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DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH

EARLY OUTCOMES AND PREDICTORS OF MORTALITY AMONG PRETERM NEONATES WITH RESPIRATORY DISTRESS SYNDROME ADMITTED AT KAWEMPE NATIONAL REFERRAL HOSPITAL; A PROSPECTIVE STUDY.

BY

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A DISSERTATION SUBMITTED TO THE DIRECTORATE OF RESEARCH AND GRADUATE TRAINING IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH OF MAKERERE UNIVERSITY.

DECLARATION

I, Wanjala Francis Xavier, affirm that this dissertation is my original work and has not been submitted to any university or institution for any academic qualification. All literature used in this study has been appropriately cited for acknowledgment.

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APPROVAL

We endorse this dissertation, done under our close supervision. We recommend its submission to Makerere University for the partial fulfillment of the award of a Master's Degree of Medicine in Pediatrics and Child Health.

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DEDICATION

This work is dedicated to the countless preterm neonates and their families whose strength and resilience continue to inspire the pursuit of better neonatal care. It is also dedicated to my family for their unwavering love, support, and encouragement throughout this journey.

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS/ACRONYMS

APH	Antepartum Hemorrhage
APGAR	Appearance, Pulse, Grimace, Activity, Respiration
BPD	Bronchopulmonary Dysplasia
CPAP	Continuous Positive Airway Pressure
CXR	Chest X-Ray
DM	Diabetes Mellitus
GA	Gestational Age
IVH	Intraventricular Hemorrhage
LBW	Low Birth Weight
NICU	Neonatal Intensive Care Unit
NCPAP	Nasal Continuous Positive Airway Pressure
PROM	Premature Rupture of Membranes
RDS	Respiratory Distress Syndrome
RR	Respiratory Rate
SGA	Small for Gestational Age
SDG	Sustainable Development Goals
SNAP-II	Score for Neonatal Acute Physiology-II
SSA	Sub-Saharan Africa

OPERATIONAL DEFINITIONS

Antenatal steroid administration: Was considered as giving corticosteroids to expectant mothers who are at risk of preterm birth to hasten the development of the fetal lungs and lower the risk of respiratory distress syndrome (1).

Apgar score: A quick method for assessing a newborn's health immediately after birth that is based on five factors: Skin color, muscle tone, respiratory effort, heart rate, and reflex response (2).

Low birth weight: A birth weight below 2500 grams, regardless of gestational age (3).

Preterm neonate: An infant born before 37 completed weeks of gestation (4).

Respiratory Distress Syndrome (RDS): The presence of at least two of the following clinical symptoms will be used to define RDS: grunting, nasal flaring, chest indrawing, intercostal or subcostal retractions, and tachypnea (respiratory rate > 60 breaths per minute). This diagnosis was confirmed by a chest X-ray showing characteristic features, including low lung volume, diffuse bilateral and symmetrical granular opacities, and air-bronchograms (5)**.**

Silverman-Anderson Score (SAS) is used to assess the severity of RDS in neonates. A score of six or higher was classified as severe, a score of four to five was classified as moderate, and a score of one to three was classified as mild (6-8).

Early outcomes: This was defined as the survival status of the neonate after 3 days of follow-up (5)**.**

ABSTRACT

Background: Respiratory distress syndrome (RDS) is a severe condition in preterm newborns, marked by a lack of surfactant, which results in high rates of illness and death. The burden of RDS is greater in low- and middle-income countries, where it significantly increases mortality rates and admissions to neonatal intensive care units. Despite global efforts to reduce neonatal mortality, RDS remains a major challenge, particularly in places like Uganda, where there is limited research specifically examining the outcomes of preterm neonates with RDS. The study aimed to determine early outcomes and predictors of mortality among preterm neonates with respiratory distress syndrome admitted to Kawempe National Referral Hospital (KNRH) in Uganda.

Methods: This was a hospital-based prospective cohort study conducted at the Neonatal Special Care Unit of Kawempe National Referral Hospital among preterm neonates aged less than 24 hours whose respiratory distress commenced within the first 6 hours of life. Quantitative data were collected using structured questionnaires, focusing on maternal and neonatal characteristics, as well as early outcomes of the preterm babies. Early outcomes comprised survival and mortality assessed within three days of follow-up. The Kaplan-Meier method estimated survival curves, with differences between these curves analyzed using the log-rank test. Bivariate and multivariate Cox proportional hazards regression was used to assess the predictors of mortality with statistical significance set at <0.05.

Results: Among the 201 preterm neonates with respiratory distress syndrome admitted to KNRH, 25(12.4%) died within the three-day follow-up, with most of the deaths (24), occurring within the first 2 days. Preterm neonates who did not receive xanthine derivatives had approximately three times higher hazard of death compared with those who received xanthine derivatives (aHR=2.99; p=0.034). Similarly, neonates delivered vaginally had more than four times increased hazard of death compared with those delivered by caesarean section (aHR=4.33; p=0.013). (Table 8).

Conclusion: Preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital experienced early mortality mainly within the first two days of life. The hospital needs to ensure timely access to caffeine therapy and consider safe delivery options for preterm births to improve survival outcomes in this high-risk population.

CHAPTER ONE: INTRODUCTION

1.1 Background

Respiratory distress syndrome (RDS) is a major cause of morbidity, and mortality among premature newborns (9). It is defined as a severe inflammatory lung condition characterized by rapid onset, leading to increased pulmonary vascular permeability, increased lung weight, and reduced aerated lung tissue (10). Respiratory distress syndrome typically appears within the first 48 hours of life usually in neonates born prior to 37 weeks of gestation, with its occurrence decreasing as gestational age increases (9). This condition mainly arises due to a lack of pulmonary surfactants that play a crucial role in lowering surface tension within the alveoli and maintaining their stability (11). If not treated, affected infants may experience fatigue, episodes of apnoea, low oxygen levels and might progress to respiratory failure (12).

In 2020, over 13.4 million babies globally were born prematurely (4). The global incidence rate of RDS ranges from 24.9% to 62.96% and is reported to increase neonatal admissions to the neonatal intensive care unit (NICU). It also accounts for 31.3% of all perinatal deaths (13). The effects of RDS are especially severe in low- and middle-income countries (14). In Sub-Saharan Africa (SSA), the burden of RDS is high with distinct variations across countries. The incidence of RDS in preterm neonates is reported to be 10.9% in Nigeria, 45.3% in Ethiopia, and 23% in Ivory Coast (15-17).

RDS is linked to high rates of neonatal mortality, especially among those born before 28 weeks of gestation, with frequent bronchopulmonary dysplasia (BPD) among survivors (9, 14, 18). Neurological complications such as intraventricular haemorrhage (IVH) are common, often leading to long-term deficits (19, 20). Various studies have identified multiple factors associated with RDS to include maternal diabetes mellitus, hypertension, mode of delivery, gender, prematurity, multiparity, birth weight, antenatal steroid administration, hyperglycaemia, surfactant, airway pressure, sepsis, antepartum haemorrhage, premature rupture of membranes, and low APGAR scores at one and five minutes after birth (21-24).

RDS is diagnosed through clinical assessment and imaging methods, such as chest X-ray (22). Clinical diagnosis of RDS among neonates is based on the presence of at least two of the following symptoms: a respiratory rate exceeding 60 breaths a minute, grunting, nasal flaring, or intercostal

or subcostal retractions (22). The aetiology of RDS is influenced by various respiratory conditions like birth asphyxia, hyaline membrane disease, tracheoesophageal fistula, meconium aspiration syndrome, transient tachypnoea, pneumonia, and pneumothorax of the newborn (22, 25, 26).

In Uganda, the incidence of preterm births is 13 per 1,000 live births, contributing to the ongoing challenge of reducing infant mortality (27). Despite the high burden of RDS among preterm neonates in resource-limited settings, there is a lack of studies focused on the outcomes of RDS in this vulnerable population. Consequently, the absence of comprehensive data hinders the formulation of effective policies and strategic interventions to reduce neonatal mortality and morbidity. This gap in evidence limits progress toward achieving Sustainable Development Goal 3.2, which aims to end preventable deaths of newborns and children under five years of age.

This study, therefore, aimed to determine the early outcomes and predictors of mortality among preterm neonates with respiratory distress syndrome admitted to Kawempe National Referral Hospital.

1.2 Statement of the Problem

Preterm neonates are at increased risk of respiratory distress syndrome, which contributes substantially to neonatal morbidity and mortality (28). At Kawempe National Referral Hospital, monthly data from the special care unit at KNRH indicate 634 neonates were admitted to the Special Care Unit in November 2024, of whom 197 died, representing a mortality rate of approximately 31%. Among these deaths, 39 were attributed to RDS, making it the leading reported cause of mortality during that period. Severe RDS is also associated with intraventricular haemorrhage and long-term neurodevelopmental impairments, including motor and cognitive deficits (29).

The Government of Uganda and the Ministry of Health have implemented several interventions to reduce neonatal mortality, including establishing neonatal care units, strengthening maternal and child health policies, and expanding healthcare facilities such as Kawempe National Referral Hospital (30, 31). However, the continued burden of RDS and associated mortality at KNRH undermines these efforts. Previous studies have reported that limited access to advanced neonatal care, infections and immature lung development may influence mortality among neonates with RDS (22, 24). However, there is limited empirical evidence on the early outcomes and predictors

of mortality among preterm neonates with RDS at KNRH. This study therefore assessed the early outcomes and predictors of mortality among preterm neonates with RDS admitted to Kawempe National Referral Hospital.

1.3 Justification

Premature neonates face an increased risk of developing RDS (9). This condition typically manifests within the first 48 hours of life, consequently increasing the risk of morbidity and mortality among premature newborns (32). In Tanzania, a study by Bulimba, Cosmas (6) at Muhimbili National Hospital, reported that 3 in every 10 preterm neonates with RDS died within the first seven days of life. This highlights the need for early diagnosis and intervention. Furthermore, the use of Antenatal Corticosteroids (ACS) in Tanzania has demonstrated a 58% reduction in RDS incidence and a 75% decrease in neonatal mortality (33).

In Uganda, however, there remains a lack of comprehensive data on RDS outcomes. This study aims to fill that gap by providing relevant information to enhance medical care through close monitoring and timely interventions, potentially improving survival rates for preterm neonates with RDS. By identifying key predictors of mortality, the study will enable healthcare providers to tailor treatments based on individual risk factors, ensuring more effective and personalized care. Additionally, this research aligns with Sustainable Development Goal 3, Target 3.2, which seeks to end preventable deaths of newborns and reduce neonatal mortality to at least as low as 12 per 1,000 live births by 2030. By generating context-specific evidence and informing clinical practice, the study has the potential to directly support Uganda's progress toward achieving this target, contributing to global efforts to improve neonatal survival. Furthermore, this research will contribute to the scientific body of knowledge regarding neonatal RDS

1.4 Research Questions

1. What are the early outcomes of preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital?
2. What are the predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital?

1.5 Study Objectives

1.51 General Objective

To determine early outcomes and predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital.

1.52 Specific Objectives

1. To determine early outcomes of preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital.
2. To determine the predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital.

1.61 Conceptual Framework

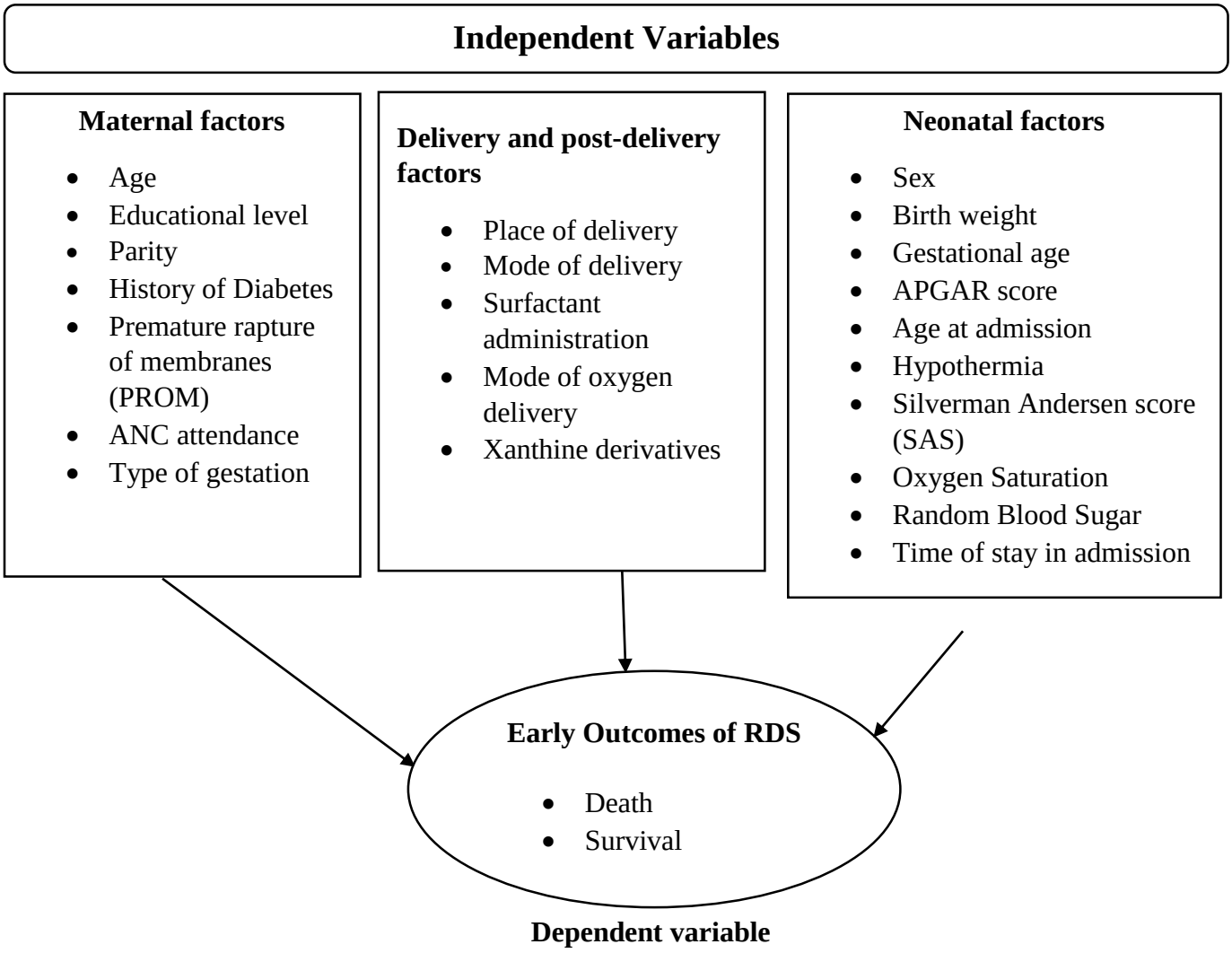


Figure 1: Showing the Conceptual Framework

1.62 Narrative

Maternal factors such as age, diabetes history, parity, education level, antenatal care (ANC) attendance, antenatal steroid administration, and premature rupture of membranes (PROM) can significantly impact the outcomes of preterm neonates with RDS. Advanced maternal age and conditions like diabetes can heighten the risk of premature birth and related complications, including RDS. Mothers with diabetes face an increased risk of having neonates with RDS due to delayed fetal lung maturation resulting from high blood glucose levels. Parity can influence the timing and circumstances of birth, which in turn affect neonatal health outcomes. Educational level

and ANC attendance affect prenatal care and maternal health monitoring, impacting the timely detection and management of pregnancy-related issues.

Delivery and post-delivery factors such as mode of delivery, place of delivery, surfactant administration, and respiratory support are critical in determining neonatal outcomes in RDS. The mode and place of delivery determine access to specialized care, crucial for managing RDS and other neonatal complications. Post-delivery interventions like surfactant administration and provision of respiratory support directly influence the severity and progression of respiratory distress and improve survival chances in preterm neonates.

Neonatal factors such as birth weight, gestational age, sex, APGAR score, hypothermia, age at admission, Silverman Andersen score (SAS), and oxygen saturation are essential in determining the outcomes for preterm neonates with RDS. Low birth weight and premature birth (gestational age) are primary risk factors for developing RDS due to underdeveloped lungs. APGAR scores at birth reflect immediate neonatal health status, impacting initial management and prognosis. Monitoring for hypothermia and age at admission are crucial as they affect the severity and progression of RDS symptoms. The Silverman Andersen score (SAS) provides a standardized assessment of respiratory distress severity, guiding treatment decisions. Oxygen saturation levels are vital indicators of respiratory function and response to therapy, crucial for managing RDS and predicting outcomes in preterm neonates.

CHAPTER TWO: LITERATURE REVIEW

2.0 Introduction

This literature review examines early outcomes and risk factors associated with respiratory distress syndrome (RDS) in preterm infants. Information was gathered from sources such as PubMed, Google Scholar, BMC, and other online search engines. The review aims to offer a thorough understanding of the outcomes and factors contributing to RDS in preterm neonates.

2.1 Pathophysiology of Respiratory Distress Syndrome

Respiratory distress syndrome (RDS), also referred to as hyaline membrane disease, primarily results from surfactant deficiency in the immature lungs of preterm neonates (34). Surfactant, produced by type II alveolar epithelial cells, is essential for reducing alveolar surface tension, thereby preventing alveolar collapse during expiration and facilitating efficient gas exchange (34). In its absence, widespread atelectasis occurs, leading to impaired oxygenation, reduced lung compliance, and increased work of breathing. The resultant intrapulmonary right-to-left shunting contributes to refractory hypoxemia, while progressive alveolar collapse and poor compliance further exacerbate hypercapnia and respiratory acidosis (35, 36).

The structural immaturity of the premature lung compounds this problem. Surfactant synthesis begins in the late canalicular stage of fetal lung development and rises significantly during the third trimester. Consequently, the incidence of RDS is inversely proportional to gestational age: more than half of neonates born before 28 weeks are affected, while the risk declines to less than 2% at 35-36 weeks (37). Prematurity is also associated with a highly compliant chest wall and reduced alveolar surface area, both of which exacerbate alveolar instability and ventilatory inefficiency (38). Histopathological examination of affected lungs often reveals the formation of eosinophilic “hyaline membranes” composed of plasma proteins, fibrin, and necrotic epithelial cells that line collapsed alveoli, giving rise to the term “hyaline membrane disease” (34).

The failure of adequate ventilation produces severe ventilation-perfusion mismatch. While some alveoli remain perfused but unventilated, others collapse completely, producing areas of shunt physiology that are unresponsive to supplemental oxygen. These abnormalities manifest clinically as persistent hypoxemia and respiratory failure (35). With prolonged inadequate gas exchange, neonates develop respiratory muscle fatigue and worsening acidosis, which can quickly become fatal without intervention (37).

In addition to immaturity, intrauterine and perinatal factors may influence the pathophysiology of RDS. Antenatal inflammation, such as chorioamnionitis, has paradoxical effects, as inflammatory cytokines may accelerate lung maturation in some cases but can also damage pulmonary tissue and impair surfactant function in others (39, 40). Beyond environmental influences, rare genetic defects affecting surfactant production or metabolism can also precipitate RDS, even in term infants. Mutations in genes encoding surfactant proteins B and C, or the ABCA3 transporter, disrupt surfactant synthesis and packaging, leading to severe neonatal respiratory failure unresponsive to standard therapies (41).

Recovery from RDS is dependent on the regeneration of alveolar epithelium and restoration of surfactant production. As type II pneumocytes proliferate and resume normal function, alveolar stability improves, leading to better gas exchange and gradual resolution of respiratory symptoms (34, 42). However, some infants, particularly those requiring prolonged ventilatory support, may develop chronic lung injury such as bronchopulmonary dysplasia, underscoring the long-term consequences of disrupted pulmonary development in the neonatal period (43).

2.2 Burden of Respiratory Distress Syndrome

The global prevalence of neonatal respiratory distress syndrome remains uncertain. However, available studies indicate that RDS constitutes a major burden of neonatal morbidity and mortality worldwide, particularly in resource-limited settings.

In Afghanistan, a retrospective study at the French Medical Institute for Mothers and Children in Kabul found that 51.3% of 78 preterm neonates developed RDS. Stratified by gestational age, the prevalence was highest among extremely preterm (100%), followed by early preterm (55.6%), moderate preterm (44%), and late preterm (35.7%). A similar pattern was observed by birthweight, with RDS occurring in 100% of extremely low birthweight, 56.2% of very low birthweight, and 58.8% of low birthweight neonates (44). In India, a prospective observational study at Jawaharlal Nehru Medical College Hospital, Aligarh, reported a prevalence of 7.1% for neonatal respiratory distress, with RDS accounting for 35.5% of the cases (45).

In Sub-Saharan Africa, several studies highlight the significant contribution of RDS to neonatal admissions and deaths. In Ethiopia, a study conducted among neonates admitted to the neonatal intensive care units of Gurage Zone public hospitals reported an RDS prevalence of 45.1% (46).

Similarly, in Egypt, respiratory distress accounted for 52.9% of neonatal intensive care admissions at Assiut University Children's Hospital (47). Data from Kenya further emphasize the fatal impact of RDS; of 165 neonatal deaths investigated through the Child Health and Mortality Prevention Surveillance (CHAMPS) program between 2017 and 2021, RDS was present in the causal chain for 43 cases (26.1%) (48).

In Uganda, RDS has been consistently identified as a leading complication among preterm neonates. A prospective cohort study at Mbarara Regional Referral Hospital (MRRH) enrolled 538 preterm neonates between October 2019 and September 2020 and found that 37.5% were diagnosed with RDS (49). Another study at the same hospital reported that 25% of neonates admitted to the neonatal unit presented with RDS, with nearly half of the admissions being preterm (46%) and 44% of low birthweight (50).

2.1 Early outcomes of preterm neonates with respiratory distress syndrome

Respiratory distress syndrome (RDS) is a prevalent and severe condition in preterm neonates, marked by immature lungs and inadequate surfactant production. This results in symptoms like nasal flaring, chest retractions, and fluctuating oxygen levels (13).

Research indicates considerable differences in survival rates for preterm neonates with RDS. For example, a study at Muhimbili National Referral Hospital in Tanzania found an overall mortality rate of 31.3% among these infants, with increased mortality rates observed in those with birth weights under 1500 grams and gestational ages less than 32 weeks (6). Similarly, another study from Ethiopia indicated mortality rates as high as 34% in some settings, emphasizing the critical impact of birth weight and gestational age on survival (51).

A study on outcomes of respiratory distress syndrome managed at Moi Teaching and Referral Hospital, Eldoret, Kenya found that mortality was high, with 68 deaths (72.3%) recorded during the study period, 58 (61%) of which occurred within the first 10 days of life (52). A related study discovered that neonates born before 28 weeks of gestation experienced the highest mortality rate of 63.07%. Those born between 28-32 weeks had a mortality rate of 27.27%, which further decreased to 21.41% for neonates born between 33-36 weeks. The lowest mortality rate, 13.73%, was observed in neonates born after 37 weeks of gestation (22).

According to a study done at Adama Hospital and Medical College, adverse outcomes were observed in 62.8% of preterm admissions with RDS. In contrast, just ninety-nine newborns (37.2%) were released in excellent health or after demonstrating a notable clinical improvement. (53).

Respiratory complications are a major concern for preterm infants with RDS, often requiring intensive respiratory support. Fernandes and Chawla (42) found that 50-70% of neonates with RDS require mechanical ventilation, which increases the likelihood of developing bronchopulmonary dysplasia and its potential long-term health impacts. Early surfactant administration notably decreases the need for mechanical ventilation and reduces the incidence of BPD (54).

Preterm infants with RDS face an elevated risk of brain damage and developmental issues, making neurological outcomes particularly concerning. Wang and Song (36) identified a strong link between severe RDS and an increased risk of intraventricular hemorrhage (IVH), which can lead to long-term neurodevelopmental deficits such as delayed cognitive and motor skills. Pande and Vagha (44) also noted that these infants are at a higher risk for periventricular leukomalacia (PVL), a severe brain injury associated with significant neurodevelopmental challenges.

Cardiovascular complications related to RDS, such as patent ductus arteriosus (PDA), are notably serious. Pourarian and Farahbakhsh (43) found that RDS can lead to heart failure and other severe cardiovascular issues. Early closure of PDA is essential for improving survival rates and minimizing complications like pulmonary hemorrhage (20).

Preterm neonates with RDS also face complications such as retinopathy of prematurity (ROP) (18, 24). Research shows that minimally invasive surfactant therapy reduces the risk of these complications by decreasing the need for invasive mechanical ventilation (6, 55).

Recent advances in minimally invasive surfactant therapy (MIST) and non-invasive ventilation (NIV) have shown positive results for preterm infants with RDS. Studies on positive airway pressure (NCPAP) and nasal intermittent positive pressure ventilation (NIPPV) demonstrated that both methods significantly improved oxygenation and ventilation following MIST, though the NIPPV group experienced longer durations of respiratory support and higher rates of complications like retinopathy of prematurity (55).

2.2 Predictors of mortality among preterm neonates with respiratory distress syndrome

2.2.1 Maternal factors

RDS in preterm neonates is significantly influenced by various maternal factors. These factors include maternal age, ANC attendance, educational level, parity, mode and place of delivery, fever, diabetes, premature rupture of membranes, and marital status.

Maternal Age

Previous studies have shown no difference in the outcomes of RDS among preterm babies (6, 56). However, evidence suggests that age-related biological factors and potential complications contribute to the increased risk of RDS in neonates born to younger and older mothers. Neonates of young mothers (≤ 19 years) may often face a higher risk of RDS due to increased incidences of preterm births (57). These neonates typically have underdeveloped lungs and a surfactant deficiency, increasing their vulnerability to RDS (54). However, neonates of older mothers (≥ 35 years) may be more susceptible to RDS due to a higher frequency of medical complications like preeclampsia and gestational diabetes, which can lead to preterm births (58).

Educational Level

Educational attainment significantly influences maternal health behaviors and access to healthcare. Marinonio, Costa-Nobre (59) reported that neonates of mothers having seven or fewer years of schooling are 1.18 times more likely to die due to RDS compared to those born to mothers with more than seven years of schooling (RR: 1.18; 95% CI: 1.09–1.29). This suggests that education promotes health literacy and better utilization of prenatal care services, leading to reduced risks of preterm birth and RDS.

Parity

A study in Gondor, Ethiopia, discovered that neonates born to first-time mothers have 2.49 times greater odds of mortality compared to those born to mothers with previous births (AOR: 2.49; 95% CI: 1.05 - 5.87) (32). A study conducted in Brazil reported that preterm neonates belonging to mothers with multiple deliveries are 1.24 times more likely to dies from RDS compared to neonates from mothers with less or single deliveries (RR: 1.24;95% CI: 1.16–1.33) (59).

Maternal Fever

Maternal fever during labor can indicate intra-amniotic infection and raises the risk of preterm birth. A systematic review and meta-analysis found that preterm births are more common at higher temperatures compared to lower temperatures. For each 1°C increase in temperature, the odds of preterm birth rose by 1.05 times (95% CI: 1.03-1.07). Additionally, higher temperatures were associated with lower birth weights in 18 out of 28 studies (60). Research has notably linked low birth weight and preterm delivery to an increased risk of mortality from RDS (53, 61)

Maternal diabetes

Maternal diabetes is a known risk factor for preterm birth (4). A meta-analysis examining the relationship between maternal diabetes mellitus (DM) and neonatal respiratory distress syndrome (RDS) found a pooled odds ratio (OR) of 1.47 (95% CI 1.24–1.74). Specifically, the odds ratio for newborn RDS was 1.57 (95% CI 1.28–1.93) for gestational diabetes mellitus (GDM) and 2.66 (95% CI 2.06–3.44) for pre-gestational diabetes mellitus (PGDM) (62). Preterm birth is associated with an elevated risk of mortality due to delayed lung maturation, and this risk is further increased by maternal hyperglycemia, which can interfere with fetal surfactant production (54).

Premature rupture of membranes

A retrospective study conducted in Kabul city revealed that the odds of having the poor outcome are 5.7 times higher in neonates of mothers with PROM compared to those without PROM (AoR: 5.7, 95%CI: 1.5–22.1) (44). The condition often leads to preterm labor and can result in intra-amniotic infection, further increasing the risk of RDS in neonates and its associated complications.

Another study in north-west Ethiopia revealed that preterm neonates whose mothers had preterm premature rupture of membranes were 3.54 times more likely to face respiratory distress-related death compared to those without such experience (AOR=3.54; 95% CI: 1.167, 10.739) (56).

Antenatal care (ANC) attendance

Regular antenatal care (ANC) attendance is essential for monitoring and managing maternal and fetal health, significantly reducing the risk of preterm birth and RDS. Marinonio, Costa-Nobre (59) found that neonates whose mothers had zero to three prenatal care visits have a 1.25 times higher risk of death related to RDS compared to those whose mothers had more than three prenatal care

visits (RR: 1.25; 95% CI: 1.18–1.32). This emphasizes the importance of ensuring access to comprehensive prenatal care for all pregnant women.

2.2.2 Delivery and post-delivery factors

Mode of Delivery

The mode of delivery significantly impacts the risk of RDS in preterm infants. Marinonio, Costa-Nobre (59) demonstrated that preterm neonates delivered vaginally have a 1.29 times higher risk of death related to RDS compared to those delivered via cesarean section (RR: 1.29; 95% CI: 1.22–1.36). Studies have also reported that elective cesarean section before labor is associated with an increased risk of RDS (11). This is likely due to the lack of hormonal and physical stimuli necessary for fetal lung maturation.

Place of Delivery

The place of delivery, particularly the level of neonatal care available, affects the outcomes of RDS. Preterm neonates born in hospitals with neonatal intensive care units (NICUs) have significantly lower risks of severe RDS and mortality. (13). A study conducted in Ethiopia revealed that preterm neonates delivered in other facilities with less specialized or lower-level facilities have 3.78 times higher odds of mortality compared to those delivered in more specialized centers. (32).

A study on the survival and mortality factors of preterm neonates admitted to Felege Hiwot Specialized Hospital in Ethiopia found that neonates born at home were 2.08 times more likely to die compared to those delivered in a hospital (AOR: 2.08; 95% CI: 1.26, 3.434) (63). The findings suggest that institutional delivery may provide better access to medical care and interventions that can positively impact neonatal outcomes compared to home birth.

Surfactant administration

According to a surfactant therapy meta-analysis and systematic review, 46% of these infants received the treatment. Additionally, the research showed that the use of surfactants was linked to a lower risk of death (OR 0.45, 95% CI: 0.32 to 0.64) in newborns receiving either invasive mechanical ventilation (IMV) or non-invasive respiratory support (NRS) (64).

A similar study conducted in Canada revealed that the composite outcome rate was higher among neonates who received one or more doses of surfactant, with an increasing rate corresponding to the number of doses. The cohort that received multiple doses of surfactant showed elevated rates of mortality and significant morbidities such as severe neurological injury, bronchopulmonary dysplasia (BPD), and stage 3 or higher retinopathy of prematurity (ROP) or treated ROP, in comparison to those who received either a single dose or no surfactant. Furthermore, in the multiple-dose groups, the length of noninvasive respiratory assistance was noticeably longer (65).

Mode of oxygen delivery

A study by Isayama and Iwami found that less invasive surfactant administration (LISA) was linked to a lower probability of survival compared to continuous positive airway pressure (CPAP) alone (OR 0.58; 95% CI, 0.35–0.93) (61). Furthermore, LISA was linked to a lower chance of experiencing an air leak (OR 0.24; 95% CI, 0.05-0.96) (61).

Another study on nasal high-flow therapy in preterm infants found that treatment failure occurred in 71 out of 278 infants (25.5%) in the high-flow group, compared to 38 out of 286 infants (13.3%) in the CPAP group (risk difference of 12.3 percentage points; 95% CI, 5.8 to 18.7; $P < 0.001$). The rate of intubation within 72 hours was similar between the high-flow and CPAP groups (risk difference of 3.9 percentage points; 95% CI, −1.7 to 9.6; $P = 0.17$), and there was no significant difference in the rate of adverse events (66).

Ramaswamy, Devi and Kumar (67) state that as neonatal care has shifted from invasive ventilation to a focus on non-invasive respiratory support, various modalities have been developed, resulting in better neonatal outcomes. They also note that numerous systematic reviews and meta-analyses have shown that synchronized nasal intermittent positive pressure ventilation (NIPPV) is more effective than other non-invasive respiratory support methods for neonates. However, they emphasize that no single non-invasive ventilation (NIV) approach is ideal for every case. Therefore, the choice of NIV should be individualized, taking into consideration its effectiveness, the specific disease pathology, available resources, the clinician's expertise, and parental preferences.

Xanthine Derivatives

Xanthine derivatives, particularly caffeine citrate, are widely used in neonatal care due to their respiratory-stimulant and bronchodilatory properties. Evidence from large randomized trials, most notably the Caffeine for Apnea of Prematurity (CAP) trial, has demonstrated that caffeine reduces bronchopulmonary dysplasia, shortens the duration of mechanical ventilation, and improves long-term survival without neurodevelopmental disability among very preterm infants (68, 69). While these studies were not limited to neonates with surfactant-deficiency RDS, the mechanisms by which methylxanthines enhance diaphragmatic contractility, antagonize adenosine receptors, and decrease ventilator dependence suggest potential mortality benefits in RDS cohorts. Comparative reviews further highlight caffeine's superiority over theophylline due to its wider therapeutic window and better safety profile (70). Thus, although direct evidence linking methylxanthine use to reduced mortality specifically from RDS is limited, its physiological effects and demonstrated impact on broader neonatal respiratory outcomes make it a plausible factor influencing survival.

2.2.3 Neonatal factors

Neonatal factors play a critical role in the development and severity of Respiratory Distress Syndrome (RDS) in preterm infants. Understanding these factors is essential for improving neonatal care and outcomes.

Sex

Male infants have been reported to generally have a higher risk of mortality. A study conducted in Brazil reveled that male preterm neonates have a 1.16 times higher risk of death related to RDS compared to female neonates (RR: 1.16; 95% CI: 1.10–1.22) (59). The underlying reasons for this disparity include hormonal and developmental differences that affect lung maturation in male fetuses (59, 71).

Birth Weight

Low birth weight is a major risk factor for RDS, primarily due to insufficient surfactant production and underdeveloped lungs. A 2022 study in Ethiopia discovered that infants with birth weights under 1000 grams were 5.771 times more likely to face poor clinical outcomes compared to those weighing between 1500 and 2500 grams (AOR: 5.771; 95% CI: 4.67–12.95). (53). A similar study in Northern Ethiopia found that infants with birth weights between 1 and 1.49 kg are 4.22 times

more likely to die from respiratory distress syndrome compared to those with birth weights of 1.5 kg or greater (AOR: 4.22; 95% CI: 1.79–9.93) (61).

Gestational Age

Gestational age directly correlates with the risk and severity of RDS. Extremely preterm infants (<28 weeks) have the highest incidence of RDS. A Study conducted in Adama NICU of Ethiopia found that infants born < 28 weeks of gestation are 4.16 times more likely to have poor clinical outcome compared to those born at 34-37 weeks (AOR: 4.16; 95% CI: 4.01–12.97) (53). A related study conducted on respiratory distress and mortality among neonates revealed that infants born at less than 28 weeks of gestation have significantly higher odds of mortality due to respiratory distress syndrome compared to full-term infants (AOR: 3.32; 95% CI: 1.07–10.22) (61).

APGAR score

According to a study done in Ethiopia, babies who had APGAR scores between 4-6 at five minutes after delivery had a 4.62 times higher chance of having a poor clinical outcome than babies who had scores between 7-10 (AOR: 4.62; 95% CI: 4.19–9.26) (53). Gebreheat and Tadesse's (54) study in Ethiopia found that infants with an APGAR score of 4-6 at one minute are more likely to develop respiratory distress syndrome compared to those with a score of 7-10 (AOR: 2.22; 95% CI: 1.54–3.19). The APGAR score reflects the immediate respiratory effort and adaptability of a neonate, which influences their later respiratory function (28).

Age at admission

The age at admission to neonatal intensive care units (NICUs) is critical in assessing the severity and prognosis of RDS. In a similar study conducted by Alzubair, Hailu and Tamirat (32), preterm neonates admitted below six hours of age have 6.14 times higher odds of mortality compared to those admitted at six hours or older (AOR: 6.14; 95% CI: 1.63 - 23.03). Early admission allows for prompt intervention and respiratory support, which can mitigate the progression of respiratory compromise (14).

Hypothermia

Hypothermia in preterm infants is associated with an increased risk of RDS mortality, primarily due to impaired respiratory and metabolic functions. A study conducted in Western Ethiopia

revealed that preterm neonates who present with hypothermia at admission have a 1.6 times higher hazard of longer time to recovery resulting into death compared to those without hypothermia (AHR: 1.6; 95% CI: 1.13, 2.26) (51). Maintaining optimal thermal regulation is crucial in preventing complications and supporting respiratory stability (37).

Silverman Andersen score (SAS)

The Silverman Andersen Score (SAS), used to assess the severity of respiratory distress, correlates with the RDS related mortality. A study on clinical profiling of preterm neonates revealed that among the neonates assessed, there were 47 in the mild category, 660 in the moderate category, and 343 in the severe category. This study showed that 3 neonates (6.38%) in the mild distress group, 61 neonates (9.38%) in the moderate distress group, and 166 neonates (49.85%) in the severe distress group died (22). This indicates that mortality rate increased with higher Anderson Silverman scores thus early recognition and management based on SAS scoring are critical in improving outcomes.

Oxygen Saturation

Abnormal oxygen saturation levels at birth and throughout the neonatal period are indicators of respiratory distress and the severity of Respiratory Distress Syndrome (RDS). Infants with consistently low oxygen saturation levels (<95%) are at a higher risk of requiring extended mechanical ventilation and developing severe lung complications that could result in death. A study in Tanzania found that preterm infants with oxygen saturation below 90% six hours after admission had a 4.45-fold increased risk of dying by day seven compared to those with saturation levels of 90% or higher (6).

Time of Stay in Admission

The duration of stay in the NICU following birth correlates with RDS outcomes. Infants requiring prolonged NICU admission (>7 days) have a higher risk of developing complications such as BPD and severe RDS leading to heightened risks of neonatal mortality. According to Bacha and Hailu (41), newborns hospitalized for three to seven days face a 1.65 times higher risk of poor clinical outcomes compared to those hospitalized for more than seven days (AOR: 1.65; 95% CI: 1.09–9.48) (41). Similarly, a study in Thailand found that preterm infants who remained in the hospital

longer had a 35.5 times greater chance of survival compared to those with shorter hospital stays (OR: 35.516; 95% CI: 1.031-1.061 (72).

Random Blood Sugar Levels

Random blood sugar (RBS) levels also serve as an important prognostic marker in neonates with respiratory distress. Both hypoglycemia and hyperglycemia are common in critically ill and preterm infants, and each has been independently associated with increased mortality risk. Hypoglycemia is linked to acute neurologic injury and poor survival, while hyperglycemia is correlated with higher rates of sepsis, intraventricular hemorrhage, and death (70, 73). Recent prediction models for neonatal acute respiratory syndromes have identified low or abnormal blood glucose values as independent predictors of severe disease and mortality (74). Given that dysglycemia reflects both systemic illness severity and metabolic instability, RBS provides a readily accessible, non-invasive measure that can meaningfully improve prognostic accuracy in neonates with RDS.

2.3 Summary of the literature review

Among premature newborns, respiratory distress syndrome (RDS) is a common and serious illness marked by lung immaturity and insufficient surfactant production. Research shows that preterm newborns with RDS have widely differing mortality rates, with mortality rates as high as 31.3% at Muhimbili National Hospital and 34% in Ethiopia. Factors influencing these outcomes include neonatal and maternal factors. Outcomes like neurological complications, mortality, cardiovascular complications, risk of retinopathy of prematurity (ROP) have been highlighted.

The literature highlights the need for comprehensive interventions to address RDS among preterm neonates. These interventions should focus on improving maternal health care, promoting early surfactant administration, and developing programs to enhance neonatal intensive care practices. Despite the recognition of these issues, research on RDS among neonates in Uganda, remains scarce. This disparity emphasizes the need for additional research to comprehend early outcomes and related variables among preterm newborns with respiratory distress syndrome in order to create focused strategies to promote their wellbeing.

CHAPTER THREE: METHODOLOGY

3.1 Study design

This was a hospital-based prospective cohort study employing quantitative methods of data collection.

3.2 Study Period

The study was conducted over three months from May 2025 to July 2025

3.3 Study setting

The study was carried out at the Neonatal Special Care Unit of Kawempe National Referral Hospital. The hospital is a 200-bed capacity hospital which was created by Uganda Cabinet Minute No. 23(2018) as a National Referral Hospital to offer preventive, curative, and rehabilitative health services, and research as well as the training of students undertaking several cadres in the medical and health fields. The hospital is located in Kampala, Kawempe Division, and approximately six kilometres from the city centre - along Kampala-Gulu highway. It offers specialized health care in obstetrics, paediatrics, adolescent health, HIV/AIDS care, research, and training, with the hospital vision being “a model specialized National Referral Hospital in the country and East Africa”.

The Neonatal Special Care Unit has a bed capacity of 60 beds with four cubicles; however at times the number goes up to 120 neonates, meaning the bed occupancy goes to twice the bed capacity. The first cubicle is where all stable neonates are admitted, whether term or preterm. The second cubicle is for term neonates and is also the receiving cubicle for term neonates. Cubicle three is for the preterm neonates and is also the receiving cubicle for preterm neonates whereas cubicle four is the neonatal intensive care unit where all critically ill neonates and those requiring mechanical ventilation are admitted.

The special care unit has one neonatologist, one senior consultant, three consultants, and seven paediatricians who cover the unit on a rotation basis throughout the week. An average of four senior house officers and six medical officers also cover the unit on a rotational basis during the day and night throughout the week. The unit is manned by about 33 nurses/midwives and also receives junior house officers and intern nurses on a rotational basis.

The Neonatal Special Care Unit provides medical care for both term and preterm neonates referred from different regions of Uganda. Preterm neonates with RDS receive respiratory support through free-flow oxygen, continuous positive airway pressure or mechanical ventilation, depending on the severity of illness. Other available treatments include surfactant, caffeine citrate or aminophylline, intravenous fluids, antibiotics (ampicillin, gentamicin, cefotaxime, amikacin, PISA, Meropenem, etc), vitamin K, dextrose 10% and thermal care. Critically ill neonates and those requiring mechanical ventilation are managed in the neonatal intensive care cubicle. Through the obstetric services, eligible mothers at risk of preterm delivery may receive antenatal corticosteroids to promote fetal lung maturation. All treatment decisions, including administration of antenatal corticosteroids, surfactant and xanthine derivatives, are made by the attending clinical team according to clinical indication and availability. On average, 340 preterm neonates are admitted each month. Among these, approximately 200 cases are diagnosed with RDS, with 150 being preterm neonates.

3.4 Study Population

3.4.1 Target population

All preterm neonates in Uganda suffering from respiratory distress syndrome

3.4.2 Accessible population

All preterm neonates admitted to Kawempe National Referral Hospital's Special Care Unit with respiratory distress syndrome.

3.4.3 Actual Population

All preterm newborns with respiratory distress syndrome admitted in the Special Care Unit at Kawempe National Referral Hospital during the study period and whose mothers provided informed consent to participate in the study

Mothers of neonates whose babies fit the eligibility requirements were the respondents.

3.4 Eligibility criteria

3.4.1 Inclusion criteria

- ✓ All preterm newborns less than 24 hours old whose respiratory distress began within six hours of birth.
- ✓ Informed consent provided by the mothers.

3.4.2 Exclusion criteria

- ✓ Preterm infants with respiratory distress syndrome who needed emergency surgery during the data collection period.
- ✓ Preterm neonates with congenital anomalies identified on clinical examination were excluded; however, this applied only to, visibly detectable anomalies, as no advanced diagnostic investigations were performed.

3.5 Sample size estimation

Objective 1:

The sample size for objective 1 was determined using the formula for estimating single proportions using results from a study conducted in Tanzania where 31.3% of the study participants had died by day 7 (6).

$$N = \frac{Z^2 \times P \times (1-P)}{D^2}$$

Where,

N = required sample size

Z = Z-value corresponding to the desired level of confidence (1.96 at 95% confidence level)

p = estimated incidence proportion the population (31.3%)

d = desired margin of error or precision (0.05)

$$N = \frac{(1.96^2) \times 0.313 \times (1-0.313)}{(0.05)^2}$$

N= 330

Objective 2:

The sample size was determined using the Fleiss formula for cohort studies using results from a study that was conducted in Tanzania by Bulimba, Cosmas (6) among preterm neonates with RDS with the 6th hour temperature as the variable of interest.

$$\boldsymbol{N_{Fleiss}}=\frac{\left[z\alpha_{/2}\sqrt{(r+1)p(1-p)}+z_{\beta}\sqrt{rp_0(1-p_0)+p_1(1-p_1)}\right]^2}{(p_0-p_1)^2r}$$

$$\boldsymbol{N_{Fleiss-cc}}=\frac{N_{Fleiss}}{4}\left[1+\sqrt{1+\frac{2(r+1)}{N_{Fleiss}r|p_1-p_0|}}\right]$$

$$\boldsymbol{P}=\frac{p_0+rp_1}{r+1}$$

Where;

α = 0.05, the probability of a type I error (or significance level) is the likelihood of incorrectly rejecting a true null hypothesis.

β = 0.2, the likelihood of a Type II error (1 - test power) represents the chance of not rejecting a false null hypothesis.

P_0 = 0.263, the proportion of preterm infants having a temperature < 36.5°C at the sixth hour who died (exposed group).

P_1 = 0.418, the proportion of preterm infants having a temperature ≥36.5°C at the sixth hour who died (unexposed group).

r =1.6, the ratio of unexposed to exposed

$N_{Fleiss-cc}$ = 131 required sample size for the population 1 group using Fleiss formula with continuity correction.

N_2 = 1.6x 131= 210

Required Sample size = N1 + N2= **341**

The larger of the two sample sizes, 341, will therefore be considered.

Correcting for finite population

Applying Cochran's finite population correction. $N_{adjusted} = \frac{n}{1+\frac{n-1}{N_{pop}}}$

Where,

n is the calculated sample size=341

N_{pop} is the estimated population of preterm neonates born with RDS over a three month period =450

The corrected Sample size = 194

Adjusting for a 5% non-response = $\frac{194}{0.95}$

The final sample size = 204

3. 7 Sampling Procedure

Systematic sampling was employed to recruit participants for the study. With an estimated population of 450 preterm neonates with RDS over three months and a sample size of 204, the sampling interval was calculated as k=2. Each day of the study, the first participant was randomly chosen from the initial three preterm neonates with RDS at the hospital. This random selection was done using a ballot paper. Subsequent participants were selected at intervals of 2. The selection was made from the Special Care Unit (SCU), and the study was conducted day and night from Monday to Sunday.

3.8 Study Variables

3.81 Dependent Variables

The dependent variable in this study was the early outcomes of preterm neonates with respiratory distress syndrome. This was determined by the infant's survival status within a three-day follow-up period, categorized as either died or survived.

3.82 Independent Variables

Maternal-related factors: Age, Educational level, Parity, Mode of delivery, Place of delivery, Fever, History of Diabetes, Premature rupture of membranes (PROM), and ANC attendance

Neonatal-related factors: Sex, Birth weight**,** Gestational age**,** APGAR score**,** Age at admission**,** Hypothermia, Silverman Andersen score (SAS), Surfactant administration, Respiratory support, Oxygen Saturation**,** Time of stay in admission**.**

3.9 Data Collection Tool

A structured questionnaire was used to collect data. It was sectioned into three categories: Maternal-related factors, Neonatal-related, and the early Outcomes. A structured daily assessment tool was also used to collect data on vital signs during the follow-up period.

3.10 Data collection procedure

Recruitment of the study team

The study team consisted of the principal investigator and four research assistants. The research assistants comprised a medical officer, two registered nurses, and a midwife, all working in the Neonatal Special Care Unit at Kawempe National Referral Hospital. Their responsibilities included completing the data collection form by administering interviews to the participants.

The research assistants underwent a two-days training on the research protocol, procedures, as well as the data collection tools.

The principal investigator (PI) was solely responsible for conducting clinical assessments and was also actively involved in conducting interviews with the participants. The PI was also involved in data entry and cleaning for quantitative data. Overall, the PI provided oversight and supervised all the research activities.

Enrolment of study participants

The registered nurses and midwives were responsible for enrolling the study participants. The study participants to be enrolled were those with respiratory distress. Systematic random sampling was used for enrollment. Each day, the first participant was selected randomly using a ballot method from the first three newborns. Subsequent participants were then enrolled at intervals of every two preterm neonates. The nurses and research assistants approached the mothers, introduced the study, and sought consent. For those who provided consent, eligibility was assessed.

Preterm neonates aged less than 24 hours who developed respiratory distress within the first six hours of life were initially identified through physical examination and clinical assessment. RDS was suspected when at least two clinical signs of respiratory distress including grunting, nasal flaring, chest indrawing, intercostal/subcostal retractions, and tachypnea (respiratory rate >60/min) were present.

A chest X-ray was then performed at the earliest clinically feasible opportunity to confirm the diagnosis. Radiological features suggestive of RDS included low lung volumes, diffuse bilateral and symmetrical granular opacities, and air bronchograms. Chest X-rays were interpreted by a qualified radiologist at KNRH. For quality assurance, the first five images and every tenth image thereafter were independently reviewed by a second radiologist. Only neonates who met both the clinical and radiological criteria were included in the final study cohort. Chest X-ray was used because it was the available imaging method at the study site and the radiology team was experienced in its interpretation. Since characteristic radiological features may be subtle during the early stages of RDS, chest X-ray findings were interpreted together with the clinical presentation rather than as an isolated diagnostic test.

Both inborn and outborn preterm neonates were included. Prematurity was determined using the Last Normal Menstrual Period (LNMP) or early trimester scans and confirmed by the Ballard score (for infants weighing 1 kg or more) or foot length (for those under 1 kg). Maternal characteristics such as age, education level, parity, delivery method, delivery place, antenatal care attendance, antenatal steroid use, and history of diabetes were gathered through interviews with the mother and verified with maternal history files and antenatal cards. Prolonged premature rupture of membranes (PROM) was defined as rupture of the amniotic sac for more than 18 hours before labor onset, based on maternal history files.

Sex and birth weight were recorded from NICU records, and the infant's age at admission was noted in hours by the research assistants. The New Ballard score was used to assess gestational age. Clinical evaluations of oxygen saturation, temperature, random blood glucose levels, and the Silverman Andersen score (SAS) were conducted at admission and six hours afterward by the principal investigator (PI) and research assistants. Body temperature was measured with a digital thermometer, defining hypothermia as a temperature below 36.5°C and fever as above 37.5°C. Pre-ductal oxygen saturation (SpO2) was assessed with a pulse oximeter, with hypoxia defined as

SpO2 below 90% in room air. Blood glucose levels were measured with a glucometer, with hypoglycemia defined as below 2.4 mmol/L and hyperglycemia as above 5.4 mmol/L.

Surfactant administration was recorded, including whether it was given to manage RDS, the number of doses, and the timing of administration. Mode of oxygen delivery was evaluated based on the ventilation modality used, including mechanical ventilation, nasal continuous positive airway pressure (CPAP), free flow. The SAS was used to grade RDS severity, with a score of ≥6 indicating severe, 4 to 5 moderate, and 1 to 3 mild distress.

APGAR scores at one and five minutes after birth were recorded from the patients' files by the PI and research assistants. Daily follow-ups occurred over three days, with daily assessments of vital signs and oxygen saturation. The outcome of preterm neonates with RDS was determined within the first three days after birth, categorizing infants as either deceased or survived based on their status at that time.

3.11 Data management

The data for each participant was checked for completeness before exiting them from the study after the follow-up period. This data was then entered electronically using the Kobo Collect software setup on the study tablets. It was then uploaded onto a secure host server. The PI performed data quality checks on the uploaded data for accuracy and completeness. Data was then coded, and the database was rechecked to ensure the accuracy and completeness of the data during data entry. The data was then exported to Stata Version 16/MP (STATA CORP, TEXAS USA) for cleaning and analysis. Completed questionnaires and consent forms were kept by the PI in a secure lockable cabin for at least three years after the completion of the study.

3.12 Data Analysis

Descriptive statistics were used to describe the study sample. Continuous variables were summarized using descriptive statistics such as means and standard deviations for normally distributed data and median and interquartile range (IQR) for skewed data, while categorical variables were summarized using frequencies and percentages and displayed in tables. The outcome variable was early outcomes of preterm neonates with RDS, which was categorized as Died=1 and Survived=0.

Objective 1

The primary endpoint of the study was mortality, assessed from the date of admission to either the date of death or the end of the study. Survival curves were estimated using the Kaplan-Meier method, and differences between these curves were analyzed with the log-rank test.

Objective 2

The predictors for mortality were estimated using the Cox proportional hazards regression model with crude and adjusted hazard ratios as the measures of association. All the variables with a p value less than or equal to 0.2 at bivariate analysis were considered for multivariate analysis. P-values ≤ 0.05 at multivariate were considered statistically significant, with a confidence interval of 95%.

3.11 Quality control

- ✓ Before actual data collection, the data collection tools underwent pre-testing with 10 participants. Results from the pre-test phase were not included in the final analysis; however, adjustments to the tools were made if necessary.
- ✓ The Principal Investigator (PI) developed Standard Operating Procedures (SOPs) for data collection.
- ✓ Research assistants underwent a two-day training on the data collection tools and procedures.
- ✓ The PI or designee cross-checked filled questionnaires for completeness and accuracy daily. Any incorrect data, missing data, or inconsistencies identified during data collection were corrected before the study concluded.
- ✓ There was a second radiographer for a second opinion.

3.14 Ethical consideration

- ✓ Ethical approval was obtained from the Makerere University School of Medicine Research and Ethics Committee (SOMREC) as well as the Department of Pediatrics and Child Health at Makerere University.
- ✓ Administrative clearance was obtained from Kawempe National Referral Hospital (KNRH) prior to the study.

- ✓ The study details were explained to the heads of the special care unit where the research was conducted.
- ✓ Informed written consent for data collection was obtained from the mothers or caretakers of the neonates participating in the study.
- ✓ For critically ill neonates requiring immediate care, informed consent was deferred until the neonate had been stabilized and the mother or legal guardian was able to receive and understand the study information. Thereafter, written informed consent was obtained.
- ✓ All data collected was treated with strict confidentiality. Access was restricted to authorized study personnel only. Electronic records were stored securely on password-protected devices, and a backup copy was maintained on a password-protected portable hard drive under the principal investigator's secure custody.
- ✓ Should any data be published, no identifying information will be included to ensure anonymity.
- ✓ Confidentiality was maintained by using study numbers instead of participant names and conducting interviews in private settings.
- ✓ Chest X-rays were performed only after clinical assessment indicated suspected RDS. Although CXR involves a small amount of radiation, its diagnostic benefit was considered greater than the potential risk. Radiation exposure was minimized by limiting imaging to a single clinically indicated chest X-ray and following standard neonatal radiation-protection procedures.

3.15 Dissemination of results

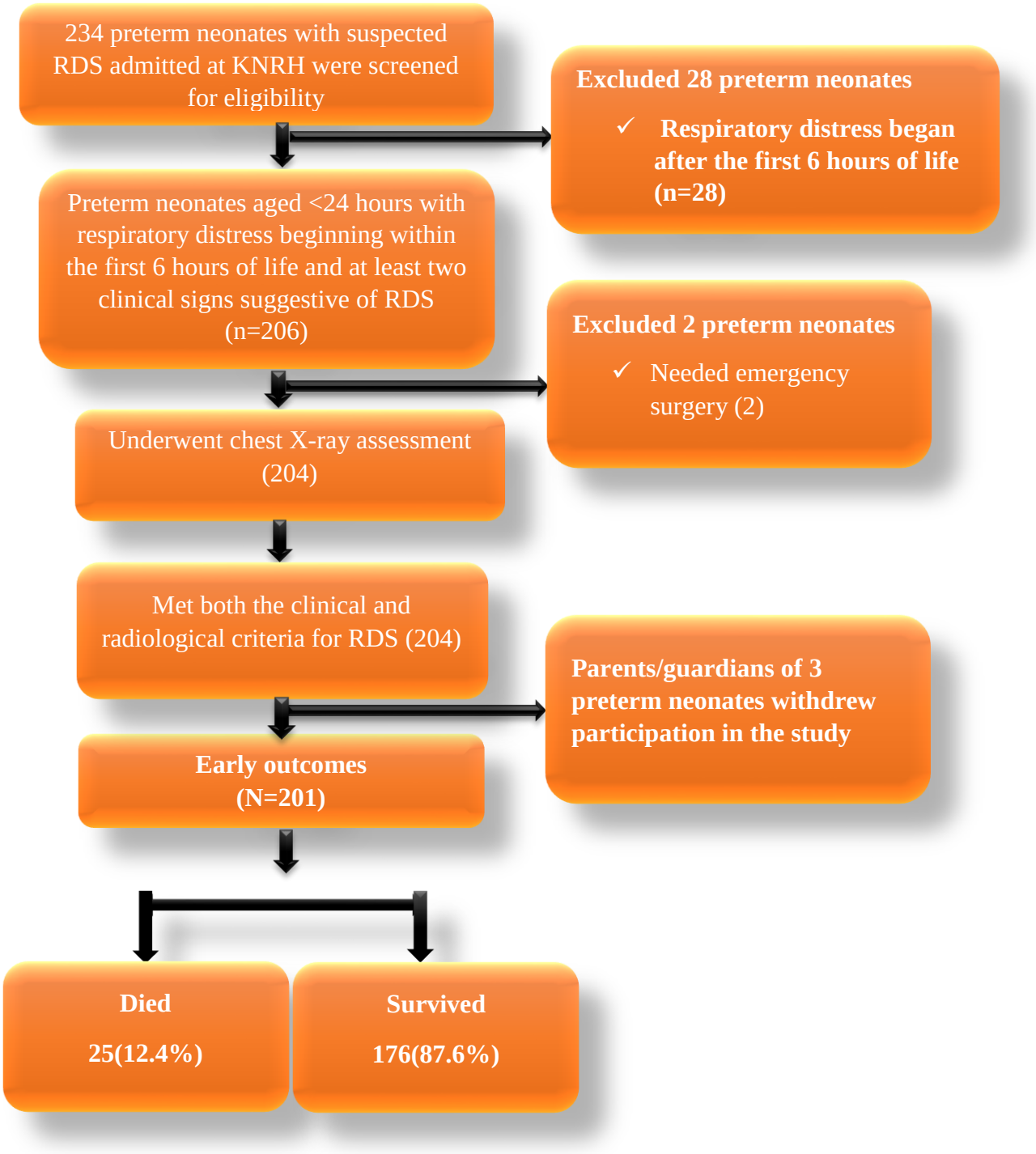
The results of this study will be compiled into a dissertation and submitted to meet the requirements for the Master of Medicine in Paediatrics and Child Health. Copies will be provided to the Albert Cook Library, the Department of Paediatrics and Child Health, the Directorate of Research and Graduate Training, and Kawempe National Referral Hospital (KNRH). Furthermore, the findings will be presented at scientific events such as conferences, workshops, and seminars, and will also be published in peer-reviewed journals.

CHAPTER FOUR: RESULTS

4.0 Introduction

This chapter presents findings on the early outcomes and predictors of mortality among preterm neonates with respiratory distress syndrome (RDS) admitted to Kawempe National Referral Hospital (KNRH). A total of 206 preterm neonates with Respiratory Distress Syndrome (RDS) were screened for eligibility, 204 were included in the study, and 3 withdrew from the study. (Fig. 2)

Figure 2: Study profile for preterm neonates with RDS admitted to KNRH



4.1 Baseline characteristics of preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital.

Neonatal-Related Characteristics

Among 201 preterm neonates with RDS admitted at KNRH, 106 (52.7%) were male. Nearly half 100 (49.8%) had a birth weight of 1000-1499g, and 113 (56.2%) had 28-31 weeks of gestation. At 5 minutes, most neonates 177 (88.1%) had an Apgar score ≥7. The majority, 113 (56.2%), were admitted within the first hour of life. Hypothermia on admission (<36°C) was common in 173 (86.1%) neonates. Severe respiratory distress (SAS ≥6) was observed in 87 (43.3%) at admission. Oxygen saturation was <90% in 96 (47.8%) neonates at admission, but improved to >95% in 130 (64.7%) at 6 hours. Random blood sugar was mostly within normal range (2.5-6.9 mmol/L) in 134 (66.7%) at admission, however at 6 hours the RBS had risen to ≥7.0 mmol/L in 138 (68.7) neonates. (Table 1)

Table 1: Neonatal Characteristics of preterm neonates with RDS admitted at KNRH

Variable	Frequency (N=201)	Percentage (%)
Sex of the neonate		
Female	95	47.3
Male	106	52.7
Birth weight (g)		
<1000g	36	17.9
1000-1499g	100	49.8
1500-2380g	65	32.3
Gestational age		
<28 weeks	37	18.4
28-31 weeks	113	56.2
32-33 weeks	31	15.4
34-36 weeks	20	10
APGAR Score at 5minutes		
<7	24	11.9
≥7	177	88.1
Age at admission in hours		
1 hour	113	56.2
2-3 hours	46	22.9
4 to <14 hours	42	20.9
Temperature at admission		
<35.5	159	79.1
35.5-37.4	39	19.4

≥37.5	3	1.5
Temperature at 6 hours		
<35.5	93	46.5
35.5-37.4	103	51.5
≥37.5	4	2.0
Silverman Anderson Score (SAS) at admission		
Mild distress (1-3)	37	18.4
Moderate Distress (4-5)	77	38.3
Severe Distress (≥6)	87	43.3
Silver Anderson Score (SAS) at 6 hours		
Mild distress (1-3)	49	24.4
Moderate Distress (4-5)	78	38.8
Severe Distress (≥6)	74	36.8
Oxygen Saturation at admission		
<90	96	47.8
90-95	74	36.8
>95	31	15.4
Oxygen Saturation at 6 hours		
<90	20	10
90-95	51	25.4
>95	130	64.7
Random Blood Sugar level at admission (mmol/L)		
<2.5	17	8.5
2.6-6.9	134	66.7
≥7.0	50	24.8
Random Blood Sugar level at 6 hours (mmol/L)		
<2.5	6	3.0
2.6-6.9	57	28.3
≥7.0	138	68.7

Delivery and post-delivery factors

Regarding the delivery and post-delivery factors, surfactant was administered to 121 (60.2%), with most 89 (73.5%) receiving it ≥24 hours after birth. CPAP was the main mode of oxygen delivery 118 (58.7%), while 69 (34.3%) received free flow oxygen and 14 (7.0%) were mechanically ventilated. Xanthine derivatives were given to 121 (60.2%) neonates. Regarding mode of delivery, 110 (54.7%) were delivered vaginally and 91 (45.3%) by cesarean section. The majority, 193 (94.0%), were delivered in health facilities, while 8 (4.0%) were delivered at home or en route. (Table 2)

Table 2: Delivery and post-delivery characteristics of preterm neonates with RDS admitted at KNRH

Variable	Frequency (N=201)	Percentage (%)
Surfactant administration		
No	80	39.8
Yes	121	60.2
Time to surfactant administration after birth (n=121)		
< 12 hours	32	26.5
≥ 12 hours	89	73.5
Mode of Oxygen Delivery		
Mechanical Ventilation	14	7.0
CPAP	118	58.7
Free Flow	69	34.3
Xanthine derivatives		
No	80	39.8
Yes	121	60.2
Mode of delivery		
Cesarean section	91	45.3
Vaginal delivery	110	54.7
Place of delivery		
Health center/clinic/Hospital	193	96.0
Home/on route to the health facility	8	4.0

Maternal-Related Characteristics

Among 179 mothers of preterm neonates with RDS, most were aged ≥25 years 101 (56.4%). More than half 96 (53.6%) had attained secondary education, while only 12 (6.7%) had no formal education. The majority had 2-3 children 76 (42.5%), and 62 (34.6%) were primiparous. None of the mothers reported a history of diabetes. Premature rupture of membranes occurred in 35 (19.6%) mothers, with 21 (60%) lasting ≥12 hours. Most mothers 164 (91.6%) attended ANC, though 121 (73.8%) had fewer than 4 visits. Single gestations predominated at 157 (89.1%), while 22 (10.9%) were multiple. Antenatal steroids were administered to 33 (18.4%) mothers, with 16 (48.5%) receiving ≥3 doses and 19 (57.6%) had the first dose administered ≥12 hours before birth. (Table 3).

Table 3: Maternal Related Characteristics of preterm neonates with RDS admitted to KNRH

Variable	Frequency (N=179)	Percentage (%)
Mothers Age		
<25 years	78	43.6
≥25 years	101	56.4
Highest level of education attained		
No formal education	12	6.7
Primary education	54	30.2
Secondary education	96	53.6
Tertiary education	17	9.5
Parity		
1 Child	62	34.6
2-3 Children	76	42.5
≥ 4 Children	41	22.9
History of diabetes		
No	179	100
Premature rupture of membranes (PROM)		
No	144	80.4
Yes	35	19.6
Duration PROM (n=35)		
< 12 hours	14	40
≥ 12 hours	21	60
ANC Attendance		
No	15	8.4
Yes	164	91.6
Number of ANC Visits (n=164)		
< 4 Visits	121	73.8
≥ 4 Visits	43	26.2
Type of gestation		
Single	179	89.1
Multiple	22	10.9
Antenatal Steroid Administration (n=179)		
No	146	81.6
Yes	33	18.4
Doses of Antenatal Steroid Administration (n=33)		
1-2 doses	17	51.5
≥ 3 doses	16	48.5
Onset of first dose to time of birth (n=33)		
<12 hours	14	42.4
≥12 hours	19	57.6

4.2 Early outcomes of preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital

Among the 201 preterm neonates with respiratory distress syndrome admitted to Kawempe National Referral Hospital, 25 (12.4%) died, yielding a mortality rate of 45.45 deaths per 1,000 person-days at risk. A total of 176 (87.6%) neonates survived during the three-day follow-up period. Three neonates were withdrew consent, reportedly due to emotional distress related to their infants' critical condition.

Survival Probability of preterm neonates with RDS admitted to Kawempe National Referral Hospital

At the beginning of follow-up (time 0), all 201 preterm neonates with RDS were at risk. By day 1, 11 neonates had died, resulting in a survival probability of 94.5%. By day 2, 13 more deaths had occurred, and the survival probability dropped to 88.1%. On day 3, 1 additional death occurred, and the survival probability further declined to 87.6%.

Table 4: Survival Probability of preterm neonates with RDS admitted to Kawempe National Referral Hospital

Day	At Risk	Deaths	Survival Probability	95% Confidence Interval
1	201	11	94.5%	0.90-0.97
2	190	13	88.1%	0.83-0.92
3	177	1	87.6%	0.82-0.91

Kaplan-Meier Survival Curve of Preterm Neonates with Respiratory Distress Syndrome

The Kaplan-Meier survival curve shows a gradual decline in survival probability among preterm neonates with respiratory distress syndrome over a 3-day follow-up period. Survival starts at 100% on day 0, drops to about 94.5% by day 1, then declines further to 88.1% on day 2, and slightly to 87.6% by day 3. Most deaths occurred within the first two days. (Figure 3)

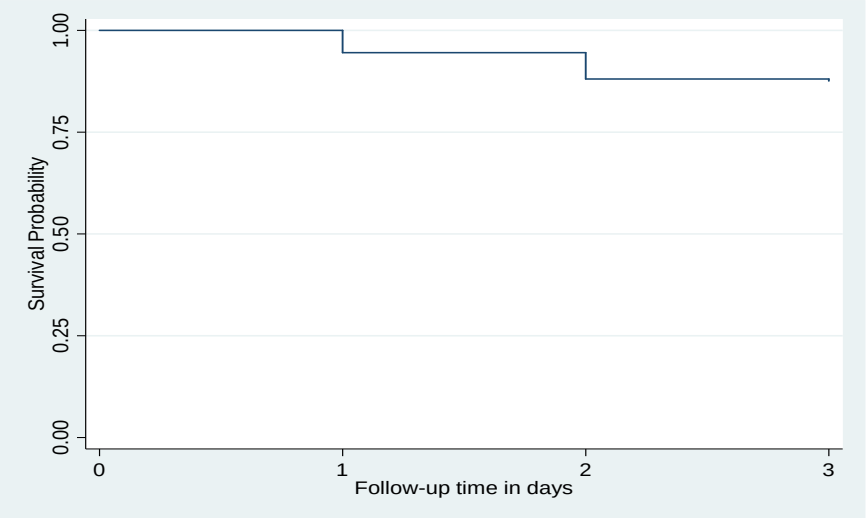


Figure 3: Kaplan-Meier Survival Curve of Preterm Neonates with Respiratory Distress Syndrome

4.3 Bivariate Analysis of predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital.

Neonatal-Related Predictors of mortality among preterm neonates with RDS admitted at KNRH

Among neonatal-related predictors, mortality was significantly higher among preterm neonates with a birth weight below 1000g (p=0.005) and those with an APGAR score less than 7 at 5 minutes (p=0.016). Severe respiratory distress at 6 hours was also strongly associated with increased risk of death (p=0.014), while oxygen saturation above 95% at 6 hours was protective (p=0.041). Borderline associations were observed with age at admission between 4-14 hours (p=0.084), severe respiratory distress at admission (p=0.067), oxygen saturation below 90% at 6 hours (p=0.096), elevated random blood sugar at admission (p=0.041), and temperature above 37.5°C at admission (p=0.003). (Table 5)

Table 5: Neonatal-Related Predictors of mortality among preterm neonates with RDS admitted at KNRH

Variable	Outcome (N=201)		cHR(95%CI)	Pvalue
	Survived (n=176)	Died (n=25)		
Sex of the neonate				
Female	83(87.4)	12(12.6)	1.00(0.46-2.19)	0.996
Male	93(87.7)	13(12.3)	1	
Birth weight				
<1000g	25(69.4)	11(30.6)	4.49(1.56-12.92)	0.005
1000-1499g	91(91)	9(9)	1.16(0.39-0.3.45)	0.794
1500-2380g	60(92.3)	5(7.7)	1	
Gestational age				
<28 weeks	29(78.4)	8(21.6)	5.08(0.64-40.65)	0.125
28-31 weeks	98(86.7)	15(13.3)	2.81(0.37-21.24)	0.318
32-33 weeks	30(96.8)	1(3.2)	0.67(0.02-10.65)	0.774
34-36 weeks	19(95)	1(5)	1	
APGAR Score at 5minutes				
<7	17(70.8)	7(29.2)	2.92(1.22-7.00)	0.016
≥7	159(89.8)	18(10.2)	1	
Age at admission in hours				
1 hour	103(91.2)	10(8.8)	1	
2-3 hors	39(84.8)	7(15.2)	1.73(0.66-4.55)	0.265
4 to <14 hours	34(81)	8(19)	2.27(0.89-5.75)	0.084
Temperature at Admission				
<35.5	137(86.2)	22(13.8)	5.35(0.72-39.71)	0.101
35.5-37.4	38(97.4)	1(2.6)	1	
≥37.5	1(33.3)	2(66.7)	40.20(3.61-447.27)	0.003
Temperature at 6 hours				
<35.5	77(82.8)	16(17.2)	2.29(0.98-5.36)	0.055
35.5-37.4	95(92.2)	8(7.8)	1	
≥37.5	3(75.0)	1(25.0)	3.58(0.45-28.68)	0.229
SAS at Admission				
Mild distress (1-3)	35(94.6)	2(5.4)	1	
Moderate Distress (4-5)	72(93.5)	5(6.5)	1.18(0.23-6.10)	0.840
Severe Distress (≥6)	69(79.3)	18(20.7)	3.91(0.91-16.85)	0.067
SAS at 6 hours				
Mild distress (1-3)	48(98)	1(2)	1	
Moderate Distress (4-5)	72(92.3)	6(7.7)	3.82(0.46-31.70)	0.215
Severe Distress (≥6)	56(75.7)	18(24.3)	12.55(1.67-94.00)	0.014
Oxygen Saturation at Admission				
<90	82(85.4)	14(14.6)	1.4(0.59-3.34)	0.446
90-95	66(89.2)	8(10.8)	1	

>95	28(90.3)	3(9.7)	0.88(0.23-3.32)	0.853
Oxygen Saturation at 6 hours				
<90	13(65)	7(35)	2.32(0.86-6.23)	0.096
90-95	42(82.4)	9(17.6)	1	
>95	121(93.1)	9(6.9)	0.38(0.15-0.96)	0.041
RBS at Admission				
<2.5	16(94.1)	1(5.9)	0.65(0.09-4.98)	0.680
2.6-6.9	121(90.3)	13(9.7)	1	
≥7.0	39(78.0)	11(22.0)	2.31(1.04-5.17)	0.041
RBS at 6 hours				
<2.5	5(83.3)	1(16.7)	1.00(0.13-7.87)	0.998
2.6-6.9	48(84.2)	9(15.8)	1	
≥7.0	123(89.1)	15(10.9)	0.69(0.30-1.58)	0.384

Delivery and post-delivery predictors of mortality of preterm neonates with RDS admitted at KNRH

Surfactant administration was significantly protective against mortality (p=0.005). Similarly, not receiving xanthine derivatives was significantly associated with increased mortality (p=0.004). Vaginal delivery showed higher mortality compared to cesarean section (p=0.032). Other factors, including time to surfactant administration (p=0.282), mode of oxygen delivery (p=0.732), and place of delivery (p=0.354), were not significantly associated with mortality. (Table 6)

Table 6: Delivery and post-delivery predictors of mortality of preterm neonates with RDS admitted at KNRH

Variable	Outcome		cHR(95%CI)	Pvalue
	Survived (n=175)	Died (n=25)		
Surfactant administration				
No	63(78.8)	17(21.3)	1	
Yes	113(93.4)	8(6.6)	0.30(0.13-0.69)	0.005
Time to surfactant administration after birth (n=121)				
<24 hours	89(88.1)	12(11.9)	1	
≥ 24 hours	19(95.0)	1(5.0)	0.41(0.05-3.13)	0.387
Mode of Oxygen delivery				
Mechanical Ventilation	14(100)	0(0)	-	-
CPAP	103(87.3)	15(12.7)	1	
Free Flow	59(85.5)	10(14.5)	1.15(0.52-2.56)	0.732
Xanthine derivatives				
No	63(78.8)	17(21.3)	3.39(1.46-7.87)	0.004
Yes	113(93.4)	8(6.6)	1	
Mode of delivery				
Cesarean section	85(93.4)	6(6.6)	1	
Vaginal delivery	91(82.7)	19(17.3)	2.73(1.09-6.84)	0.032
Place of delivery (n=179)				
Health center/clinic/Hospital	170(88.1)	23(11.9)	1	
Home/on route to health facility	6(75)	2(25)	1.98(0.47-8.40)	0.354

Maternal-Related Predictors of mortality among preterm neonates with RDS admitted at KNRH

Among maternal-related factors, having fewer than four antenatal care visits showed a borderline association with mortality among preterm neonates (p=0.070). Other variables, including Multiple gestation (p=0.116), age, parity, education level, premature rupture of membranes, and antenatal steroid administration, were not significantly associated with neonatal mortality. (Table 7)

Table 7: Maternal related predictors of mortality among preterm neonates with RDS admitted at KNRH

Variable (N=179)	Neonatal Outcome		cHR(95%CI)	Pvalue
	Survived (n=159)	Died (n=20)		
Mothers Age				
<25 years	69(88.5)	9(11.5)	1.05(0.43-2.53)	0.918
≥25 years	90(89.1)	11(10.9)	1	
Highest level of education attained				
No formal education	11(91.7)	1(8.3)	0.64(0.06-7.07)	0.717
Primary education	46(85.2)	8(14.8)	1.19(0.25-5.62)	0.823
Secondary education	87(90.6)	9(9.4)	0.77(0.17-3.55)	0.736
Tertiary education	15(88.2)	2(11.8)	1	
Parity				
1 Child	57(91.9)	5(8.1)	0.66(0.19-2.28)	0.511
2-3 Children	66(86.8)	10(13.2)	1.08(0.37-3.17)	0.883
≥ 4 Children	36(87.8)	5(12.2)	1	
PROM				
No	129(89.6)	15(10.4)	1	
Yes	30(85.7)	5(14.3)	1.32(0.48-3.65)	0.586
Number ANC Visits				
< 4 Visits	103(85.1)	18(14.9)	6.45(0.86-48.29)	0.070
≥ 4 Visits	42(97.7)	1(2.3)	1	
Antenatal Steroid Administration				
No	131(89.7)	15(10.3)	0.66(0.24-1.81)	0.416
Yes	28(84.8)	5(15.2)	1	
Type of gestation				
Single	159(88.8)	20(11.2)	1	
Multiple	17(77.3)	5(22.7)	2.20(0.82-5.85)	0.116

4.4 Kaplan-Meier Survival estimates for predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital.

Kaplan Meir Estimates by Birth weight

There is a statistically significant difference in survival between the birth weight groups (P=0.0005). Neonates with birth weight <1000g had the lowest survival probability, followed closely with those with birth weight of 1000-1499g, while neonates with birth weight 1500-2380g had the highest survival over the follow-up period (Figure 4).

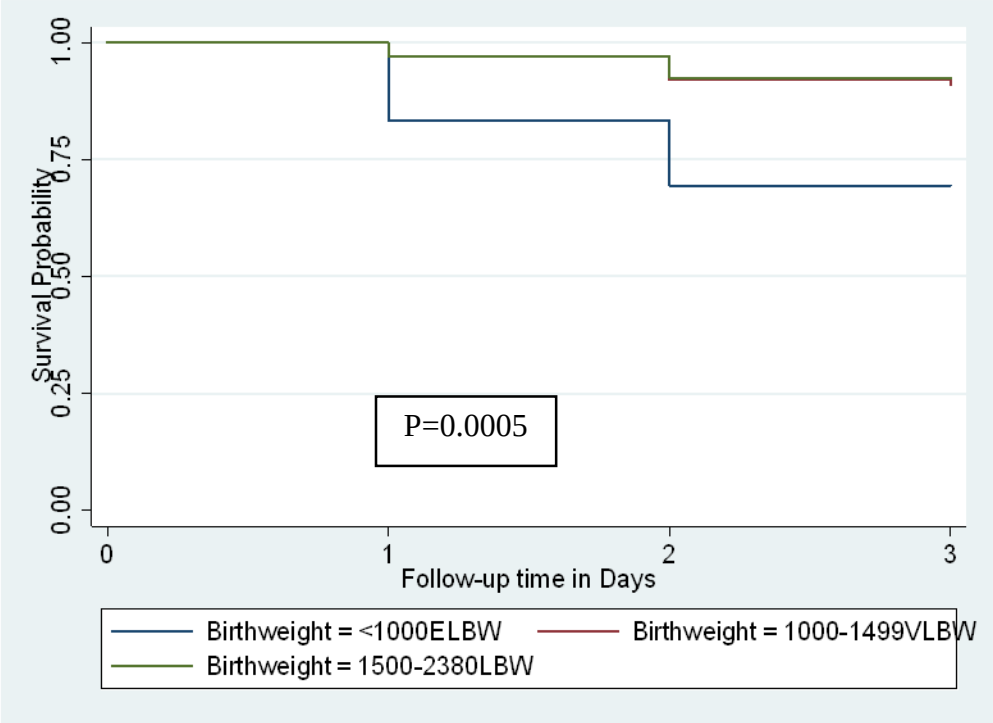


Figure 4: Kaplan-Meier Survival Estimates by Birth Weight in Preterm Neonates with RDS

Kaplan Meier survival estimates by gestational weeks

Preterm neonates born before 28 weeks had the lowest survival, with a sharp decline within the first day. Neonates born between 28-31 weeks also experienced early mortality but had better outcomes compared to the <28weeks group. However those born between 32-33 weeks showed high survival with only minimal decline, while those born between 34-36 weeks maintained nearly 100% survival over the three-day follow-up period. The survival difference between the groups, was however, not statistically significant (log-rank test, p=0.0655).

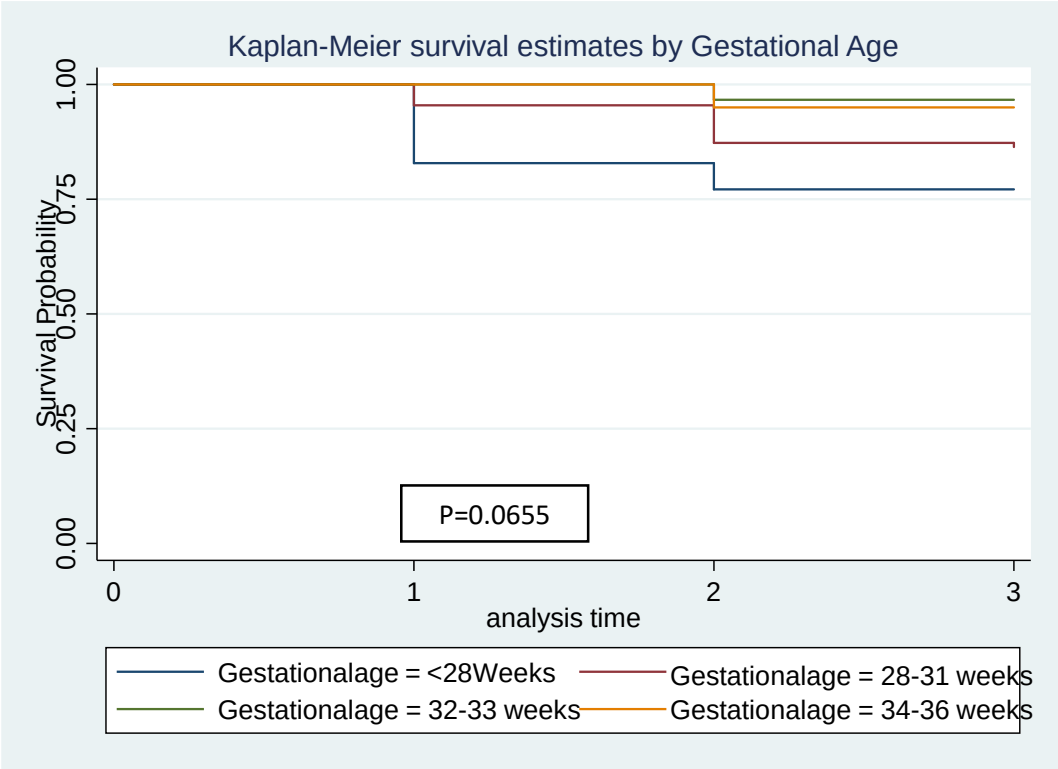


Figure 5: Kaplan-Meier Survival Estimates by Gestational Age in Preterm Neonates with RDS

Kaplan-Meier Survival Estimates by Xanthine Derivatives

Infants who received xanthine derivatives had significantly better survival than those who did not, with survival remaining near 100% during follow-up. In contrast, infants who did not receive xanthine derivatives experienced a marked decline in survival within the first two days, with survival probabilities dropping to below 80% by day three. The difference was statistically significant (log-rank test, p=0.0018).

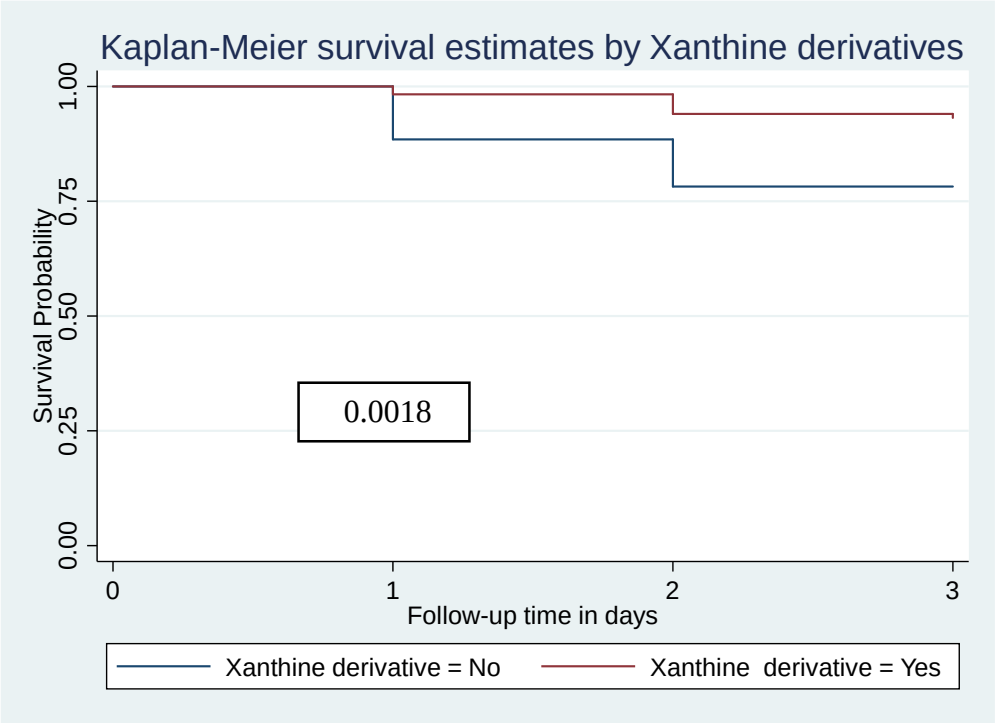


Figure 6:Kaplan-Meier Survival Estimates by Xanthine Derivatives

Kaplan-Meier survival estimates by mode of delivery

Infants delivered by cesarean section had slightly higher survival compared to those delivered vaginally. Survival among the cesarean group remained above 95% throughout the three-day follow-up, while the vaginal delivery group showed a sharper decline to about 80% by day three. The difference was statistically significant (log-rank test, p=0.0213).

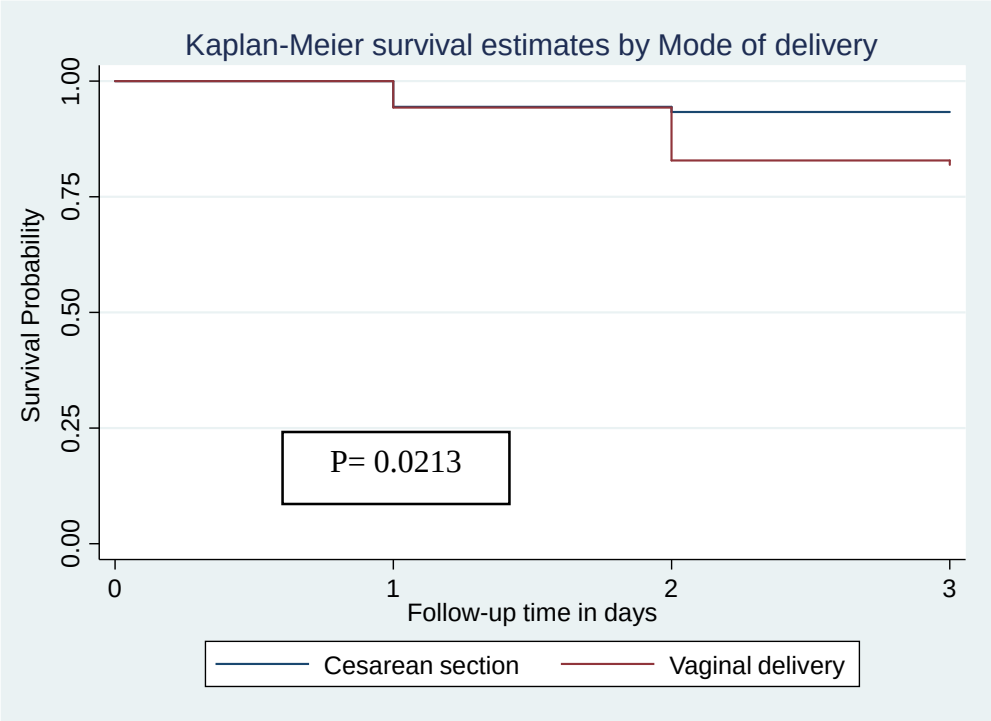


Figure 7: Kaplan-Meier estimates by mode of delivery

4.5 Multivariate Analysis of predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital.

All variables with a p-value <0.2 at bivariate analysis were considered for multivariate analysis. Confounding was tested at multivariate analysis, and the final model for multivariate included administration of xanthine derivatives, mode of delivery, birth weight, random blood sugar at admission, number of antenatal care visits, and oxygen saturation at six hours.

After adjustment for potential confounders, administration of xanthine derivatives and mode of delivery remained significant predictors of mortality. Preterm neonates who did not receive xanthine derivatives had approximately three times higher hazard of death compared with those who received xanthine derivatives (aHR=2.99; p=0.034). Similarly, neonates delivered vaginally had more than four times increased hazard of death compared with those delivered by caesarean section (aHR=4.33; p=0.013). (Table 8).

Table 8: Predictors of mortality among preterm neonates with RDS admitted at KNRH

Variable	cHR(95%CI)	aHR(95%CI)	Pvalue
Xanthine derivatives			
No	3.39(1.46-7.87)	2.99(1.09-8.23)	**0.034**
Yes	1	1	
Mode of delivery			
Cesarean section	1	1	
Vaginal delivery	2.73(1.09-6.84)	4.33(1.37-13.73)	**0.013**
Birth weight			
<1000g	4.49(1.56-12.92)	2.04(0.63-6.64)	0.236
1000-1499g	1.16(0.39-0.3.45)	0.62(0.18-2.08)	0.437
1500-2380g	1	1	
RBS at Admission			
<2.5	0.65(0.09-4.98)	1.04(0.13-8.44)	0.969
2.6-6.9	1	1	
≥7.0	2.31(1.04-5.17)	2.13(0.79-5.76)	0.135
Number ANC Visits			
< 4 Visits	6.45(0.86-48.29)	4.53(0.59-34.69)	0.145
≥ 4 Visits	1	1	
Oxygen Saturation at 6 hours			
<90	2.32(0.86-6.23)	0.59(0.15-2.35)	0.451
90-95	1	1	
≥95	0.38(0.15-0.96)	0.29(0.10-0.83)	0.061

CHAPTER FIVE: DISCUSSION

5.0 Introduction

The study aimed to determine early outcomes and predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital. 25(12.4%) of the preterm neonates with RDS died. The predictors of mortality included Lack of xanthine derivatives administration and vaginal delivery.

5.1 Early outcomes of preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital.

The findings indicate an early mortality rate of 12.4% among preterm neonates with RDS, with 25 deaths occurring within the three-day follow-up period. Mortality was concentrated within the first 48 hours, with only one additional death occurring on Day 3. This early clustering of deaths may be explained by the physiological vulnerability of preterm neonates during the immediate postnatal period, when surfactant deficiency, immature respiratory mechanics, hypoxaemia, respiratory fatigue and temperature instability are most pronounced (37, 75). Delayed surfactant administration may also have contributed to early deterioration. Although 60% of neonates received surfactant, most (73.6%) received it after 12 hours of life, beyond the optimal "golden window" of 1-2 hours post-birth, which may have reduced its early protective effect (76). In addition, Antenatal corticosteroid administration was reported in only 33 mothers. This low coverage is concerning because antenatal corticosteroids are recommended for mothers at risk of preterm delivery to reduce neonatal respiratory morbidity and mortality (77). This finding may therefore reflect missed opportunities for timely administration, especially among referred mothers. However, because information on antenatal corticosteroid use was mainly obtained from maternal reports, under-reporting or recall bias cannot be excluded.

Furthermore, the intensive care context at KNRH, while commendable, remains constrained by limited staffing, delayed triage, and resource shortages, all of which may delay recognition of deteriorating neonates and escalate mortality rates during this critical timeframe. Our findings are consistent with current national newborn situation analysis in Uganda which indicates that over half of the neonatal deaths occur within the first week of life, particularly in the first 24 hours, and are mainly due to birth asphyxia, infections, and complications of preterm birth (78). This

reinforces our observation of concentrated early deaths at KNRH and highlights the urgency of improving timeliness in surfactant administration, respiratory support, and rapid postnatal triage

When compared to findings from other low- and middle-income countries (LMICs), the mortality rate at KNRH appears relatively lower. Studies conducted in Tanzania (31.3%) (6), Ethiopia (37.4%) (79), and Bangladesh (36.5%)(80), all reported higher mortality rates. However, these studies had longer follow-up periods, ranging from 7 to11 days, which allows capturing of later deaths that might occur from complications such as infections, or persistent respiratory failure, hence the accumulation of more deaths over time. A study conducted in Kenya, conversely, reported an exceptionally high mortality rate of 72.3% among neonates with RDS, with most deaths (61%) occurring within the first 10 days (52). The possible reason for this difference might be because the study in Kenya was within preterm neonates with low birth weight which facilitates neonatal death while the current study included all birth weight groups of preterms.

Our findings show higher mortality compared to a study in Saudi Arabia, which reported a rate of 5.1% among neonates with RDS (13). This study was conducted among term neonates, who generally have better outcomes than the preterm neonates included in our study. Additionally, the study was conducted in a well-resourced setting with timely and advanced neonatal care. Similarly, a study in China reported a lower mortality of 8.06% (81). The discrepancy of results with China study might be due to the difference in NICU setup like using bubble CPAP for treatment, other advanced treatment technologies, surfactant administration-based treatment, and study design differences. Another possible reason for the difference between this study and the study in China is, that the study conducted in China was on term neonates who have better survival probability.

The findings from KNRH highlight the importance of early intervention in the management of preterm neonates with RDS. The concentration of deaths within the first 48 hours highlights the need to improve timeliness in surfactant administration. While mortality outcomes at KNRH are lower than in several comparable LMIC settings, they remain suboptimal and point to need for actionable areas for quality improvement in the care of preterm infants with RDS.

5.2 Predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital.

Neonates who did not receive xanthine derivatives had a threefold higher hazard of death compared to those who did. This finding is biologically plausible, as caffeine and related methylxanthines stimulate the central nervous system, enhance respiratory drive, and improve diaphragmatic contractility (82, 83). These effects reduce the frequency of apnea, decrease the need for mechanical ventilation, and may exert anti-inflammatory and neuroprotective benefits that improve survival (83, 84). Evidence from the CAP trial demonstrated that caffeine reduced bronchopulmonary dysplasia and improved survival without neurodevelopmental disability at 18 to 21 months, although in-hospital mortality reduction was less clear (68, 69). Subsequent meta-analyses have also reported lower rates of severe morbidities and, in some cohorts, improved survival with early caffeine initiation (85, 86). Ensuring early and consistent access to caffeine, particularly in resource-limited settings, could be a low-cost strategy to reduce mortality. Despite this well-documented benefit, the use of xanthines in our cohort was limited, even though the majority of neonates were delivered within the hospital setting. This points to a potential implementation gap, possibly related to inconsistent availability of caffeine, lack of standardized protocols, or delayed initiation in the immediate postnatal period. Strengthening supply chains, ensuring guideline adherence, and integrating early xanthine initiation into routine neonatal care could therefore be a feasible and impactful strategy to improve survival among preterm infants with RDS at KNRH.

Mode of delivery was independently associated with mortality in this study. Neonates delivered vaginally had a higher hazard of death compared with those delivered by caesarean section. One possible explanation is that caesarean deliveries, particularly when planned or anticipated for high-risk preterm births, may allow better preparation for immediate neonatal resuscitation, respiratory support and early postnatal care, thereby reducing risks of hypoxia, birth trauma, and intrapartum complications (87). In contrast, vaginal deliveries in this setting may have included preterm births that occurred rapidly, unexpectedly, or after referral delays, with less time to optimise neonatal support at birth. This could partly explain the higher mortality observed among neonates delivered vaginally.

Our findings are consistent with a study by Marinonio, Costa-Nobre (59), which demonstrated that preterm neonates delivered vaginally had a higher risk of death related to RDS compared to those delivered via cesarean section. Similarly, cesarean section deliveries have shown survival advantages in specific subgroups, such as singleton breech presentations (88). However, another study reported that elective cesarean section before labor is associated with an increased risk of RDS (11). In the present study, caesarean sections were not separated into elective and emergency procedures, and this limits further interpretation of the finding. Therefore, the observed association therefore, warrants further investigation, particularly with separation of caesarean deliveries into elective and emergency procedures.

5.3 Study strengths and Limitations

A strength of this study is the use of chest X-rays to confirm Respiratory Distress Syndrome, which minimized misclassification and improved diagnostic accuracy, thereby strengthening the validity of our findings. Additionally, to the best of our knowledge, this is the first prospective cohort study in Uganda assessing early outcomes of preterm neonates with RDS. Furthermore, the study design allows for establishment of temporal relationship between the predictors and outcomes.

However, the study was conducted at a single centre, which may limit the generalizability of the findings to other settings with different resources. The study also did not comprehensively investigate comorbidities such as neonatal sepsis, intraventricular haemorrhage, congenital heart disease and other neonatal complications, which could have been possible causes of death as well. Additionally, the effectiveness of CPAP was not assessed, which could have influenced the study outcomes. Furthermore, the study mostly relied on maternal responses which may have been limited by recall and reporting bias for some key variables like antenatal steroid use. Finally, although lung ultrasound is a radiation-free method for diagnosing RDS, it was not used because it was not routinely available and the study team lacked adequate expertise in neonatal lung ultrasound.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

This study found that early mortality among preterm neonates with respiratory distress syndrome at Kawempe National Referral Hospital occurred mainly within the first two days of life, highlighting the vulnerability of the immediate postnatal period. Lack of xanthine derivative administration and vaginal delivery were independently associated with mortality. These findings highlight the importance of ensuring timely access to caffeine therapy and considering safe delivery options for preterm births to improve survival outcomes in this high-risk population.

6.2 Recommendations

Kawempe National Referral Hospital should ensure early and consistent administration of xanthine derivatives for preterm neonates with RDS.

Kawempe National Referral Hospital should strengthen multidisciplinary delivery planning for high-risk preterm births to ensure timely obstetric decision-making, preparedness for neonatal resuscitation, and early respiratory support.

Future studies should employ more comprehensive methods to rule out comorbidities beyond overt clinical anomalies and should be conducted across multiple centres to enhance generalizability of findings

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APPENDICES

APPENDIX I: INFORMED FORM

Title of Proposed Study: Early outcomes and predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital. A prospective study.

Investigator: Wanjala Francis Xavier (Master of Medicine in Pediatrics and Child Health, Makerere University)

Email: wanjalafrancis@gmail.com **Phone:** +256-701159131

Background and rationale of the study: Babies born before 37th weeks may have difficulties in breathing. These babies have trouble breathing because their lungs are not fully ready to work on their own. This happens because the lungs haven't developed enough to make a special substance that helps keep the airways open, making it easier to breathe. When babies struggle to get enough air, it can be very serious and sometimes life-threatening. In Uganda, where many babies are born too early, this is a big problem, but there is not enough research to understand how to best help these babies survive and get better. This study aims to learn more about what helps or harms these babies, so doctors can improve the care they provide.

A description of sponsors of the research project and the organizational affiliation of the researchers: The study is sponsored by the student himself and the student is affiliated with Makerere University.

Purpose: This study aims to investigate the early outcomes and predictors of mortality among preterm neonates with respiratory distress syndrome admitted to Kawempe National Referral Hospital in Uganda.

The estimated duration the research participant will take to in the research project: This study will take approximately 30 minutes.

Procedures: Preterm infants under 24 hours of age with respiratory distress will be enrolled and evaluated for lung problems. Clinical assessments will include checking for chest indrawing and rapid breathing, while chest X-rays will confirm. The infants' oxygen levels, temperature, and

blood glucose will be monitored, and the severity of their condition will be graded. The mother will be interviewed about her medical history, and daily follow-ups of the infant's condition will take place over three days to track outcomes.

Who Will Participate in the Study? 200 preterm neonates < 24 hours of age whose respiratory distress commenced < 6 hours after birth term neonates referred to the Special Care Unit at Kawempe National Referral Hospital will participate in the study. Each participant will take approximately 30 minutes in the study.

Risks/Discomforts: While your baby participates in this study, they may experience some discomfort during routine procedures like blood glucose tests (a small prick on the heel) or when being placed under monitoring equipment. There is also a small risk of irritation from repeated monitoring or handling. However, all procedures involved are standard care for preterm infants, and the study will not involve any additional or experimental interventions that could cause harm. The research team will take all necessary precautions to minimize discomfort and risks throughout the study.

Benefits: The study offers no direct benefits to the participants however, the information you will provide will be very valuable in improving medical care through close monitoring and timely interventions, potentially improving survival rates for preterm neonates.

Confidentiality: All participant information will be kept confidential and only accessible by the research team, Makerere School of Medicine Research Ethics Committee and Uganda National Council for Science and Technology. I will ensure that your child's name is not be used in the study questionnaires nor will it be attached to any published results. I will use corresponding unique identifiers in the form of serial numbers connected to these consent forms in the study questionnaire.

Alternatives: Your child's participation is entirely voluntary and you deserve the right to pull out of the study any time you feel you can't continue with the study. There are no other alternatives as the child will continue with the normal care.

Cost: There will be no cost to participants for participating in this study.

Compensation for Participation: Every participant who consents to participate will receive 10,000 Uganda shillings as compensation for their time participating in this study.

Reimbursement: There will be no reimbursement for the study

Questions about the study: Questions pertaining this study may be addressed to the principal investigator (Wanjala Francis Xavier) via email: wanjalafrancis@gmail.com or phone: +256-701159131

Questions about participants' rights: If you have any questions about your rights as research participants, you may address them to the chairperson Makerere School of Medicine Research Ethics Committee (REC)- Professor Ocama Ponsiano on his phone (+25677241190).

Statement of Voluntariness: Participation in this study is voluntary. Participants have the right to withdraw at any time without consequences.

Dissemination of Results: Study findings from this study will be compiled into a dissertation and submitted to fulfill the requirements for the Master of Medicine in Pediatrics and Child Health. A copy will be submitted to the Albert Cook Library, Department of Pediatrics and Child Health, Directorate of Research and Graduate Training, and at Kawempe National Referral Hospital. Additionally, the results will be shared through presentations at scientific events such as conferences, workshops, and seminars, as well as published in peer-reviewed journals.

Ethical approval: This study has been approved by Makerere University School of Medicine Research and Ethics Committee.

STATEMENT OF CONSENT

..... has described to me what is going to be done, the risks, the benefits involved and my rights regarding this study. I understand that my decision to participate in this study will not alter my child's usual medical care. In the use of this information, my identity will be concealed. I am aware that I may withdraw at anytime. I understand that by signing this form, I do not waive any of my legal rights but merely indicate that I have been informed about the research study in which I am voluntarily agreeing to participate. A copy of this form will be provided to me.

Name ……Signature of parent/guardian for minors (If applicable)…Date ……...

Name……Signature of witness (if applicable)……Date…….

Name …….Signature of interviewer/Person obtaining informed consent ……Date …….

APPENDIX II: INFORMED CONSENT FORM- LUGANDA VERSION

Ennamba mu kunoonyereza: .....

Title of Proposed Study: Early outcomes and predictors of mortality among preterm neonates with respiratory distress syndrome admitted at Kawempe National Referral Hospital. A prospective study.

Akuliddemu okunoonyereza:

Dr. Wanjala Francis Xavier, omuyizi asoma ddiguli ey'okubiri mu kujjanjaba abaana, okuva mu kitongole ekivunaanyizibwa ku bulamu bw'abaana n'okubajjanjaba ekiyitibwa Department of Paediatrics and Child Health, College of Health Sciences mu yunivaasite e Makerere, ennamba y'essimu: +256-701159131, **Email:** wanjalafrancis@gmail.com

Ebikwata ku kunoonyereza n'ensonga lwaki okunoonyereza kukolebwa:

Abaana abazaalibwa nga tebanaweza wiiki asatu mu musanvu bayinza okubeera n'obuzibu mu kussa. Abaana bano baba n'obuzibu mu kussa kubanga amawuggwe gaabwe gaba teganakula bulungi okusobola okukola nga geetengeredde. Obuzibu buno bubaawo kubanga amawuggwe gaba tegakuze kimala okusobola okukola ekirungo ekisobozesa ebituli omuyita empewo okweggula okusobozesa omwana okussa obulungi. Abaana bwe batawanyizibwa okufuna empewo ebamala, kiba kizibu ky'amaanyi era ekiyinza okuteeka obulamu bwaabwe mu katyaabaga. Kino kizibu kinene, naddala mu Uganda abaana bangi mwe bazaalibwa nga tebanatuuka. Wabula tewanabeerawo kunoonyereza kukoleddwa kumala okusobola okutegeera ngeri ki gyetuyinza okuyamba abaana bano obutafa n'okubeera obulungi. Okunoonyereza kuno kugendereddwamu okumanya ebisingawo ku biki ebiyinza okuyamba oba okukosa abaana bano, olw'okusobozesa baddokita okulongoosa mu bujjanjabi bwe babawa.

Abasasulidde okunoonyereza n'ekitongole omuva omunoonyereza:

Okunoonyereza kuno kusasuliddwa omunoonyereza akuliddemu okunoonyereza kuno ye kennyini, era ng'ava mu kitongole ekivunaanyizibwa ku bulamu bw'abaana n'okubajjanjaba ekiyitibwa Department of Paediatrics and Child Health, College of Health Sciences mu yunivaasite y'e Makerere,

Ekigendrerwa ky'okunoonyereza:

Okunoonyereza kuno kugendereddwamu okuzuula biki ebiyinza okuva mu bujjanjabi obukozesebwa okujjanjaba ekizibu ky'obutassa bulungi mu baana abazaaliddwa nga tebanatuuka n'ensonga eziyinza okuvaako okufa mu baana abo ababa baweereddwa ebitanda mu ddwaliro lya gavumenti ekkulu ery'e Kawempe.

Ebbanga eyeetabye mu kunoonyereza ly'asuubirwa okumala nga yeetaba mu kunoonyereza: Okunoonyereza kuno ojja kukwetabamu okumala eddakiika amakumi asatu.

Ebinaakolebwa mu kunoonyereza:

Abaana abanaaba bazaaliddwa nga tebanatuuka era abanaaba tebanawezza ssaawa abiri mu nnya okuva lwe bazaaliddwa bajja kuwandiisibwa mu kunoonyereza kuno era bajja kukeberebwa okulaba oba balina ekizibu ky'obutassa bulungi. Okukeberebwa okunaakolebwa mujja kubaamu okukebera ekifuba, okulaba oba ekifuba kyenyika omwana bw'aba assa wamu n'okusiza okumu okumu. Obungi bwa okisigyeni omwana gw'alina, ebugumu ly'omubiri gwe ne sukaali ali mu musaayi gwe bijja kulondoolebwa. Maama w'omwana ajja kubuuzibwa ebibuuzo ebikwata ku byafaayo by'obulwadde bw'omwana era okwetegereza embeera y'omwana kujja kukolebwa okumala ennaku satu, okusobola okulaba biki ebiva mu kujjanjabibwa.

Baani abaneetaba mu kunoonyereza?

Okunoonyereza kuno kujja kwetabwamu abaana ebikumi bibiri abanaaba bazaaliddwa nga tebanatuuka, nga basindikiddwa okufuna obujjanjabi mu kifo ekiyitibwa Special Care unit mu ddwaliro lya gavumenti ekkulu e Kawempe, era abanaaba bawezeza essaawa amakumi abiri mu nnya oluvanyuma lw'okuzaalibwa, nga n'ekizibu ky'obutassa bulungi kyebalina kyatandise mu bbanga eriri wansi w'essaawa mukaaga. Buli aneetaba mu kunoonyereza kuno ajja kukubeeramu okumala eddakiika ezikunuukiriza mu makumi asatu.

Ebizibu/Okukaluubirizibwa okusuubirwa okuba mu kunoonyereza:

Omwana wo bw'anaaba yeetabye mu kunoonyereza kuno, ayinza okuwulira okukaluubirizibwa okuva mw'ebyo ebikolebwa bulijjo mu kujjanjaba, okugeza obulumi okuva mu kayiso akamufumitibwa ku kisinziiro okupima obungi bwa ssukaali ali mu musaayi oba bw'anaateekebwa mu kyuuma okumwetegereza. Wabula, byonna ebinaakolebwa by'ebyo ebikolebwa bulijjo ku

baana abazaaliddwa nga tebanatuuka era okunoonyereza kuno tekujja kugattako kintu kyonna ekiyinza okuleeta obulabe. Abanoonyereza bajja kufaayo okukendeeza obuzibu n'okukaluubirizibwa okuyinza okubaawo mu ebbanga lyonna okunoonyereza lye kunaamala.

Okuganyulwa okusuubirwa okuva mu kwetaba mu kunoonyereza:

Aneetaba mu kunoonyereza kuno tajja kuganyulwamu mu butereevu. Wabula, ebyo by'onootubuulira bijja kuba byamugaso mu kulongoosa enzijjanjaba y'abaana okuyita mu kubeetegereza n'okubaako ebikolebwa mu bwangu okusobola okulinnyisa omuwendo gw'abaana abawona oluvanyuma lw'okuzaalibwa nga tebanatuuka**:**

Okukuuma ebyaama/obwatwekisize:

Byonna ebikwata ku baneetaba mu kunoonyereza bijja kukuumibwa nga byakyaama era bijja kumanyibwa banoonyereza, abakungu okuva mu kakiiko akalung'amya okunoonyereza n'abakungu okuva mu kitongole ekivunaanyizibwa ku kunoonyereza mu ggwanga ekiyitibwa Uganda National Council for Science and Technology. Nja kufaayo okulaba nti amannya g'omwana wo tegakozesebwa ku nkalala okuli ebibuuzo ebinaabuuzibwa yadde okulagibwa mw'ebyo ebinaava mu kunoonyereza ebinaafulumizibwa. Nja kukozesa nnamba, era nga zino zezijja okukwanaganyizibwa wakati wa foomu ekkiririzibwako okwetaba mu kunoonyereza n'enkalala okuli ebibuuzo.

Ebirala ebiyinza okukolebwa nga teweetabye mu kunoonyereza.

Okwetaba kw'omwana wo mu kunoonyereza kuno kwakyeyagalire era oli waddembe okuva mu kunoonyereza kuno obudde bwonna w'owulirira nti tokyayagala kweyongerayo na kunoonyereza kuno. Tewali kirala kyetuyinza kukola nga teweetabye mu kunoonyereza, okuggyako omwana okuweebwa obujjanjabi obugabibwa bulijjo.

Eby'okusasulira:

Abaneetaba mu kunoonyereza tebajja kusasuzibwa ssente neemu okwetaba mu kunoonyereza kuno.

Okuliyirirwa olw'okwetaba mu kunoonyereza:

Buli anakkiriza okwetaba mu kunoonyereza ajja kuweebwa silingisi za Uganda omutwalo gumu (Shs. 10,000) okuliyirira obudde bwe bw'anaaba awaddeyo okwetaba mu kunoonyereza kuno.

Okuddizibwa ssente:

Tewajja kuba kuddizibwa ssente yonna olw'okwetaba mu kunoonyereza kuno.

Ebibuuzo ebikwata ku kunoonyereza:

Ebibuuzo byonna ebikwata ku kunoonyereza kuno bijja kubuuzibwa omunoonyereza akukiddemu okunoonyereza, Dr. Wanjala Francis Xavier) ng'okozesa ennamba ye ey'essimu: 0701159131 oba email ye: wanjalafrancis@gmail.com

Ebibuuzo ebikwata ku ddembe ly'eyeetabye mu kunoonyereza:

Bw'oba olina ekibuuzo kyonna nga kikwata ku ddembe lyo ng'eyeetabye mu kunoonyereza, osobola okutuukirira ssentebe w'akakiiko akalung'amya okunoonyereza akayitibwa School of Medicine Research Ethics Committee (SOMREC), polofeesa Ocama Ponsiano ng'okozesa ennamba y'essimu 077241190.

Obwakyeyagalire bw'okwetaba mu kunoonyereza:

Okwetaba mu kunoonyereza kuno kwakyeyagalire. Abaneetaba mu kunoonyereza balina eddembe okukuvaamu obudde bwonna awatali kubonerezebwa kwonna.

Okubuulira abakwatibwako ebyo ebivudde mu kunoonyereza:

Ebinaava mu kunoonyereza kuno bijja kuwandiikibwa mu kitabo ekijja okuweebwaayo okutuukiriza ebyetaago by'okuweebwa ddiguli ey'okubiri mu kujjanjaba abaana. Ekitabo kino era ekijja kuweebwa etterekero ly'ebitabo eriyitibwa Albert Cook Library, n'eri ekitongole ekivunaanyizibwa ku bulamu bw'abaana n'okubajjanjaba ekiyitibwa Department of Pediatrics and Child Health, eri Directorate of Research and Graduate Training, n'eri eddwaliro lya gavumenti ekkulu ery'e Kawempe. Ebinaava mu kunoonyereza era, bijja kugabanibwako n'abantu abalala okuyita mu misomo n'enkung'aana n'okuwandiikibwa mu bitabo omufulumira ebivudde mu kunoonyereza.

Olukusa okukola okunoonyereza:

Okunoonyereza kuno kwaweereddwa olukusa okukolebwa akakiiko akalung'amya era akakwasisa empisa mu kunoonyereza akayitibwa Makerere University School of Medicine Research and Ethics Committee.

OKUKKIRIZA OKWETABA MU KUNOONYEREZA

.....anyinnyonnyodde ebigenda okukolebwa mu kunoonyereza, ebizibu ebisuubirwa, okuganyulwa n'eddembe lyange mu kunoonyereza kuno. Nkitegedde nti okusalawo kwange okwetaba mu kunoonyereza kuno tekujja kukosa bujjanjabi omwana wange bw'aweebwa bulijjo. Mu kukozesa ebyo bye naababuulira mu kunooyereza, amannya gange n'ebirala ebinkwatako tebijja kulagibwa. Nkitegedde nti nsobola okuva mu kunoonyereza kuno obudde bwonna. Nkitegedde nti bwenteeka omukono gwange ku foomu eno, mbeera sseggyeeko ddembe lyange nalimu mu mateeka, wabula okulaga obulazi nti ntegeezeddwa ku kunoonyereza kwe nzikkirizza okwetabamu nga siwaliriziddwa. Kkopi ya foomu eno ejja kumpeebwa

Amannya g'omuzadde/Alabirira omwana: _____

Omukono/Ekinkumu ky'omuzadde: .....Ennaku z'omwezi: .....

Amannya g'omujulizi: .....

Omukono gw'omujulizi: ..... Ennaku z'omwezi: .....

Amannya g'omunoonyereza akoze ku foomu eno: .....

Omukono gw'omunoonyereza: ..... Ennaku z'omwezi: .....

APPENDIX III: QUESTIONNAIRE

Study ID ……. **Date of Data Collection** ……

Maternal Factors	
1. Mother's age 2. Maternal Initials	_____ _____
2. Highest level of education attained	[ ] No formal education [ ] Primary education [ ] Secondary education [ ] Tertiary education
3. Number of births had	_____
4. Mode of delivery for the current baby	[ ] Vaginal delivery [ ] Cesarean section
5. Place of delivery for the current baby	[ ] Home/enroute to health facility [ ] Health center/clinic/Hospital
6. History of diabetes	[ ] Yes [ ] No
7. Mother experienced premature rupture of membranes (PROM)	[ ] Yes [ ] No
7a). If yes, how long did the rupture of membranes last before onset of birth (in hours)?	_____
8). Did you attend ANC during pregnancy?	[ ] Yes [ ] No
8a). If yes, how many ANC Visits did you attend?	_____
9a). Antenatal Steroid Administration	[ ] Yes [ ] No
9b) How many doses?	_____
9c) Onset of first dose to time of birth	[ ] 0-24 hours [ ] >24-48 hours

	[ ] >48 hours
Neonatal characteristics	
10. Sex of the neonate	[ ] Male [ ] Female
11. Weight at birth (grams)	_____
12. Gestational age at birth in weeks	_____
13. APGAR score within 5 t0 10 minutes of birth	[ ] 4-7 [ ] >7 [ ] Not recorded
14. Age at admission (hours)	_____
15. Admission temperature	_____
16. Temperature at 6 hours after admission	_____
17. Silverman Andersen score (SAS) at admission	[ ] 1-3(mild) [ ] 4-5(moderate) [ ] ≥6(severe)
18. Silverman Andersen score (SAS) at 6 hours following admission	[ ] 1-3(mild) [ ] 4-5(moderate) [ ] ≥6(severe)
19. Oxygen saturation at admission	[ ] <90 [ ] ≥90
20. Oxygen saturation at 6 hours following admission	[ ] <90 [ ] ≥90
21a. Surfactant administration	[ ] Yes [ ] No
21b. Specify the time surfactant was administered	[ ] Within 12 hours [ ] After 12 hours

21b If yes, what was the total number of doses received?	_____
22. Respiratory support initiated	[ ] Continuous Positive airway pressure (CPAP) [ ] Nasal intermittent positive pressure ventilation (NIPPV) [ ] bi-level CPAP [ ] Heated humidified high-flow nasal cannula (HHHFNC) [ ] Nasal high-frequency ventilation (NHFV) [ ] Non-invasive neutrally adjusted ventilatory assist (NIV-NAVA) [ ] Oxygen by Nasal prongs [ ] Others _____(specify)
23. Random Blood sugar levels at admission	_____
24. Random Blood sugar levels at 6 hours following admission	_____
Section 3: Outcome	
25. Outcome of the neonate	[ ] Survived [ ] Died
25a. Specify the date of death	_____
26. Total Duration of Stay in Hospital (Days):	_____

Thank you for your participation in this study.

APPENDIX IV: TRANSLATED QUESTIONNAIRE (LUGANDA)

Ennamba mu kunoonyereza…… Ennaku z'omwezi**:** ……

Ebikwata ku Maama	
1. Emyaka gya Maama 2. Ennukuta ezisooka ku mannya ga Maama	_____ _____
2. Eddaala Maama lyeyakomako mu kusoma	[ ] Teyasomako mu kibiina [ ] Pulayimale [ ] Ssekendule/Ssiniya [ ] Ttendekero eryawaggulu
3. Emirundi gyeyaakazaala	_____
4. Engeri omwana gw'alina kati gyeyamuzaalamu	[ ] Yasiindika [ ] Yalongoosebwa
5.Ekifo omwana gw'alina kati gyeyamuzaalira	[ ] Awaka/Yazaalira mu kkubo ng'agenda mu ddwaliro [ ] Mu kalwaliro/Kiliniki/Ddwaliro
6. Olina obulwadde bwa ssukaali?	[ ] Yee [ ] Nedda
7. Maama yayabika ensundwe	[ ] Yee [ ] Nedda
7a). Bwekiba, Yee, okwabika ensuundwe kwaamala bbanga ki ng'ebisa tebinatandika(essaawa)?	_____
8). Wagendanga mu ddwaliro okunywa eddagala ng'oli lubuto?	[ ] Yee [ ] Nedda
8a). Bwekiba 'Yee', mirundi emeka gyewagenda mu ddwaliro okunywa eddagala?	_____
9a). Waweebwa eddagala eriziyiza omwana okuzaalibwa nga tanatuuka?	[ ] Yee [ ] Nedda
9b) Waweebwa ddoozi meka?	_____

9c) Ddoozi esooka yakuweebwa ddi nga tonnazaala	[ ] 0-24 hours [ ] >24-48 hours [ ] >48 hours
Ebikwata ku mwana	
10. Ekikula ky'omwana	[ ] Musajja [ ] Mukazi
11. Obuzito bwe mukuzaalibwa (grams)	_____
12. Ebbanga olubuto kwe lwazaalibwa(mu wiiki)	_____
13. Omuwendo ogulaga obulamu bw'omwana nga yaakazaalibwa mu ddakiika eziri wakati w'ettaano ne kkumi.(APGAR score)	[ ] 4-7 [ ] >7 [ ] Tegwawandiikwa
14. Emyaka gye mu kiseera mweyaweerwa ekitanda mu ddwaliro(Emyaka mu ssaawa)	_____
15. Ebugumu ly'omubiri gwe (Temperature) mu kiseera mweyaweerwa ekitanda mu ddwaliro	_____
16. Ebugumu ly'omubiri gwe (Temperature) oluvanyuma lw'essaawa omukaaga ng'aweereddwa ekitanda mu ddwaliro.	_____
17. Omuwendo ogulaga okukoowa omwana kweyalina nga tannasibwako okisigyeni(oxygen)	[ ] 1-3(mild) [ ] 4-5(moderate) [ ] ≥6(severe)
18. Omuwendo ogulaga okukoowa kw'omwana nga wayise essaawa mukaaga oluvanyuma lw'okuweebwa ekitanda mu ddwaliro.	[ ] 1-3(mild) [ ] 4-5(moderate) [ ] ≥6(severe)

19. Obungi bwa okisigyeni(oxygen) eyali mu musaayi mu kiseera omwana mweyaweerwa ekitanda mu ddwaliro.	[ ] <90 [ ] ≥90
20. Obungi bwa okisigyeni(oxygen) eyali mu musaayi oluvanyuma lw'essaawa omukaaga ng'omwana aweereddwa ekitanda mu ddwaliro	[ ] <90 [ ] ≥90
21a. Omwana yaweebwa eddagala eriziyiza ebituli ebiri mu mawuggwe ge obutazibikira/okwekwata awamu?	[ ] Yee [ ] Nedda
21b Bwekiba 'Yee', omwana yafuna omugatte gwa ddoozi meka?	_____
22. Okuyambibwako okussa	[ ] Continuous Positive airway pressure (CPAP) [ ] Nasal intermittent positive pressure ventilation (NIPPV) [ ] bi-level CPAP [ ] Heated humidified high-flow nasal cannula (HHHFNC) [ ] Nasal high-frequency ventilation (NHFV) [ ] Non-invasive neutrally adjusted ventilatory assist (NIV-NAVA) [ ] Oxygen by Nasal prongs [ ] Others _____(specify)
23. Obungi bwa ssukaali w'omumusaayi ku lunaku lwe yaweebwa ekitanda mu ddwaliro	_____
24. Obungi bwa ssukaali w'omumusaayi oluvanyuma lw'essaawa omukaaga ng'omwana aweereddwa ekitanda mu ddwaliro	_____
Ekitundu eky'okusatu(Ebyaava mu kujjanjabibwa)	

25. Ebyaava mu kujjanjaba omwana	[ ] Omwana yawona [ ] Omwana yaffa
26. Ennaku zonna awamu zeyamala mu ddwaliro:	_____

Weebale kwetaba mu kunoonyereza kuno.

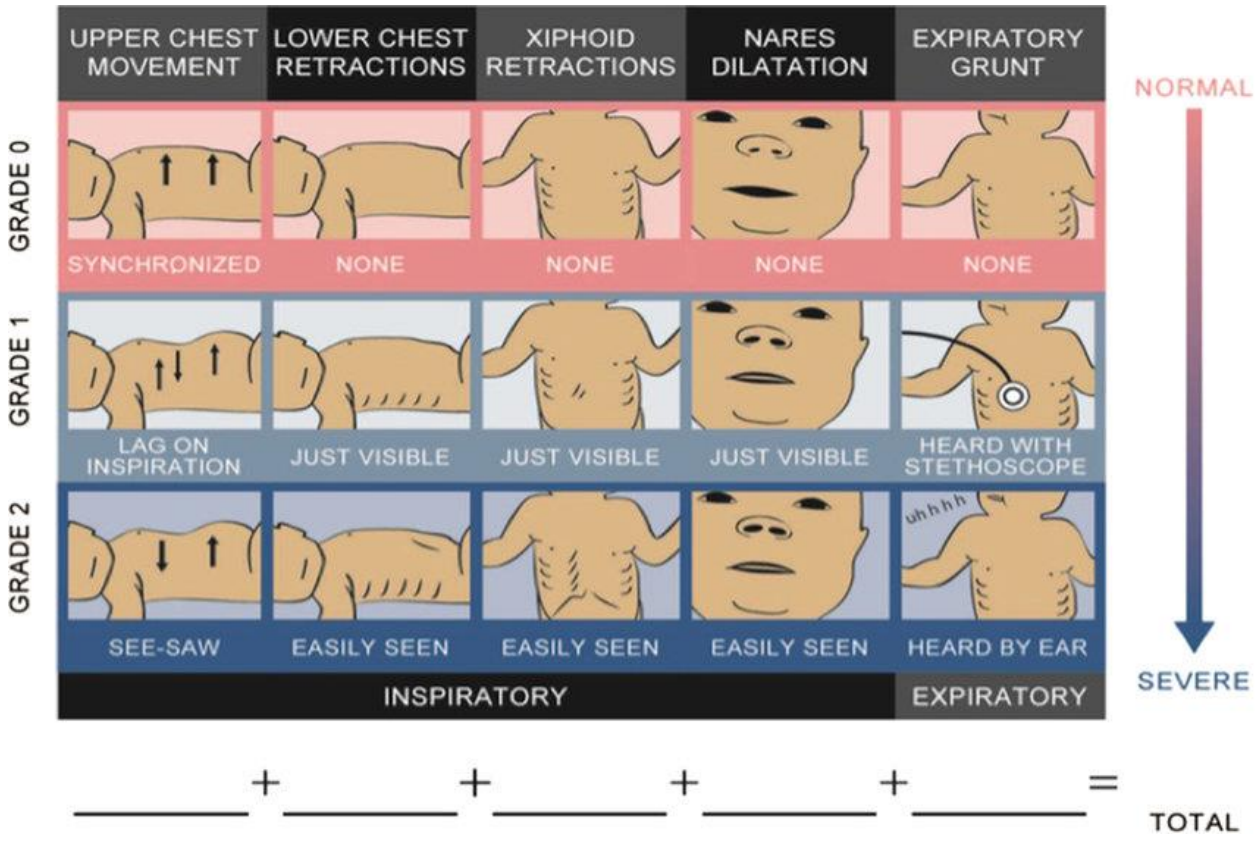
APPENDIX V: TOOL FOR DAILY ASSESEMENTS (EACH DAY FOR 3 DAYS)

Study ID NO: _____

Age: _____ Birth weight: _____

No.	Day of assessment:	Day 1- at admission	Day1 at 6 hours	Day 2 morning	Day 2 evening	Day 3 morning	Day 3 evening
1	Time of assessment:						
2	Temperature (°C):						
3	Respiratory rate:						
4	Oxygen Saturation:						
5	Silverman Andersen Score (SAS):						
6	Glucose level:						
7	Surfactant administered						
8	Dose (mg):						
9	Duration after birth:						
10	Type of Respiratory Support: 1- Free flow 2- CPAP, 3-Mechanical ventilation						
11	Xanthine derivatives given today (Yes/No):						
12	If Yes, caffeine citrate or aminophylline?						
13	Time administered:						
14	Dose:						
15	Assessed by (Name/Signature):						

APPENDIX VI: SILVERMAN ANDERSEN RESPIRATORY SEVERITY SCORE



APPENDIX VII: WORKPLAN

Activities	Jun -24	Jul -24	Aug -24	Sep -24	Oct -24	Nov -24	Dec -24	Jan -25	Feb -25	Mar -24	APr -25	May -25	Jul -25
Proposal development													
Proposal Presentation													
Proposal Submission to IRB for Review													
Data Collection													
Data entry and Analysis													
Discussion and Dissertation report													
Dissertation review by supervisors													
Dissertation presentation													
Dissertation Submission													
Dissemination of Results													

APPENDIX VIII: BUDGET

No.	Item	Quantity	Unit Price	Total Cost
1	**Stationary**			
a)	Photocopying Papers	3 reams	18,000	54,000
b)	Ruled Papers	1 ream	12,000	12,000
c)	File Folders	4 pieces	2,000	8,000
d)	Pens	4	500	2,000
	Sub Total			**76,000**
2	**Refreshments for research training**			
a)	Break fast	2 days (4 RA)	5,000	40,000
b)	Lunch	2 days (4 RA)	10,000	80,000
	Sub Total			**120,000**
3	**Internet services**	2 days	2,000	16,000
	Sub total			**16,000**
4	**Printing and Binding**			
A.	Printing			
a)	Questionnaires	200 copies (3pgs)	200 per page	120,000
b)	Proposal	4 copy (50pgs)	2,00 per page	40,000
c)	Report	4 copy (80pgs)	200 per page	64,000
	Sub Total			**224,000**
B.	**Binding**			
a)	Proposal	4 copies	3,000	12,000

b)	Report	4 copies	3,000	12,000
	Sub Total			**24,000**
4.	Supervision fee			200,000
5	Compensation fee for participants	200	10,000	2,000,000
	Compensation for research assistants	4 Ras	400,000 (per month)	4,800,000
6	Biostatician		800,000	800,000
7	Chest X-rays	200	30,000	6,000,000
8	Glucometer -One touch	1	200,000	200,000
9	Glucometer strips	16	50,000	800,000
10	Pulse oximeter	1	120,000	120,000
	Grand Total			**15,380,000**