was admitted in NICU. Out of 400 neonates admitted with respiratory distress, 314 (78.5%) neonates were discharged and 86 (21.5%) were dead. The out born death rate (21.9%) was marginally more as compared to inborn (21.35%) neonates with respiratory distress. RDS was the most common cause of deaths in neonates with respiratory distress admitted in our NICU followed by birth asphyxia [21].

In another cross sectional study on neonatal respiratory distress which was conducted from March 2013 to December 2014 in Nepal Medical College and Teaching Hospital. Overall, 87.2% of neonates survived and 12.8% were died. Most common causes of death were septic shock, respiratory failure and sudden cardiopulmonary arrest [22].

A cross-sectional study carried out in Saudi Arabia, Taif city, King Abdulaziz Hospital from January to June 2016 (6 months period, Percentage of dead cases was 2.4% [23].

A prospective, consecutive, cross-sectional and descriptive study done on determinants of outcome in new-borns with respiratory distress in Osogbo, Nigeria, 40.2% of preterms died mainly from hyaline membrane disease [24].

Based on a study done in Neonatal mortality and associated factors in the specialized neonatal care unit Asmara, Eritrea A retrospective cross-sectional study was carried out to investigate neonatal mortality and associated factors among neonates admitted to the SNCU, Asmara, Eritrea. RDS accounted for the highest (n = 38, 48.1%) cause of mortality followed by sepsis (n = 15, 19%) and congenital malformation (n = 8, 10.1%) [25].

A prospective, cross-sectional, observational study in five hospitals in Ethiopia, Were done on preterm infants born in the study hospitals at younger than 37 gestational weeks, between July 1,

2016, to May 31, 2018, 4919 preterm infants were enrolled in the study and 3852 were admitted to neonatal intensive care units. By 28 days of post-natal age, 1109 (29%) of those admitted to the neonatal intensive care unit died. Complete diagnostic autopsy was done in 441 (40%) and minimally invasive tissue sampling in 126 (11%) of the neonatal intensive care unit deaths. The main primary causes of death in the 1109 infants were established as respiratory distress syndrome (502 [45%]); sepsis, pneumonia and meningitis (combined as neonatal infections; 331 [30%]), and asphyxia (151 [14%]). Hypothermia was the most common contributory cause of preterm mortality (770 [69%]). The highest mortality occurred in infants younger than 28 weeks of gestation (89 [86%] of 104), followed by infants aged 28–31 weeks (512 [54%] of 952), 32–34 weeks (349 [18%] of 1975), and 35–36 weeks (159 [8%] of 1888)[26].

A hospital-based prospective descriptive analytical cross-sectional study was conducted in 2020 at Gondar university hospital on Determinant factors of immediate outcomes of Neonatal Respiratory Distress Syndrome in Gondar university hospital, Ethiopia Gondar, Ethiopia, a total of 162 neonates were enrolled; the result showed that there were 87 (53.7%) males and 75(46.3%) females. Of these 106 (65.4%) were discharged with Improvement, 4 (2.5%) discharged with complications, and 52 (32.0%) die[27].

An institution-based retrospective follow-up study on the burden of hyaline membrane disease, mortality and its determinant factors among preterm neonates admitted at Debre Tabor General Hospital among preterm neonates admitted with the diagnosis of RDS 49.5% (106 per 214) were died [20].

2.2 .Associated factors of respiratory distress syndrome among preterm neonates

A multicenter Italian survey, on risk factors for respiratory distress syndrome in the newborn show that, risk factors have been evaluated using data from a large survey conducted between 1980 and 1989 in selected periods in eleven perinatal units placed in five Italian regions. A total of 1624 live born infants consecutively delivered at the collaborating centers, at delivery 26–37 weeks gestational age and without clinically evident congenital anomalies were included in the survey. The risk of RDS markedly increased with decreasing birth weight: compared to babies weighing more than 2500 g at birth the RR estimates were respectively 1.4, 4.5, 8.8 and 39.3 in

those weighing <2000-2500 g, × 1500–2000 g, × 1000–1500 g and 1000 g or less. Likewise, compared to babies born between the 35th and the 37th week of gestation, the RR of RDS was 3.3 and 21.5 in those born between the 31st-34th or before the 31st week of gestation. Multiple pregnancy, gestational or chronic diabetes, pregnancy-induced or chronic hypertension and premature rupture of the membranes were not related to the risk of RDS. Compared to vaginal births, babies delivered by intrapartum cesarean section had an increased risk of RDS (RR 1.8, 95% CI from 1.2 to 2.7), but babies delivered by elective cesarean section were at not significantly decreased risk (RR 0.5, 95% CI 0.3 to 1.1). Low Apgar score at 1st and 5th minute (less than 7) was associated with an increased risk of RDS, the RR estimates being, compared to babies with Apgar score equal to 7 or more, 7.9 at 1 minute of age and 8.4 for 5 minutes of age [28].

A Population Based Study on preeclampsia and the risk of broncho pulmonary dysplasia in VLBW infants, a retrospective cohort study assessing the association between preeclampsia and the risk of developing BPD in very-low-birth-weight (VLBW) infants registered in the Premature Baby Foundation of Taiwan from 1997 through 2006, reveal that, infants with maternal preeclampsia had a higher gestational age, higher incidence of cesarean section and being small for their gestational age, lower incidence of respiratory distress syndrome, patent ductus arteriosus, and sepsis. BPD occurred significantly less frequently in the maternal preeclampsia group (24.1% vs. 36.7%; adjusted odds ratio: 0.78; 95% confidence interval, 0.62–0.98). Subgroup analysis showed that the association between preeclampsia and BPD was significant only in those VLBW infants with a gestational age between 31–34 weeks[29].

A study done in India on the influence of maternal risk factors on pulmonary maturity in preterm newborns was a prospective cohort study of 142 preterm babies who were selected randomly and were assessed for the development of RDS. The result showed that Prolonged rupture of membranes, higher socio-economic class, male gender, intrauterine growth restriction were risk factors for RDS, whereas pregnancy induced hypertension, maternal anemia, lower socio-economic class, female gender, appropriate for gestational age (AGA) babies, and antenatal steroid causes accelerated pulmonary surfactant maturity in preterm newborn [30].

Study done on respiratory distress in newborn which was conducted at AVBRH, Wardha, Maharashtra, India to study morbidity and mortality of respiratory distress in neonates admitted in NICU. Males were affected more than females M:F ratio was 1.36:1 many of them were delivered by CS. 122 (43.72%) inborn and 38 (36.19%) out born neonates had diagnosis of TTN who presented with respiratory distress in NICU whereas 74 (25.1%) inborn 33 (31.4%) and out born neonates had RDS. %) [21].

Across sectional study on neonatal respiratory distress was conducted from March 2013 to December 2014 in Nepal Medical College and Teaching Hospital. It was found that 59.6% vaginally delivered babies and 39.4% CS babies had respiratory distress. The commonest cause of respiratory distress in this study was Meconium Aspiration Syndrome (MAS) in 23 (21.1%) patients. In HMD, 80.0% of cases were of <32 weeks with mean birth weight of 1240 grams ±140 gm. In most of the cases, antenatal steroid was not given as they presented late in the hospital. Maternal risk factors like PROM, maternal fever, foul smelling liquor, hypertension, and diabetes mellitus were present in HMD. HMD (p=.02)were observed significantly more in a caesarean section deliveries [22].

A cross-sectional study carried out in Saudi Arabia, Taif city, King Abdulaziz Hospital from January to June 2016 (6 months period). About 56.7% don't have ANC follow up,4.4% of mothers were diabetic, 3.3% of mothers had hypertension, 20.4% had PROM, 3.3% had history of Abruptio placenta, 4.4% had history of placenta previa , 35.6% of mothers delivered by normal labor, 63.3% delivered by cesarean section. 47.3% of babies received antenatal steroids, 32% were treated by antibiotics. 60.4% of newborn were put on a ventilator, 61.8% were treated by surfactant therapy. All the newborns were 1 day age at the time of the research, 57.1% of newborn were male gender, 4.4% of babies were extreme preterm, 86.5% were preterm, 4.4% were late preterm and 4.7% were full term. 53.5% of patients had Apgar score of > 7 while 46.5% had Apgar score 1< 7. While 92.5% had Apgar score 5 > 7 and 7.6% had Apgar score 5 < 7 [23].

Study done on Respiratory Distress and Its outcome among neonates admitted to neonatal Intensive Care Unit of Assiut University Children Hospital, Egypt, Majority of neonates were from rural, single born and preterm (65.1%, 75.6% &68.8% respectively). On the other hand only 26.5% of neonates had normal birth weight. Moreover, 87.9 % of neonates were delivered at hospital and 43.7% of them were delivered by emergency C.S. Majority of cases of hyaline

membrane disease were preterm and low Birth weight (96.2% & 93.7% % respectively), with statistical significant difference. Majority of hyaline membrane diseased neonates who treated by surfactant or CPAP were recovered (75.8% & 66.7% respectively) with significant statistically difference. The only significant independent factors associated with mortalities of neonates of respiratory distress were residence, causes of RD, birth weight and place of delivery. Rural, low birth weight and home delivery neonates were risky of mortalities than others [31].

A prospective, consecutive, cross-sectional, and descriptive study was done on the determinants of outcome in newborns with respiratory distress in Osogbo; Nigeria.Respiratory distress was commoner at the extremes of gestational ages; below 34 weeks and above 41 weeks. Respiratory distress was significantly commoner among the preterms than term new-borns. Respiratory distress was commoner at the extremes of birth weight; below 1.50 kg and above 4.01 kg. Comparing birth weight <2.50 kg to ≥2.50 kg, significant higher proportion of low birth weight babies had respiratory distress. Commoner causes of respiratory distress among the preterms were respiratory distress syndrome, septicaemia, anaemia, congenital anomalies of respiratory tract and cardiovascular causes. Though higher proportion of males, babies delivered by spontaneous vertex delivery (SVD), low birth weight and preterms died, this was not statistically significant level ($p>0.1$). However, significantly higher proportion of outborns died [24].

An institution-based retrospective follow-up study on incidence of respiratory distress and its predictors among neonates admitted to the neonatal intensive care unit, Black Lion Specialized Hospital Findings, in multivariable analysis, being male, neonates born via caesarean section, home delivery, maternal DM, preterm birth, neonatal sepsis, PROM, and an Apgar score of less than 7 were the factors which continued as statistically significant predictors of RD. The hazard ratio for RD in male neonates was 2.4 times higher than their female counter parts. The study also showed that the hazard ratio for RD among neonates born via caesarean section had nearly two times the risk compared to neonates born vaginally. The risk of RD in neonates born at home was almost three times higher than those delivered at a health institution. This result also indicated that neonates delivered from mothers who had DM had a 2.3 times higher risk of RD as compared with their non-DM counterparts. Moreover, as the gestational age increased by one week, the rate of RD decreased by 10%. The risk of RD also increased three fold for a neonate who had an Apgar score of less than 7 as compared with one having an Apgar score greater than or equal to 7.

Additionally, neonatal sepsis increases the risk of RD by 60%. The last predictor for RD was to be born from mothers experiencing PROM, with neonates having a 1.1,1.1(1.8,1.5) times higher risk of RD than their counterparts not experiencing PROM [19].

A hospital-based prospective descriptive analytical cross-sectional study was conducted on 2020 at Gondar university hospital, on Determinant factors of immediate outcomes of Neonatal Respiratory Distress Syndrome in preterm neonates in Gondar, Ethiopia a total of 162 neonates were enrolled; the result showed that, those admitted below 6 hours of age was 6.14 times higher than those admitted aged 6 hours and above. Babies born to primiparous mothers were more than twice as likely to die as babies born to multiparous mothers. Neonates who were delivered in other facilities had 3.78 times increased odds of mortality[27].

An institution-based retrospective follow-up study on the burden of hyaline membrane disease, mortality and its determinant factors among preterm neonates admitted at Debre Tabor General Hospital Predictors of RDS done by both bi-variable and multivariable logistic regression were undertaken. In binary logistic regression gestational age, number of antenatal care visit, parity, birth order, birth weight, maternal complications, APH, 5th minute Apgar score and PPROM were significantly associated with HMD. Whereas, in multivariable analysis; Gestational age, 5th minute Apgar score and birth weight were statistically significant. In this study, new born with less than 34 weeks of gestation were 2.64 times more likely to develop hyaline membrane disease than neonates born greater than or equal to 34 weeks of gestation. Similarly preterm neonate born with less than 7 APGAR score of 5th minute were 2.2 times more likely to have hyaline membrane disease in contrast with new-borns with APGAR score of greater than seven. Those preterm neonates born with birth weight of less than 1500 gram were 2.4 times more likely to have hyaline membrane disease than new-born with birth weight of greater than 1500gram [20].

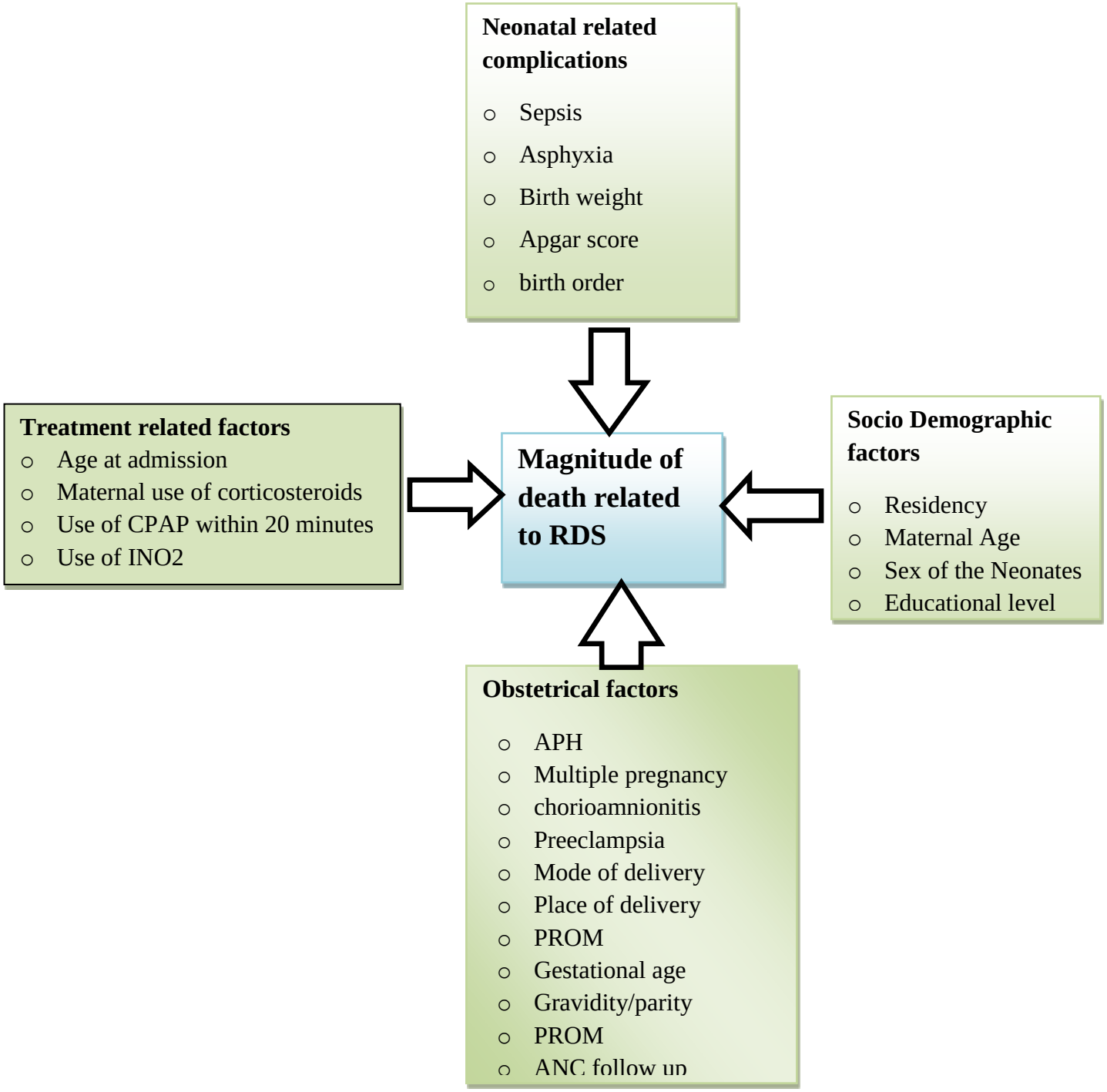

Figure 1: Conceptual Frame Work of magnitude of death related to RDS and associated factors at Tibebe ghion comprehensive specialized hospital North West Ethiopia.

3. METHODS AND MATERIALS

3.1 Study Design and Period

Hospital based prospective follow up study was conducted among preterm newborns admitted to Tibebe Ghion comprehensive specialized hospital with the diagnosis of RDS from January 1, to August 30,2022.

3.2 Study Area

The study was conducted in Tibebe ghion comprehensive and specialized hospital, a tertiary teaching hospital and one of the health institutions in Ethiopia providing different services.

It is located in the northwest part of Ethiopia 560 KM away from Addis Ababa in Amhara Regional State. Tibebe Ghion comprehensive specialized hospital has four major departments which are internal medicine, surgery, obstetrics and gynecology and pediatrics and child health.

It has also minor departments including ophthalmology, ear nose throat (ENT), Psychiatry, anesthesiology, dermatology and radiology.

The Neonatal ICU ward in Tibebe Ghion has separate compartments for preterm and term newborns. It has also separate room for KMC and maternal side as well. The ward is equipped with phototherapy machines and incubators too. There are around 200 cases of admission per month and on average 8 cases per day admission and around 100 preterm neonates per month among them around 38 were with the diagnosis of RDS. The commonest cases admitted are preterm newborns with their complications (HMD, Sepsis, and jaundice) and term newborns with asphyxia with encephalopathy, MAS, Hyper bilirubinemia, sepsis and anemia due to different reasons. The care is being provided with structured services involving Interns, Residents and senior physicians along with nursing staffs.

3.3 Source and Study Population

3.3.1 Source population

All preterm newborns with the diagnosis of RDS admitted to Tibebe Ghion comprehensive and specialized hospital to the Neonatal intensive care unit ward.

3.3.2 Study Population

All preterm newborns with the diagnosis of RDS admitted to Tibebe Ghion comprehensive specialized hospital Neonatal Intensive Care Unit from January 1, to August 30, 2022.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

- ✓ All newborns whose GA is ≥28 weeks to≤ 37 weeks and postnatal age ≤ 96 hours with the diagnosis of RDS admitted to Tibebeghion comprehensive specialized hospital during the study period.

3.5 Sample size and Sampling technique

3.5.1 Sample size determination

The required minimum sample size is calculated based on the two specific objectives of the study. For the first study a single population proportion formula is used. The proportion (40%) is taken from a study conducted in Debre Tabor General Hospital [20]. Based on this, the sample size is determined based on the following single population proportion formula as;

$N= (Z\alpha /2)^2*P (1-P)/d^2$

$n= (1.96)^2*0.4(1-0.4)/ (0.05)^2=369$

since the source population is < 10,000 I used final sample size correction:

$Nf= ni/ (1+ni/N)$

$Nf=369/ (1+369/1100)= 275$

After adding 5% non-respondents, the final sample size will be 289 newborns.

Where; n= The desired sample

Ni=the initial sample

NF=final sample size

N=number of newborns admitted during the study period

P=the proportion of preterm neonatal RDS is 40% taken from the study done at Debretabor general hospital.

Zα/2=critical value at 95% confidence level of certainty (1.96)

d=the margin of error between the sample and the population =5%

The sample size for the second objective is calculated based on factors and assumptions of 95% confidence level, 80% power and 1:1 ratio of unexposed to exposed using Epi Info 7 software, as shown in the table below.

Table 1: Sample size based on factors associated with outcomes of respiratory distress

Factor	% of outcome in unexposed	AOR	Sample size
Gestational age (<34wk)	14.2	2.6	238
5th minute APGAR score (<7)	27.4	2.2	246
Birth weight (<1500g)	21.6	2.4	222

Therefore, the largest sample size is obtained and was considered from the first objective.

3.5.2 Sampling technique

In the 8 months period of admissions, consecutive sampling technique was used to select the study participants. Since the flow of cases due to preterm RDS is low, around 38 cases per month, the data was collected using the consecutive sampling method until the sample size was fulfilled.

3.6 Study Variables

Dependent variable

RDS related death (yes, no)

Independent variables

Socio Demographic factors

- Residency
- Maternal Age
- Sex of the Neonates
- Level of education of the mother

Neonatal related complications

- Sepsis
- Asphyxia
- Birth weight
- Birth order
- Body temperature (hypothermia)

Obstetrical factors

- APH
- Multiple pregnancy
- chorioamnionitis
- Preeclampsia
- Mode of delivery
- Place of delivery
- Gestational age
- Parity
- PPROM
- ANC follow up

Treatment related factors

- Age at admission
- Maternal use of corticosteroids
- Use of continuous air way pressure within 20 minutes of delivery
- Use of Intra nasal oxygen

3.7 Operational Definition

RDS: A neonate between 28 weeks to 37 weeks of gestation who presented with tachypnea, grunting and respiratory distress and diagnosed by the physician with preterm RDS.

Neonate: An infant whose age is ≤ 28 days postnatally.

LBW: birth weight <2500 grams.

Maternal complication: was considered if mother had an obstetric hemorrhage, eclampsia and preeclampsia, premature rupture of membrane (PROM), emergency cesarean section, and retained.

RDS related death: A preterm neonate who died within 96 hours of delivery with the diagnosis of RDS after admission to the hospital.

3.8 Data collection instrument

Data was collected based on structured and pretested questionnaires during the time of admission and the outcomes of the neonates were seen and filled on the questionnaire after 96 hours of postnatal age. The questions on the questionnaire were developed from different authors who did similar research on this topic and from standard text books from the English version [1, 19, 20].

3.9 Data collection procedure

Selection and training of data collectors were given, and then data was collected by pediatric residents over an 8-month period. Since the flow of cases due to preterm RDS is low, around 38 cases per month, the data was collected using the consecutive sampling method until the sample size was fulfilled. The method of data collection was using the face-to-face interview method to find the primary data from the mothers, and the secondary data was taken from the patient chart.

3.10 Data quality Control

A pretest was done among 5% of cases in December, a month before the study period at the same hospital. Based on the pretest result, unclear questions in the questionnaire were corrected. The principal investigator was also supervising the data collection throughout the entire data collection period. Completeness of data was cross-checked by the principal investigator among randomly selected patients during data collection.

3.11 Data analysis

The collected data was coded and checked for completeness and entered to SPSS version 23.0 for analysis. Descriptive statistics like frequency, mean and median was used to describe the data. Binary logistic regression method was fitted to identify factors associated with preterm neonatal RDS among newborns admitted to Tibebe Ghion comprehensive and specialized hospital with p value less than 0.25.

Odds ratio with 95% confidence interval was estimated to determine the strength of association. Variables with Odds ratio having p value <0.05 in multivariable analysis was considered to be as an independent predictor of RDS.

4. ETHICAL CONSIDERATIONS

Ethical clearance was obtained from the ethical review committee of school of medicine, Bahir Dar University. Permission was obtained from the department of pediatrics and child health. During the data collection, the data collector explained clearly about the purpose of the research to

the participants' mother and participation was based on willingness and informed consents was taken.

5. RESULTS

5.1 Socio demographic characteristics of the mother and neonate

As shown in Table 2, the mean age with standard deviation (±SD) of mother was 28.26 (±5.26) years. About 90.3% of mothers were in the age group of 20–34 years. The majority (65.7%) of them were from the rural area. Regarding the educational status of mothers, 28.4 % of them were unable to read and write. Fifty six percent of neonates were male newborn with mean gestational age (±) of 30.82(±1.85) weeks.

Table 2: Socio demographic characteristics of the mother and neonate with its outcome who had preterm neonatal admission at Tibebe ghion comprehensive specialized hospital NICU, Northwest Ethiopia, from January 1 to August 30, 2022

Variables		**Outcome of the neonate**		
		Improved	**Died**	**Total**
Sex of the new born	Female	79(65.7%)	47(34.3%)	126(100%)
	Male	87(53.3%)	75(46.7%)	163(100%)
Age of the mother	<20	0(0%)	18(100%)	18(100%)
	20-34	157(60.1%)	104(39.9%)	261(100%)
	=>35	9(90%)	1(10%)	10(100%)
Residency of the mother	Urban	55(55.5%)	44(44.5%)	99(100%)
	Rural	111(58.4%)	79(41.6%)	190(100%)
Maternal level of education	Can't read & write	58(70.7%)	24(29.3%)	82(100%)
	Read & write	44(57.9%)	32(42.1%)	76(100%)
	Primary	24(45.2%)	29(54.8%)	53(100%)
	Secondary	13(36.1%)	23(63.9%)	36(100%)
	Above secondary	27(64.3%)	15(37.7%)	42(100%)

5.2 Obstetric related factors

As demonstrated in Table 3, about ninety eight percent of mothers had ante-natal care (ANC) follow-up. Around (56.4%) mothers were primiparous. Seventy five percent of preterm neonates were single births. Around (92.7%) of neonates were delivered at health facility. Seventy four percent neonates were delivered via SVD. None of the mothers had chorioamnionitis. About (28.4%) of mothers had preeclampsia and 12.5% of mothers had PPROM.

Table 3: Obstetric related factors of mother with its outcome who had preterm neonatal admission at Tibebe ghion comprehensive specialized hospital NICU, Northwest Ethiopia, from January 1 to August30, 2022

Variables		**Outcome of the neonate**		
		Improved	**Died**	**Total**
Gestational age	<34	154(55.6%)	123(44.4%)	277(100%)
	>=34-37	12(100%)	0(0%)	12(100%)
Place of delivery	Home	18(85.7%)	3(14.3%)	21(100%)
	Health facility	148(55.2%)	120(44.8%)	268(100%)
Mode of delivery	SVD	130(60.7%)	84(39.3%)	214(100%)
	CS	36(48%)	39(52%)	75(100%)
ANC follow up	Yes	160(56.5%)	123(43.5%)	283(100%)
	No	6(100%)	0(0%)	6(100%)
Chorioamnionitis	Yes	0(0%)	0(0%)	0(0)%)
	No	166(57.4%)	123(42.6%)	289(100%)
Preeclampsia	Yes	36(44%)	46(56%)	82(100%)
	No	130(62.8%)	77(37.2%)	207(100%)
Multiple pregnancy	Yes	34(47.2%)	38(52.8%)	72(100%)
	No	132(60.8%)	85(39.2%)	217(100%0
Number of newborns	Singleton	132(60.8%)	85(39.2%)	217(100%)
	twin	30(47.6%)	33(52.4%)	63(100%)
	Triplet and above	4(44.4%)	5(55.6%)	9(100%)
Parity	Primiparous	91(55.8%)	72(44.2%)	163(100%)
	Multiparous	75(59.5%)	51(40.5%)	126(100%)
PPROM	Yes	29(80.5%)	7(19.5%)	36(100%)
	No	137(54.1%)	116(45.9%)	253(100%)

5.3 Neonatal related factors

As depicted in Table 4, the majority (79.2%) of neonates weigh between 1000-1500 gm. Nearly four-fourth (79.9%) of neonates were appropriate for gestational age by anthropometric measurement. All neonates had diagnosed with sepsis. Around 4.0% of neonates were diagnosed with asphyxia. Eighty four percent of neonates were hypothermic up on temperature measurement.

Table 4: Neonatal related complications and its outcome of preterm neonates who had preterm neonatal admission at Tibebe ghion comprehensive specialized hospital NICU, Northwest Ethiopia, from January 1 to August 30, 2022

		Outcome of the neonate		
Variables		**Improved**	**Died**	**Total**
Neonatal sepsis	Yes	166(57.4%)	123(42.6%)	289(100%)
	No	0(0%)	0(0%)	0(0%)
Asphyxia	Yes	1(8.3%)	11(92.7%)	12(100%)
	No	165(59.6%)	112(40.4%)	277(100%)
Body temperature of the new born	Hypothermia	133(54.5%)	111(45.5%)	244(100%)
	Normal	33(78.6%)	12(21.4%)	42(100%)
Birth weight of the new born	Below 1000 gm.	2(11.1%)	16(88.9%)	18(100%)
	1000 to 1500 gm.	124(54.1%)	105(45.9%)	229(100%)
	above1500 gm.	40(95.2%)	2(4.8%)	42(100%)
Anthropometry measurement	SGA	25(43.1%)	33(56.9%)	58(100%)
	AGA	141(61%)	90(39%)	231(100%)

5.4 Treatment related factors and RDS related death

Around (91.6%) of neonates were admitted at the NICU after the age of 20 minutes. About 7.3% of neonates use CPAP within 20 minutes of delivery. Sixty seven percent of mothers did not take corticosteroid during pregnancy. Among 289 neonates admitted with the diagnosis of RDS (42.6%) neonates were died due to preterm RDS within 96 hours of age after delivery.

5.5 RDS related death and associated factors of preterm neonatal RDS

Both bi-variable and multivariable logistic regressions were undertaken. In binary logistic regression sex of the neonate, mode of delivery, anthropometry, maternal level of education, preeclampsia, multiple pregnancy, PPROM and body temperature of the neonate were significantly associated with preterm neonatal RDS related death. Whereas, in multivariable analysis; preeclampsia and PPROM were statistically significant.

As described in Table 5, preterm neonates born from preclamptic mother were 51 % less likely to die with RDS than those who were delivered from non preeclamptic mothers. (AOR = 0.488; 95% CI: 0.256, 0.929).Those neonates who were born to mothers having PPROM were 3.54 times more likely to die than those who were delivered from mothers who have no PPROM.(AOR=3.54;95% CI:1.167,10.739)

Table 5: Associated factors of RDS related death among preterm neonatal admission at Tibebe ghion comprehensive specialized hospital NICU, Northwest Ethiopia, from January 1 to August 30, 2022

Variables		RDS related death				
		No	Yes	COR	P value	AOR
Sex of the new born	Female	79	47	0.705(0.439,1.131)	0.209	
	Male	87	75	1		
Anthropometry	SGA	25	33			
	AGA	141	90	1		
Preeclampsia	Yes	36	46	2.159(1.283,3.626)	0.029	0.488(0.256,0.929)
	No	130	77	1		
Multiple pregnancy	Yes	34	38	1.736(1.014,2.969)	0.65	
	NO	132	85	1		
Maternal level of education	Can't read & write	58	24		0.111	
	Read & write	44	32		0.732	
	Primary	24	29	2.175(0.947,4.997)	0.407	
	Secondary	13	23	3.185(1.259,8.054)	0.085	
	Above secondary	27	15	1		
PPROM	Yes	29	7	0.285(0.120,0.675)	0.025	3.544(1.169,10.739)
	No	137	116	1		
Body temperature of the new born	Hypothermia	133	111	2.295(1.132,4.655)	0.359	
	Normal	33	12	1		

6. DISCUSSION

Respiratory distress syndrome (RDS) is a common problem in preterm infants. In this study, Among 289 preterm neonates admitted with the diagnosis of RDS (42.6%) of neonates were died due to preterm RDS within 96 hours of age after delivery and admission to hospital which is consistent with (95% CI 36.1 to 48.4%) the study done in Nigeria, 40.2% [24] , Eritrea 48.1% [25] ,multicenter prospective, cross-sectional, observational study in five hospitals in Ethiopia 45% [26] but lower than in Debretabor general hospital ,Ethiopia,49.5% [20], it might be due to the study done in Debretabor general hospital ,the neonates were followed until discharge which is beyond 96 hours and it might include deaths caused by other than RDS, but higher than study done in Nepal 12.8% [22], in India 21.5% [32] in Saudiarabia 2.4% [23], and in Gondar university hospital, Ethiopia 32% [27]. The significant differences in the outcome of the present study with previous studies with lower RDS values can be attributed with different reasons. The first could be, the current study include only preterm neonates. In addition, majority of preterm newborns in Saudiarabia were treated with surfactant therapy. In the study done at Gondar University, the difference could be due to the difference in sample size. The other possible explanation could be a difference in the study setting, period, and socio economic difference among countries.

In multivariate analysis, those newborns born to preeclamptic mothers and PPROM mothers were associated factors for RDS-related death. According to the current study, preterm newborns born to preeclamptic mothers were 51% less likely to die than those born to non-preeclamptic mothers. As far as my personal information is concerned, there is no similar study conducted on the effect of preeclampsia on RDS related deaths, but many studies have been conducted on the effect of preeclampsia on the burden of RDS. So as the burden increases, the mortality also increases. On the burden of RDS, this study is similar to studies done in Italy [28], in Taiwan [29] and in India [30]. The decreased association of preeclamptic mothers with neonatal RDS-related deaths might be related to maternal hypertension causing placental insufficiency that results in utero stress. Due to that, there will be an increased release of stress hormones like steroids, which results in increased production of surfactant and early lung maturation. The other reason could be that

preeclamptic mothers have a higher tendency to be admitted before the onset of labor, so that most of the mothers have a chance of taking corticosteroid before delivery [33].

Those preterm newborns born to PPROM mothers were 3.54 times more likely to die than those who were delivered from mothers who have no PPROM. As far as my personal information is concerned, there is no similar study conducted on the effect of PPROM on RDS related deaths, but many studies have been conducted on the effect of PPROM on the burden of RDS. This is similar with studies done in Nepal [22],Black lion hospital, Addis Ababa, Ethiopia [19] and India [30],this could be due to risk of neonatal sepsis is higher in neonates born to PPROM mother due to maternal ascending infection and there may be concomitant oligohydraminous due to leakage of liquor that may result in cord compression resulting in inutero asphyxia.

7. LIMITATION OF THE STUDY

Since the study was a hospital-based study, the results may not be generalized to a wider population.

8. CONCLUSION and RECOMMENDATIONS

8.1 Conclusions

From the present study it can be concluded that the death rate of preterm neonatal RDS was high. Preterm neonate born to preeclamptic mothers PPROM mothers and newborn were associated factors that decrease and increase RDS related death respectively.

8.2 Recommendations

Based on the results of this study the following recommendations were made.

- To decrease the death related to preterm neonatal RDS, the hospital where the study was conducted should give emphasis on treatment strategies of RDS, including antenatal corticosteroids, surfactants, and advanced respiratory care of the neonate[9].
- Nowadays, the hospital is implementing treatment strategies for neonate with RDs such as nasal continuous positive airway pressure. However, the hospital is not implementing exogenous surfactant administration intubation and put on mechanical ventilation. Therefore, the hospital should give emphasis on delivering Nasal CPAP to labor ward, orienting the midwives on early application of nasal CPAP within 20 minutes of delivery, early referral to the NICU, prevention of hypothermia, update and integrating other treatment strategies (surfactant administration) for RDS neonates as per the protocol[34].
- In this study, PPROM increases the risk of RDS-related death in neonates, so the hospital managers and the health professionals working in the gynecology/obstetric department should teach the mothers about the prevention of PPROM. Even though it is difficult to prevent , they should be advised on risk factors of PPROM, like on prevention of bacterial vaginosis, Cervical length less than 2.5 cm for early screening and circlage, Poor nutrition Socio-economic status should be advised on nutritional support.

9. REFERENCES

1. Martin R: **Pathophysiology, clinical manifestations, and diagnosis of respiratory distress syndrome in the newborn**. *U: UpToDate, Garcia-Prats JA, Kim MS ur: UpToDate* 2022.
2. Roth-Kleiner M, Post M: **Similarities and dissimilarities of branching and septation during lung development**. *Pediatric pulmonology* 2005, **40**(2):113-134.
3. Herriges M, Morrisey EE: **Lung development: orchestrating the generation and regeneration of a complex organ**. *Development* 2014, **141**(3):502-513.
4. Gao Y, Cornfield DN, Stenmark KR, Thébaud B, Abman SH, Raj JU: **Unique aspects of the developing lung circulation: structural development and regulation of vasomotor tone**. *Pulmonary circulation* 2016, **6**(4):407-425.
5. Ablow R: **Respiratory distress syndrome (hyaline membrane disease)**. *Critical reviews in diagnostic imaging* 1981, **14**(4):321-363.
6. Hiles M, Culpan A-M, Watts C, Munyombwe T, Wolstenhulme S: **Neonatal respiratory distress syndrome: chest X-ray or lung ultrasound? A systematic review**. *Ultrasound* 2017, **25**(2):80-91.
7. Wang J, Liu X, Zhu T, Yan C: **Analysis of neonatal respiratory distress syndrome among different gestational segments**. *International journal of clinical and experimental medicine* 2015, **8**(9):16273.
8. Gregorio-Hernández R, Arriaga-Redondo M, Pérez-Pérez A, Ramos-Navarro C, Sánchez-Luna M: **Lung ultrasound in preterm infants with respiratory distress: experience in a neonatal intensive care unit**. *Eur J Pediatr* 2020, **179**(1):81-89.
9. Yadav S, Lee B, Kamity R: **Neonatal respiratory distress syndrome**. 2020.
10. Li Y, Wang W, Zhang D: **Maternal diabetes mellitus and risk of neonatal respiratory distress syndrome: a meta-analysis**. *Acta diabetologica* 2019, **56**(7).
11. Smith PB, Ambalavanan N, Li L, Cotten CM, Laughon M, Walsh MC, Das A, Bell EF, Carlo WA, Stoll BJ: **Approach to infants born at 22 to 24 weeks' gestation: relationship to outcomes of more-mature infants**. *Pediatrics* 2012, **129**(6):e1508-e1516.
12. Hubbard RM, Choudhury KM, Lim G: **Treatment patterns and clinical outcomes in neonates diagnosed with respiratory distress syndrome in a low-income country: a report from Bangladesh**. *Anesthesia and analgesia* 2018, **126**(5):1684.
13. Jacob J, Kamitsuka M, Clark RH, Kelleher AS, Spitzer AR: **Etiologies of NICU deaths**. *Pediatrics* 2015, **135**(1):e59-e65.
14. Dyer J: **Neonatal respiratory distress syndrome: tackling a worldwide problem**. *Pharmacy and Therapeutics* 2019, **44**(1):12.
15. Thygesen SK, Olsen M, Østergaard JR, Sørensen HT: **Respiratory distress syndrome in moderately late and late preterm infants and risk of cerebral palsy: a population-based cohort study**. *BMJ open* 2016, **6**(10):e011643.
16. Thygesen SK, Olsen M, Pedersen L, Henderson VW, Østergaard JR, Sørensen HT: **Respiratory distress syndrome in preterm infants and risk of epilepsy in a Danish cohort**. *European journal of epidemiology* 2018, **33**(3):313-321.
17. Chao Y-S, Grobelna A: **Curosurf (poractant alfa) for the Treatment of Infants At Risk For or Experiencing Respiratory Distress Syndrome: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines**. 2019.
18. Kamath BD, MacGuire ER, McClure EM, Goldenberg RL, Jobe AH: **Neonatal mortality from respiratory distress syndrome: lessons for low-resource countries**. *Pediatrics* 2011, **127**(6):1139-1146.

19. Mekonen H, Habtewold TD, Endalamaw A, Petrucka PM, Shiferaw WS: **Incidence of respiratory distress and its predictors among neonates admitted to the neonatal intensive care unit, Black Lion Specialized Hospital, Addis Ababa, Ethiopia**. 2020.
20. Minuye Birihane B, Alebachew Bayih W, Yeshambel Alemu A, Belay DM, Demis A: **The burden of hyaline membrane disease, mortality and its determinant factors among preterm neonates admitted at Debre Tabor General Hospital, North Central Ethiopia: A retrospective follow up study**. *Plos one* 2021, **16**(3):e0249365.
21. Kommawar A, Borkar R, Vagha J, Lakhkar B, Meshram R, Taksandae A: **Study of respiratory distress in newborn**. *International Journal of Contemporary Pediatrics* 2017, **4**(2):490-494.
22. Rijal P, Shrestha M: **Scenario of neonatal respiratory distress in tertiary hospital**. *Birth* 2018, **14**(10):6.
23. Qari SA, Alsufyani AA, Muathin SH, El Margoushy NM: **Prevalence of Respiratory Distress Syndrome in Neonates**. *The Egyptian Journal of Hospital Medicine* 2018, **70**(2):257-264.
24. Adebami OJ, Joel-Medewase VI, Agelebe E, Ayeni TO, Kayode OV, Odeyemi OA, Oyedeji GA: **Determinants of outcome in newborns with respiratory distress in Osogbo, Nigeria**. *Int J Res Med Sci* 2017, **5**(4):1487-1493.
25. Andegiorgish AK, Andemariam M, Temesghen S, Ogbai L, Ogbe Z, Zeng L: **Neonatal mortality and associated factors in the specialized neonatal care unit Asmara, Eritrea**. *BMC public health* 2020, **20**(1):1-9.
26. Muhe LM, McClure EM, Nigussie AK, Mekasha A, Worku B, Worku A, Demtse A, Eshetu B, Tigabu Z, Gizaw MA: **Major causes of death in preterm infants in selected hospitals in Ethiopia (SIP): a prospective, cross-sectional, observational study**. *The Lancet Global Health* 2019, **7**(8):e1130-e1138.
27. Alzubair YA, Hailu Y, Tamirat KS: **Determinant factors of immediate outcomes of Neonatal Respiratory Distress Syndrome in Gondar, Ethiopia**. *South Sudan Medical Journal* 2022, **15**(1):5-11.
28. Luerti M, Parazzini F, Agarossi A, Bianchi C, Rocchetti M, Bevilacqua G: **Risk factors for respiratory distress syndrome in the newborn: a multicenter Italian survey**. *Acta obstetricia et gynecologica Scandinavica* 1993, **72**(5):359-364.
29. Yen T-A, Yang H-I, Hsieh W-S, Chou H-C, Chen C-Y, Tsou K-I, Tsao P-N, Group TPIDCS: **Preeclampsia and the risk of bronchopulmonary dysplasia in VLBW infants: a population based study**. *PloS one* 2013, **8**(9):e75168.
30. Agashe US, Borade A, Gulawani S, Dhongade R: **INFLUENCE OF MATERNAL RISK FACTORS IN PULMONARY MATURITY IN PRETERM NEWBORN**.
31. Abou-Faddan HH, Abdelaziz N: **Respiratory Distress and Its Outcome among Neonates Admitted to Neonatal Intensive Care Unit of Assiut University Children Hospital, Egypt**. *Egypt The Egyptian Journal of Community Medicine* 2018, **36**(2).
32. Lakhkar B, Kommawar A, Borkar R, Vagha J, Meshram R, Taksandae A: **Study of respiratory distress in newborn**. 2017.
33. Chander A, Fisher AB: **Regulation of lung surfactant secretion**. *American Journal of Physiology-Lung Cellular and Molecular Physiology* 1990, **258**(6):L241-L253.
34. Mingione MJ, Pressman EK, Woods JR: **Prevention of PPROM: current and future strategies**. *The Journal of Maternal-Fetal & Neonatal Medicine* 2006, **19**(12):783-789.

10. ANNEX

Annex I: Information sheet

Title of the research project: outcome and associated factors of respiratory distress syndrome among preterm neonates admitted at Tibebeghion specialized hospital, Bahirdar, Amhara national regional state ,north west Ethiopia, bahirdar Ethiopia in 2022GC.

Name of the principal investigator: Dr. KIDANE MEHERET

Name of the Organization: Bahirdar University, college of Medicine and Health science, school of medicine department of pediatrics and child health**.**

Introduction: This information sheet and consent form is prepared with the aim to study the outcome and associated factors of respiratory distress syndrome among preterm neonates admitted at Tibebe ghion specialized hospital to the neonatal ward in Bahirdar town in 2022GC. The research group includes the principal investigator,trained data collectors ,supervisors and advisory from Bahirdar university **.**

Purpose of the research project

The main aim of this study is to assess the outcome and associated factors of respiratory distress syndrome among preterm neonates admitted at Tibebe ghion specialized hospital in 2022GC.

Procedure

The study participants are newborns with their mothers admitted to Tibebe ghion specialized hospital in 2022GC and I kindly invite you to take part in this study. If you are willing to participate, I will be so happy and I need you to understand clearly about the purpose of this study and show your agreement. Finally you are kindly requested to give us genuine information.

RISK and/or Discomfort

Participating in this interview, you will not be risked but will spend 15 minutes for it**.**

Benefit of participation

Even though participation has no direct benefit, your information is very important for development of guidelines in the future**.**

Confidentiality: we will not mention your name and the information collected from you will be secured**.**

Incentives/ payment for participation

You will not be provided any incentive or payment by participating in this study.

Right to refusal / withdrawal

You have full right not to participate or to withdraw at any time**.**

Contacts and Questions

Principal Investigator: Dr. KIDANE MEHERET: Mob +251911703291 or Email:

Advisors: Dr. WORKIE SHITA : Mob +251911413048 or Email:

Mr. GIZACHEW WORKU: Mob; 0918287094

Email;giz.work12@gmail.com

Annex II: English Consent form

A questioner prepared to assess magnitude of RDS related death and associated factors of respiratory distress syndrome among pre term neonates admitted at Tibebe ghion specialized hospital in 2022GC.

Hello, how are you?

My name is _____. I am from Bahirdar University in department of pediatrics and child health. Now I am collecting data to assess the RDS related death and associated factors of respiratory distress syndrome among pre term neonates admitted at Tibebe ghion specialized hospital in 2022GC .The purpose is to collect data to assess RDS related death and associated factors of respiratory distress syndrome among pre term neonates. The data will be beneficial for future plan and policy makings for better management and prevention of Preterm neonatal RDS.

The result will be important in the next studies. Then we are going to ask you some questions for 15 minutes and to see the medical records of your baby. Your willingness is appreciable and your genuine response helps us to generate solutions in the future. Your response and medical record will be fully confidential and your name will not be mentioned. If you are not comfortable your refusal is kept right and if you have any doubt you can ask any question and have the right to withdraw the response.

Are you willing to take part in the interview?

Yes_____ No_____

If yes, let's continue.

Respondent code (MRN):_____ Date of interview_____.

Interviewer name_____ signature_____.

Supervisor name _____ signature_____.

Thank you for your willingness.

IV: Questionnaries

Newborn's and profile

S.No	Questions	Coding category
1.1	Sex of the newborn	1.Female
		2.Male
1.2	Age of newborn at admission	1.less than 20 min 2. greater than 20min
1.3.	Gestational age	1.<34 weeks 2.>= to 34 weeks
1.4.	Place of delivery	1.Home
		2.Health facility
1.5.	Mode of delivery	1.Vaginal
		2.C/S
1.6	Number of fetuses in the current pregnancy	1.Singleton
		2.Twin
		3.Triplet or above
1.7	Anthropometry measurements	1.SGA

		2.AGA
2.1	Age of the mother	-----years
2.2	Residence	1.Urban
		2.Rural
2.3	Level of education	1.Cannot read and write
		2.Read and write
		3.primary
		4.secondary
		5.Above secondary
3.1	Did you have ANC follow up?	1.Yes
		2.No
3.2	Any obstetrical complication during current pregnancy?	APH 1.yes 2.no
		Chorioamnionitis 1.yes 2.no
		Preeclampsia/eclampsia 1.yes 2.no
		PROM 1.yes

		2.no
3.3	Any chronic medical diseases?	1.Yes
		2.No
3.4	Parity	1.Primiparous
		2.Multiparous

Treatment associated factors

No	Question	Category
4.1	Treatment associated factors	Maternal use of corticosteroids Use of 1.Yes 2.No
		INO2 1.Yes 2.No
		Use of CPAP 1.Yes 2.No

Neonatal related complications

S.No	Neonatal related complications
5.1	Birth weight 1.<1000gm 2.1000-1500gm 3.>1500gm
5.2	Asphyxia 1.yes 2.no
5.3	Body temperature of the new born. 1.hypothermia 2.Normal
5.4	RDS related death 1.Yes 2.No