

**SHORT TERM SURVIVAL OF PREMATURE INFANTS
ADMITTED TO THE NEW BORN UNIT AT MOI
TEACHING AND REFERRAL HOSPITAL, KENYA**

BY

**MAKOKHA FELICITAS OKWAKO MBChB (UoN)
SM/PGCHP/01/11**

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Medicine (Child Health and Paediatrics) of School of Medicine, Moi
University**

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DECLARATION

Student's declaration

I declare that this research thesis is my original work and that it has not been presented for a degree in any other university. No part of this thesis may be reproduced without the prior written permission of the author and /or Moi University

Dr. Makokha Felicitas Okwako

SM/PGCHP/01/11

Sign.....

Date.....

Supervisors' declaration

This research thesis has been submitted for examination with our approval as University supervisors.

Prof. Winstone Nyandiko M.

Associate Professor and Pediatrician

Department of Child Health and Paediatrics, Moi University

Sign.....

Date.....

Dr. Eren Oyungu

Senior Lecturer and Pediatrician

Department of Medical Physiology, Moi University

Sign.....

Date.....

DEDICATION

I would like to dedicate this thesis to my family: my husband Vincent and my sons Edgar, Levinus and Brennan for being the pillar of my strength.

ABSTRACT

Background: Prematurity is a major contributor to neonatal mortality globally and it accounts for 28% of all neonatal deaths. Preterm infants are at an increased risk of neonatal morbidity and mortality compared to full term infants. In order to achieve the fourth Millennium Development Goal, there is need for reduction of neonatal deaths especially those ascribed to prematurity. Data on hospital based survival rates for preterm infants is important for decision making by obstetricians, neonatologists and hospital management in predicting outcomes of care and development of interventions to improve outcomes of care.

Objective: To determine the proportion of premature infants admitted to the newborn unit at Moi Teaching and Referral Hospital who survive to discharge.

Methodology: This was a prospective descriptive study conducted in the newborn unit at Moi Teaching and Referral Hospital in Eldoret, Kenya. The study subjects were infants born before 37 completed weeks of gestation. A minimum sample size of 175 premature infants was required. Consecutive sampling was used to identify subjects. Data was collected using a pretested structured questionnaire and analyzed using STATA version 10.0. Descriptive statistics were used for continuous variables and frequency listing for categorical data. Cox Proportional Hazards model was used to determine factors associated with survival and Kaplan-Meier survival curves drawn.

Results: A total of 175 neonates were enrolled into the study and followed until discharge or death. There were 82 (46.9%) male and 93 (53.1%) female infants. There were 27 (15.4%) extremely preterm (less than 28 weeks), 54 (30.9%) very preterm (28 to less than 32 weeks) and 94 (53.7%) moderate to late preterm (32 to less than 37 weeks) infants. Neonatal sepsis (88.6%), hypothermia (67.4%) and respiratory distress syndrome (64.6%) were the main diagnoses made. The overall survival to hospital discharge was 60.6% (95% CI 0.53-0.68). The survival rate was 29.6% for infants born less than 28 weeks gestation, 50% for those born at 28-31 weeks and 75.5% for those born at or above 32 weeks. Of the infants who did not survive, 11 (15.9%) died within the first 24 hours while 56 (81.2%) died by the end of the first week. Gestation age of 32 weeks (HR 0.39, 95% CI 0.18-0.8), birth weight >1000g (HR 0.27, 95% CI 0.20-0.78) and maternal antenatal care attendance (HR 0.52, 95% CI 0.3-0.9) were associated with better survival. Caesarian section mode of delivery, versus spontaneous vertex delivery, was associated with increased risk of death (HR 4.26, 95% CI 1.88-9.66).

Conclusions: Two thirds of premature infants admitted to MTRH new born unit survived to discharge. The survival gestation age limit was 28 to less than 32 weeks category (50% chance of survival as per WHO). Increasing gestation age, birth weight over 1000g and maternal antenatal care clinic attendance were associated with better survival.

We therefore recommend that whenever possible preterm birth delivery should be delayed until after 28 weeks gestation.

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ACRONYMS/LIST OF ABBREVIATIONS

ANC	Antenatal care
CI	Confidence interval
Cm	Centimeter
CPAP	Continuous positive airway pressure
ELBW	Extremely low birth weight
g	Gram
GA	Gestational age
GBS	Group B Streptococcus
HIV	Human Immunodeficiency Virus
IMR	Infant mortality rate
IREC	Institutional Research and Ethics Committee
IVH	Intraventricular hemorrhage
HR	Hazard ratio
KDHS	Kenya Demographic Health Survey
Kg	Kilogram
KNH	Kenyatta National Hospital
LBW	Low birth weight
LGA	Large for gestational age
MNCH	Maternal Newborn and Child Health
MTRH	Moi Teaching and Referral Hospital
NBU	New born unit
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
PDA	Patent ductus arteriosus
RDS	Respiratory distress syndrome
SGA	Small for gestational age
UNICEF	United Nations Children's Fund
UN-MDGs	United Nations Millennium Development Goals
VLBW	Very low birth weight
WHO	World Health Organization

OPERATIONAL DEFINITIONS

Neonate	New born infant; less than 28 days old
Infant	Child up to 12 months old
Prematurity	A birth that occurs before 37 completed weeks of gestation.
Low birth weight	Weight at birth less than 2500g
Very low birth weight	Weight at birth between 1000g and 1499g
Extremely low birth weight	Weight at birth less than 1000g
Neonatal mortality	Death occurring within the first 28 days of life
Moderate to late preterm	Gestational age of 32 to less than 37 weeks
Very preterm birth	Gestational age of 28 weeks to less than 32 weeks
Extremely preterm birth	Gestational age below 28 weeks
Infant mortality	Death occurring before the first birth day
Perinatal mortality	Death occurring between 28 weeks gestational age and within 28 days of life
Post neonatal mortality	Death after 28 days to 12 months of life
Under five mortality	Death between birth and the fifth birthday
Day 1	The day of birth
Small for gestational age	Weight less than 10 th percentile for age
Large for gestation	Weight more than 90 th percentile for age
Hospital discharge	Act of allowing a patient to leave hospital after recovery or attaining recommended weight if the neonate had low birth weight
Hypothermia	Axillary skin temperature less than 35.5 degrees Celsius
Survival limit	Gestational age and birth weight at which a prematurely born fetus/infant has a 50% chance of survival

CHAPTER ONE: INTRODUCTION

1.1 Background Information

Preterm birth is the leading cause of neonatal deaths and the second leading cause of death after pneumonia in children under five years (1, 2). Mortality rates among premature infants correlate with birth weight and gestational age with decreases in both associated with poorer survival. Reliable data show that preterm births rates are increasing globally (1, 2). An equivalent of 1 in every 10 children are born preterm and around one million children die each year due to complications of preterm birth (1). In order to achieve the fourth Millennium Development Goal (MDG) of reducing the under five mortality rate by two thirds, there has to be a substantial reduction in neonatal deaths and especially those ascribed to prematurity.

It has been shown that deaths from preterm birth complications can be reduced by over 75% even without neonatal intensive care services (2). However, low coverage, poor quality, and inequities in the provision of essential antenatal interventions remain a challenge in many sub-Saharan African countries (3). With an average of only 42% of births occurring in health facilities, there is a coverage gap for obstetric and newborn care that needs to be addressed (4). The burden on health systems imposed by care of preterm infants in high-income countries is considerable and well recognized. Indeed it was estimated that the cost of care for a single preterm birth in the USA was US\$ 51 600 in the year 2005 (5). This cost is unachievable in low-income countries but is actually of greater magnitude as preterm birth rates are higher and the resources available fewer, characterized by understaffed hospitals with ill equipped or non-existent neonatal care units which ultimately result in higher neonatal mortality rates (6).

Over 90% of babies born in low-resource settings before 28 weeks gestation die in the first few days of life (< 10% die in high-income nations), a 10:90 survival gap. In developed

countries, 50% of babies born at 24 weeks survive, whereas in low-resource nations, this survival rate is not achieved until 32 weeks of gestation (2).

Most published trials of neonatal care focus on incremental gains with high-technology care for example changes in ventilation methods which in fact has limited relevance to the resource limited settings where 99% of neonatal deaths occur (7).

Over 60% of preterm deliveries worldwide occur in Sub-Saharan Africa and South Asia regions where resources for neonatal care are limited and progress to reduce neonatal mortality has been slow (2, 7, 8).

It has also been shown that strengthening existing programs within health facilities could prevent many deaths, even without high-tech equipment and supplies. Many newborn deaths could be prevented with facility-based interventions such as neonatal resuscitation, thermal care around the time of birth for all neonates, early and exclusive breastfeeding, baby hats, blankets, infection prevention (basic hand washing with soap and clean environment), and continuous positive airway pressure as well as antenatal steroids and Kangaroo Mother Care for preterm babies (9).

Friberg et al (10) argues that since low resource countries cannot be expected to scale up all essential Maternal Neonatal and Child Health (MNCH) interventions simultaneously, prioritization and phasing are required in order to generate success that will lead to increased investment and trust in health systems. Using coverage of skilled attendance at birth as a marker of health system access and equity of service delivery, Kenya was categorized in middle health system context (skilled birth attendance 30-60%) which provided a framework for assessment of priority MNCH interventions. In their model they demonstrated that increasing coverage for essential MNCH interventions could lead to 85% reduction in neonatal mortality in resource limited countries like Kenya. This study sought to determine short term survival of preterm infants as baseline information that would be used to inform Moi Teaching and Referral Hospital (MTRH) management, obstetricians, pediatricians,

neonatologists and other stakeholders on the current hospital based outcomes of preterm infants. This information will be important for decision making on the new born unit's survival limit and expected outcomes of care.

Previous studies done at Kenyatta National Hospital (KNH) and MTRH have focused on neonatal survival rates of low birth weight infants. Although concordance exists between the three low birth weight categories and the three prematurity categories, they are not interchangeable since not all low birth weight infants are preterm hence need for this study that specifically focuses on preterm infants.

Previous studies done in Kenya and other Sub Saharan countries have demonstrated high neonatal mortality rates with extremely and very low birth weight babies having the lowest survival rates. A prospective study done at KNH in 1996 showed an overall neonatal survival rate of infants less than 2000 grams to be 62.2%. None of the 23 infants born weighing less than 1000g survived to hospital discharge (11). In a prospective study done in MTRH in 1999, the seven day mortality rate of infants admitted to the special care nursery was reported to be 19.7%. Fifteen percent of the neonates admitted to the special care unit at the time of that study were preterm (12).

An unpublished study done in MTRH in the same special care unit in the year 2006 showed that the neonatal mortality of low birth weight infants was 51.6%. This was at a time when there was no continuous positive airway pressure (CPAP) for respiratory support. Similarly, none of the infants born weighing less than 1000g survived to hospital discharge (13).

A retrospective study done in Nigeria reviewing records of infants born between 1998 and 2001 in a tertiary hospital without CPAP showed an overall neonatal mortality of 19.4% with 31.9% of the mortality being attributed to prematurity (14).

It has been shown that those countries with low neonatal mortality rate achieved it even before the technological advancements seen today (15). Since preterm infants are more vulnerable compared to term infants, determining their hospital based survival rate will

provide useful baseline data which future development of strategies to improve neonatal care outcomes in MTRH would refer to.

1.2 Problem Statement

Globally 15 million babies are born prematurely and neonatal deaths account for forty percent of all deaths occurring in children under five years of age (1, 2).

According to the Kenya Demographic Health Survey (KDHS) of 2008-09, Kenya has a high neonatal mortality rate of 31/1000 live births with neonatal deaths accounting for 60% of the infant mortality rate (16).

Some of the effective high impact interventions that have reduced child, infant and neonatal mortality in developed countries are being implemented low income countries. But lack of data and contextual information for priority setting in the resource-constrained settings has hampered similar progress in developing countries.

MTRH is the second largest public hospital in Kenya, has the second largest public new born unit in the country and serves as a referral centre for all health facilities in the Western part of Kenya. The number of premature infants admitted to the new born unit has increased over the last five years and according to a clinical audit done in the year 2011, in which third of the infants admitted to the new born unit every month were preterm (12). In MTRH, there has been improvement in staff training on neonatal resuscitation, infection prevention by hand washing with soap and general hygiene, appropriate antibiotic treatment for neonatal sepsis, Kangaroo mother care, thermal provision around the time of delivery and thereafter. In addition CPAP respiratory support is now available for use in neonates with respiratory distress syndrome (RDS). Those improvements coupled with additional space and human resource were expected to improve short term neonatal survival in variance with the higher neonatal mortality among low birth weight infants reported in the same hospital in the 2006 study (13). This study therefore sought to determine survival to hospital discharge of

premature infants admitted to the new born unit at MTRH following the expansion and increase in the number of premature infants admitted to the unit.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology of Prematurity

Birth weight and gestation age have traditionally been used as strong indicators of the risk of neonatal death. World Health Organization (WHO) reported that 9.6% of all births were preterm in 2005, which translated to about 12.9 million births. Approximately 85% of this burden was concentrated in Africa and Asia, where 10.9 million births were preterm. About a half a million preterm births occurred in Europe and the same number occurred in North America (17).

Over the past two decades, the LBW rate has increased primarily because of increased number of preterm births. In the United states, in 2008, about 12.3% of all live births were less than 37 completed weeks gestational age and low birth weight infants accounted for 8.2% of live births in both 2007 and 2008 (18).

The KDHS report does not collect data on preterm births but reports data on low birth weight. According to the KDHS 2008/09, it was reported that 6% of the live births weighed less than 2500g (16). MTRH new born unit offers neonatal care to premature infants born in the hospital, those born at home and those referred from lower level health facilities.

2.2 Factors associated with prematurity

About two-thirds of preterm births are spontaneous; these births follow preterm premature ruptured membranes and preterm labour or related diagnoses, such as cervical insufficiency. Even though the primary and major determinant of birth weight is gestational age, there are other secondary factors that either directly or indirectly determine the weight of a baby at birth. It is difficult to separate completely factors associated with prematurity from those associated with low birth weight.

In a retrospective study done in Northern Tanzania to determine risk factors associated with low birth weight, it was found that gestational age below 37 weeks was strongly associated

with low birth weight. A strong positive correlation existed between preterm birth, intrauterine growth restriction and low socioeconomic status (19).

Pregnant women from families with low socioeconomic status have been shown to have higher rates of maternal under-nutrition, poor utilization of antenatal services, lower maternal age, short interval pregnancies, pregnancy related illnesses and lower maternal education level; most of which have been associated with preterm birth and low birth weight (19, 20).

In a retrospective review of 2,216 deliveries at the labour ward of the University of Nigeria, Enugu for two years, maternal age <20 years and ≥ 35 years was associated with relatively high incidence of low birth weight. Other factors identified as risk factors for delivery of LBW infants in the same study included lack of antenatal care, female gender, grand multiparty and multiple gestation (20).

Additionally, in a retrospective study done in Calabar, Nigeria to determine factors that influenced the incidence of preterm births; previous induced abortion, nulliparity, out of wedlock birth and lack of antenatal care were found to significantly increase the incidence of preterm delivery. Women with multiple pregnancy or previous preterm birth were at an increased risk of preterm delivery. Antenatal complications particularly malaria and anemia were also noted to be risk factors (21).

In a South African study done to determine obstetric causes of very low birth weight (VLBW) found that hypertension disease was present in 44.7% of the deliveries, spontaneous preterm labour in 28.8% of the cases, preterm premature rupture of membranes and congenital anomalies in 9.5% and 1.3% respectively (22).

Utilization of antenatal services in Kenya has been good with the proportion of women seeking ANC services from a trained medical provider in their most recent birth rising from 88% to 92% in the past five years. But only 15% of the mothers received ANC care during the first trimester (16).

In a study done in rural South Africa, maternal human immunodeficiency virus (HIV) infection was shown to cause small for gestation infants but not preterm births. However, infants of HIV positive mothers in this study had a 3-fold significantly increased hazard to infant death (23).

However, in a study done in Rural Mozambique between 2003 and 2006, there was no statistical difference observed in adverse pregnancy outcomes such as low birth weight, spontaneous abortion, preterm birth and still birth between HIV positive and negative mothers (24).

2.3 Spectrum of disease and Management in Premature Infants

Premature infants are at risk for developing short-term complications that result from anatomic or functional immaturity during the neonatal period.

The risk of complications increases with decreasing gestational age with serious morbidities occurring in the extremely premature infants. Immature organs of a premature infant have functional limitations leading to many physiologic challenges when adapting to the extra-uterine environment.

2.3.1 Respiratory

Respiratory distress syndrome (RDS) – occurs in 60-80% of premature infants less than 28 weeks gestation, 15-30% of those between 34-36 weeks and 5% of term babies (25).

Deficient synthesis or release of surfactant, together with small respiratory units and a compliant chest wall in preterm babies, produces atelectasis and results in perfused but not ventilated alveoli, which causes hypoxia.

In a study done in KNH new born unit in 1996 to determine survival of infants weighing less than 2000g at birth, it was reported that 43% developed RDS (11).

Another study conducted in the same unit, four years later, to quantify morbidity and mortality of low birth weight infants showed that the leading diagnosis on admission or discharge of low birth weight infants was respiratory distress syndrome at 69% (26).

For these reasons, preterm birth deliveries in MTRH are attended by clinicians experienced in neonatal resuscitation, mostly pediatrics residents.

Most effective prevention of RDS is prolongation of gestation and prevention of extreme prematurity whenever possible.

The management of RDS involves use of antenatal steroids, postnatal supplemental oxygen, exogenous surfactant and ventilatory support. Surfactant therapy for preterm infants with or at risk of RDS improves survival and reduces risk of pneumothorax (25).

Exogenous surfactant and mechanical ventilatory support are the two interventions that are not available in MTRH newborn unit.

Nasal bubble CPAP is the main respiratory support modality for premature neonates with RDS in MTRH new born unit.

Apnea is a common problem in preterm infants that may be due to immaturity of the respiratory centre or an associated illness. Apneic spells are considered clinically significant if the episodes are greater than twenty seconds duration or when shorter episodes are accompanied by hypoxia and/or bradycardia. Several theories exist regarding the pathogenesis of apnea of prematurity, none of which have been confirmed as being the single cause to date. One theory describes the role of adenosine as a central respiratory inhibitor. Adenosine is a nucleoside component of compounds such as adenosine triphosphate and cyclic adenosine monophosphate, which are crucial to numerous biochemical processes. In term infants, apnea is always worrisome and demands immediate diagnostic evaluation. Periodic breathing must be distinguished from prolonged apneic pauses because the latter may be associated with serious illnesses. Apnea is a feature of many primary diseases that affect neonates. These disorders produce apnea by direct depression of the central nervous

system's control of respiration (hypoglycemia, meningitis, drugs, hemorrhage, seizures), disturbances in oxygen delivery (shock, sepsis, anemia), or ventilation defects (pneumonia, RDS, persistent pulmonary hypertension of the newborn, muscle weakness).

In a retrospective study in KNH using records of low birth weight infants admitted from January to December 2000, 42% of the infants experienced apneic attacks during the admission period (26).

Because of limited availability of pharmacotherapeutic agents such as caffeine in MTRH new born unit, apnea is managed using methylxanthine, aminophylline.

2.3.2 Cardiovascular

Persistent patency of the ductus arteriosus is a major cause of morbidity and mortality in premature infants. Prematurity has been identified as the major predisposing factor to patent ductus arteriosus (PDA). In a prospective cohort study done at the University College Hospital, Ibadan, 35% of the preterm babies were found to have PDA compared to the overall incidence of 24.5% amongst all admissions (27).

In infants born prior to 28 weeks of gestation, a haemodynamically significant PDA can cause cardiovascular instability, exacerbate respiratory distress syndrome, prolong the need for assisted ventilation and increase the risk of bronchopulmonary dysplasia, intraventricular hemorrhage, renal dysfunction, cerebral palsy and mortality (25).

Cyclo-oxygenase inhibitors such as indomethacin and ibuprofen remain the mainstay of medical therapy for PDA, and can be used both for prophylaxis as well as for rescue therapy to achieve PDA closure. Surgical ligation is also effective and is used in infants who do not respond to medical management. Although both medical and surgical treatment have proven efficacy in closing the ductus, both modalities are associated with some adverse effects.

Because the ductus does undergo spontaneous closure in some premature infants, early identification of infants with a symptomatic PDA in MTRH new born unit is done through

clinical examination and echocardiography. Both medical management by clinicians and ligation of PDA by cardiothoracic surgeon is available at MTRH.

2.3.3 Hematologic

Anemia of prematurity occurs in low birth weight infants 1–3 mo after birth, is associated with hemoglobin levels below 7–10 g/dL, and is clinically manifested as pallor, poor weight gain, decreased activity, tachypnea, tachycardia, and feeding problems. Repeated phlebotomy for blood tests, shortened red blood cell survival, rapid growth, and the physiologic effects of the transition from fetal (low PaO₂ and hemoglobin saturation) to neonatal life (high partial pressure of oxygen and hemoglobin saturation) contribute to anemia of prematurity. The oxygen available to neonatal tissue is lower than that in adults, but a neonate's erythropoietin response is attenuated for the degree of anemia and, as a result, hemoglobin and reticulocyte count levels are low. In MTRH, anemia of prematurity is managed by transfusing packed red blood cells based on the available transfusion guidelines.

Folic acid and iron supplementation is started after two weeks and four weeks respectively to prevent anemia of prematurity. Transfusion is thought to improve oxygen transport and cardio-respiratory function thus reducing need for oxygen use and ventilatory support.

However packed red cell transfusion in preterm infants has been shown to increase the risk of necrotizing enterocolitis. In a retrospective study in the USA, the infants who received packed red cell transfusion had increased adjusted odds of developing NEC compared with infants who did not receive a transfusion (28).

2.3.4 Gastrointestinal

Hyperbilirubinemia –Preterm infants are at a greater risk of developing jaundice compared to term or normal birth weight infants.

Premature babies are prone to hyperbilirubinemia due to increased load of bilirubin to be metabolized by the liver (polycythemia, shortened red cell life as a result of immaturity or

transfused cells, increased enterohepatic circulation due to slow gastric movement, infection) and reduced ability to conjugate bilirubin due activity of the liver transferases due to prematurity.

In a Swedish population based study conducted to determine morbidity in moderately preterm infants, that is, infants born at 30 to 34 completed gestational weeks, 59% of the infants had hyperbilirubinemia (29).

A systematic review of nine studies to evaluate the efficacy of prophylactic phototherapy in preterm infants found that it helped to maintain a lower serum bilirubin concentration and may have an effect on the rate of exchange transfusion and the risk of neurodevelopmental impairment. However, it was recommended further well-designed studies that could enable to determine the efficacy and safety of prophylactic phototherapy on long-term outcomes including neurodevelopmental outcomes be done (30).

In MTRH new born unit, pathological neonatal jaundice is treated using phototherapy and exchange transfusion depending on the bilirubin levels and the clinical characteristics of the patient in reference to standard normograms.

Necrotizing Enterocolitis

Necrotizing enterocolitis (NEC) is the most common cause of gastrointestinal-related morbidity and mortality in the neonatal intensive care unit (NICU). The incidence of NEC is 1–5% of infants in neonatal intensive care units (25).

NEC is rare in term infant whereas in preterm infants it begins at 10-15 days after birth. The cause of NEC remains unclear but is most likely multifactorial. The risk factors for developing NEC are prematurity, enteral feeding, ischemia, infective agents and bacterial colonization of the gut. In a retrospective study done in Tel Aviv, Israel to determine short-term effects in human milk fed versus formula fed preterm infants; it was found that the rates of NEC were lower in the group of infants that were fed on human milk (31).

Preterm infants receiving certain treatments have been shown to have increased incidence of developing NEC. In a retrospective controlled cohort study conducted in the USA, preterm infants from 23 to less than 31 weeks who had received more packed red cell transfusions and more weeks of antibiotic therapy for nosocomial infection developed NEC than did infants who had not (32). Almost all preterm infants in MTRH newborn unit are fed on breast milk and whenever NEC is suspected, enteral feeding is stopped and the infant put on parenteral antibiotics. Complicated cases of NEC are managed by pediatric surgeons.

Nutritional problems

Preterm nutrition contributes significantly to their short term and long term outcomes.

Premature infants born weighing less than 1500 grams are not able to coordinate sucking, swallowing, and breathing. Feeding into the gastrointestinal tract (enteral feeding) helps with gastrointestinal tract development and growth (25).

The introduction of enteral feeds for very low birth weight (VLBW) infants may however be delayed due to severe respiratory distress or concern that early introduction may not be tolerated and may increase the risk of necrotizing enterocolitis.

Delay in enteral feeding may diminish the functional adaptation of the immature gastrointestinal tract and prolong the need for total parenteral nutrition which is not available in most resource limited new born units like MTRH. Early trophic feeding by giving infants very small volumes of breast milk during the first week after birth, may promote intestinal maturation, enhance feeding tolerance and decrease time to reach full enteral feeding.

According to WHO guidelines on optimal feeding of low birth weight infants in low and middle income countries, LBW infants including those with VLBW should be fed on their mother's own milk and that is what is being implemented in MTRH new born unit (33).

2.3.5 Metabolic

Hypothermia — Premature infants are at greatest risk for hypothermia immediately after birth in the delivery room and even during admission in the NBU.

Rapid heat loss occurs in premature infants because of their relatively large body surface area, thin skin and inability to produce enough heat. Heat is lost by conduction, convection, radiation, and evaporation. Hypothermia may contribute to metabolic disorders such as hypoglycemia or acidosis. In extremely premature infants of less than 26 weeks gestation, hypothermia is associated with increased mortality and, in survivors, pulmonary insufficiency.

In a population-based cohort study of 8782 very low birth weight infants born in California neonatal intensive care units in 2006 and 2007, 56.2% of the infants were found to be hypothermic. Low birth weight, cesarean delivery and a low Apgar score were associated with hypothermia in that study (34).

Standard newborn care in the delivery room to prevent hypothermia in MTRH new born unit is achieved by maintaining the room temperature at a minimum of 25°C, drying the baby thoroughly immediately after birth then removal of any wet blankets and use of pre-warmed radiant heaters if resuscitation is needed.

Premature low birth weight neonates <1500g are nursed in incubators warmer to avoid hypothermia in MTRH new born unit. Since the incubators are limited, when available patients exceed the incubator numbers, Kangaroo mother care is utilized. Triaging is done based on the gestation age, birth weight and other clinical symptoms.

Hypoglycemia

Premature babies are prone to hypoglycemia due to inadequate glycogen stores. Since glycogen is deposited during the third trimester of pregnancy, infants born prematurely have diminished reserves. There is evidence that hypoxemia and ischemia may potentiate the role of hypoglycemia in causing permanent brain damage (25).

In MTRH newborn unit, premature neonates born before arrival have a random blood sugar level taken and appropriate interventions in form of intravenous dextrose solution or feeding started as soon as possible.

2.3.6 Renal

Electrolyte imbalance

Premature infants are prone to developing hyponatremia due to urinary losses of sodium disproportionate to the intake and daily requirement.

In a comparative cohort study conducted in KNH in 1998 to evaluate the impact of early neonatal morbidity on serum sodium levels, sick preterm infants were found to develop significant hyponatremia more often than their healthy counterparts (35).

This justifies the analysis of serum electrolytes and other renal function markers in preterm infants during admission.

The smallest sickest infants are at greatest risk of metabolic bone disease due to hypocalcaemia. Progressive osteopenia with demineralized bones and occasionally pathologic fractures may develop. The major cause is inadequate intake of calcium to meet the requirements for growth. Poor intake of phosphorus and vitamin D are additional risk factors. Contributing factors include prolonged parenteral nutrition, vitamin D and calcium malabsorption, intake of unsupplemented human milk, immobilization, and urinary calcium losses from chronic diuretic use (25).

In MTRH new born unit, supplementation of vitamin D is done using multivitamin formulation containing vitamin D that is given from two weeks of age helps to prevent rickets of prematurity.

2.3.7 Central Nervous System

Intraventricular hemorrhage

Intraventricular hemorrhage (IVH) is a major complication of prematurity. IVH typically occurs in the germinal matrix, which is a richly vascularized collection of neuronal-glial precursor cells in the developing brain. It increases in frequency with decreasing gestational age and birth weight. The etiology of IVH is multifactorial and is primarily attributed to the intrinsic fragility of the germinal matrix vasculature and the disturbance in the cerebral blood flow. Severe intraventricular hemorrhage is noted in approximately 25% of infants 501–750 g; in 12% between 751 and 1,000 g; in 8% between 1,001 and 1,250 g; and in 3% between 1,251 and 1,500 g (25).

In a prospective study conducted in Nigeria between 1992 and 1994, transfontanelle ultrasound scans were performed on 93 very low birth weight neonates. Twenty two percent of the neonates had mild IVH, whereas 7.5% had moderate to severe IVH (36). There is no routine screening for IVH using cranial ultrasound in MTRH new born unit as it done in developed countries.

2.3.8 Infectious disease

Neonatal sepsis

Premature babies are prone to sepsis due to immature immune system and under developed natural barrier mechanisms. Two patterns of neonatal sepsis have been described: early-onset disease, which presents at <3 days of age, and late-onset disease, which presents at 3 days of age or later. In the 1990s, widespread implementation of maternal chemoprophylaxis led to a 65% decrease in the incidence of early-onset neonatal Group B Streptococcus (GBS) disease in the USA; from 1.7/1,000 live births to 0.6/1,000 live births, whereas the incidence of late-onset disease remained stable at 0.4/1,000 (25). Clinical presentation of sepsis in premature infants is subtle and non-specific; therefore a high index of suspicion is very important. Signs

and symptoms of sepsis include temperature instability, respiratory distress, apnoea, feed intolerance, jaundice, lethargy or irritability. Clinical diagnosis of suspected neonatal sepsis as a cause of morbidity is done in Kenya as demonstrated in a study done in KNH where 41% of the infants had a clinical diagnosis of neonatal infection (11).

Similarly, in a retrospective conducted in KNH to quantify morbidity and mortality among low birth weight infants admitted in the year 2000, 37% had suspected sepsis out of which only 14% had a blood culture done to confirm the diagnosis (31).

The first line treatment of infants with suspected sepsis is broad-spectrum antimicrobial agents; Benzyl penicillin and an aminoglycoside. Once a pathogen is identified, after culture and sensitivity results, antimicrobial therapy is narrowed.

Prevention strategies include strict compliance with hand washing and universal precautions, limiting nurse-to-patient ratios and avoiding crowding, minimizing the risk of catheter contamination, meticulous skin care, encouraging early appropriate advancement of enteral feeding, education and feedback to staff, and surveillance of nosocomial infection rates in the new born unit (25).

2.4 Short term Survival of Premature infants

Estimates of the probability of survival of very preterm infants admitted to NICU care are vital for counseling parents on expected outcomes of care and in planning to improve neonatal services. Survival rates of preterm infants have improved over the last five decades especially in developed countries and trends well documented (2).

Developed countries have higher survival for newborns with birth weights above 1000g at 94% (20). In developed countries there were major changes in both obstetric and neonatal care during the 1990s. These changes were associated with decreases in mortality and morbidity for VLBW infants. In these such countries, they are currently concentrating on

improving outcome of babies with birth weight 500g to 1000g and they are already reporting good survival as exemplified by survival rates of 55% and 88% for neonates between 501-750 g and 751-1000g surviving respectively in the USA (25).

In Kenya and other Sub-Saharan countries, survival rates of very low birth weight and who mostly are premature infants are still low. A prospective study done at KNH in 1996 showed overall survival to hospital discharge for infants less than 2000 grams to be 62.2%. None of the 23 infants born less than 1000g survived the neonatal period in that study (11). In a prospective study done in MTRH in 1999, the perinatal mortality of neonates admitted to the special care nursery was 19.7% (12). An unpublished study done in MTRH in the same special care nursery in 2006 showed overall survival for neonates below 2000g was 48.4% (13). A retrospective study in Nigeria reviewing records of children born between 1998 and April 2001 in a tertiary hospital without CPAP had an overall mortality of 19.4% with 31.9% of the mortality attributed to prematurity (14).

All these studies demonstrated low survival rates for premature infants especially the extremely preterm babies.

2.5 Factors affecting Short term Survival of Premature infants

2.5.1 Fetal factors

Gestational age and birth weight are the most important determinants of premature infant short term survival. Mortality rates amongst premature infants correlate with birth weight and gestational age with decreases in both associated with poorer survival (25). Thus infants born with the lowest gestational age and birth weight have the largest impact on infant mortality because they have the greatest risk of death. In two different studies conducted in KNH and MTRH new born units, the neonatal mortality rate among infants weighing less than 1000g was 100% (11, 13). The gestation age specific survival rate in the KNH study was low for the extremely preterm infants with only 9% of those born less than 28 weeks gestation

surviving (11). Male gender and low Apgar score at 5 minute have also been associated with poor survival.

In a study done by in South Africa to determine survival of very low birth weight infants, male gender and low Apgar score at 5 minutes, were associated with poor survival (37).

Birth weight-specific neonatal diseases such as grade IV intraventricular hemorrhage, neonatal sepsis (severe group B streptococcal pneumonia or meningitis), and neonatal malformations e.g. pulmonary hypoplasia also contribute to a poor outcome (25).

2.5.2 Maternal factors

Lack of antenatal care clinic attendance by pregnant mothers has been associated with poor preterm infant survival. In a study done to determine survival of very low birth weight infants in a public hospital in South Africa, infants whose mothers did not attend ANC had poor survival (37). Mode of delivery has been shown to affect survival of infants with spontaneous vertex delivery having higher mortality compared to Caesarean section as reported in studies done in KNH, MTRH and South Africa (26, 37).

Maternal antenatal use of steroids by pregnant women has been associated with lower incidence of RDS and better survival (25).

2.5.3 Level of care

Premature infants are more likely to survive if they are born in high level neonatal intensive care than in lower level hospitals with limited facilities.

The new American Association of Pediatrics neonatal levels of care consist of four levels with no subdivisions:

Level I: Provides basic neonatal care for term babies; can perform neonatal resuscitation at every delivery and care for infants born at 35-37 weeks gestation who remain physiologically stable.

Level II: Provides specialty care for newborns at 32 weeks' gestation or more and weighing 1,500 grams or more with problems expected to resolve rapidly or who are convalescing from a higher level of intensive care.

Level III: Provides sub-specialty care for high-risk newborns needing continuous life support and comprehensive care for critical illnesses. This includes infants weighing less than 1,500 grams or who were less than 32 weeks' gestation at birth.

Level IV: Includes capabilities of a level III neonatal intensive care unit (NICU) as well as the ability to provide on-site pediatric medical and surgical subspecialists to care for infants with complex congenital or acquired conditions, coordinate transport systems, and provide outreach education within their catchment area. Level IV intensive care units have the highest neonatal survival rates. The relative risk of neonatal mortality for infants born with very low birth weights was twofold higher in Level II centers than in Level III centers (5).

Improvements in newborn intensive care, including the use of surfactant treatment and antenatal steroid therapy to prevent and treat neonatal respiratory distress syndrome, have resulted in decreased mortality rates of preterm infants, except in those who are at the limit of viability (17).

In a retrospective cohort study conducted in a South African tertiary public hospital, in a level II NICU focusing on deliveries conducted from the year 2000 to 2002, low survival to hospital discharge of the extremely preterm infants was attributed to the lack or limited availability of exogenous surfactant and mechanical ventilation. (37). The level of care provided at MTRH new born unit given the available facilities is at level II since there is no exogenous surfactant and no facilities for continuous ventilatory support like conventional mechanical ventilation.

CHAPTER THREE: RESEARCH QUESTION, OBJECTIVES AND JUSTIFICATION

3.1 Research Question

What proportion of premature infants admitted to the new born unit at Moi Teaching and Referral Hospital survive to discharge?

3.2 Objectives

3.2.1 Primary Objective

To determine the proportion of premature infants admitted to the newborn unit at Moi Teaching and Referral Hospital who survive to discharge.

3.2.2: Secondary Objectives

1. To determine the survival in the different gestational age categories; less than 28 weeks, 28 to less than 32 weeks and 32 to less than 37 weeks.
2. To describe the factors that are associated with short term survival of premature infants admitted to the new born unit at MTRH.

3.3 Justification of the Study

Neonatal survival data has been utilized by countries and NICUs to demonstrate trends in preterm birth outcomes over the years (2). It is difficult to formulate appropriate interventions to improve neonatal care and outcomes without reliable data on survival rate.

In KNH and MTH earlier studies done focusing on survival of low birth weight infants reported poor survival of very low birth weight and extremely low birth weight infants most of whom are known to be preterm (11,13).

In MTRH, there has been significant increase in the number of preterm infants admitted to the new born unit following the expansion of the unit. However, both the short term and long term survival of preterm infants admitted to the new born unit had not been documented (12).

Facility specific data on survival of preterm infant and causes of morbidity and mortality would help the MTRH management to develop interventional strategies aimed at improving outcomes of this vulnerable group of patients. The findings will be useful to obstetricians, paediatricians and neonatologists when making decisions on delivery and care of these preterm infants and when counseling parents on expected outcomes. Findings of this study may also be used for advocacy to improve neonatal services at MTRH and other public facilities in the country taking care of preterm infants.

Lastly, this information will help advice the peripheral facilities on appropriate referral of mothers with preterm labour to MTRH given the viability limit findings from this study.

We projected that at the current rate of preterm birth deaths and with few years remaining, Kenya is unlikely to achieve the fourth MDG target of reducing under five mortality rate by the year 2015 and even beyond 2015 (16).

CHAPTER FOUR: METHODOLOGY

4.1 Study design

This was a prospective descriptive study. Study participants were recruited at admission by the principal investigator and followed during their stay in the unit, taking note of all significant clinical events until either discharge home or death. There was no intervention by research team.

4.2 Study site

The study was conducted in the newborn unit of MTRH which is located in Eldoret town, about 300km from Nairobi, in Uasin Gishu County, Kenya. The hospital is an 800 bed capacity tertiary hospital that serves as a referral hospital for the western part of Kenya, with a catchment population of about 13 million people - 33% of Kenyan population. The hospital provides various services ranging from primary to specialized care and serves urban, peri-urban and rural populations from near and far counties. The hospital also serves patients from neighboring countries; Uganda, Sudan, South Sudan and Rwanda.

The hospital's new born unit is located in the Riley Mother and Baby hospital wing, a new extension of the hospital that was opened in 2009. The NBU has a capacity of fourteen incubators, forty eight cots and is able to provide basic neonatal services and non invasive respiratory support using nasal bubble CPAP. The unit does not have a neonatal intensive care unit (NICU) and does not provide mechanical ventilation and exogenous surfactant for preterm babies.

The staffs allocated to the unit include two neonatologists, three pediatricians, thirty five nurses, a nutritionist, paediatrics resident doctors, medical officer interns and clinical officer interns.

All premature low birth weight neonates weighing less than 1700g, born in the MTRH labour ward, born at home or referred from lower level health facilities in the catchment area are

admitted to the MTRH new born unit. They are managed using the basic Pediatric protocol in Kenya which has been adopted from the WHO guidelines.

4.3 Study Population

Premature neonates admitted to the MTRH new born unit from December 2012 to August 2013 who met the inclusion criteria were recruited. This included premature neonates born in MTRH labour ward, those referred from other health facilities and those born at home.

Inclusion Criteria

- a) Neonates who were born at less than 37 completed weeks gestational age.
- b) Preterm neonates whose mothers gave informed consent to have their infants enrolled in the study.

Exclusion Criteria

- a) Preterm infants with congenital malformations not compatible with life.

4.4 Sample Size

The Fischer's formula for calculating the sample size for a simple random sample without replacement was used as follows; $N = \frac{Z^2_{\alpha} P (1-P)}{W^2}$

Where:

Z_{α} is the standard normal deviate and =1.96 for a 95% confidence level

P is the expected proportion of premature infants who survive to discharge in MTRH, 50%. In studies done in similar resource-poor settings birth weight (not gestational age) has often been used as a proxy measure for maturity, thus getting short term survival proportion as an outcome measure is difficult. This study therefore used a median value of 50% since the exact outcome proportion is unknown.

W is the desired width of the confidence interval and = 0.05

Thus: Replacing these values in the above formulae:

$$= \frac{(1.96^2 * 0.5^2)}{(0.05)^2} = 384$$

Adjusting for finite population for premature infants admitted to MTRH new born unit based on the 2011 hospital medical records where an average of 30 premature neonates were admitted per month, for 9 months: 270

Thus: $n_f = \frac{n_0}{1 + \frac{n_0}{N}}$; N=270 (N= the population size while n_f = is the finite sample size)

$$n_f = \frac{384}{1 + \frac{384}{270}} = 158.6; \approx \mathbf{159}$$

Adjusting for transfer outs, an additional 10% more were recruited giving a final sample size of 175 premature infants.

4.5 Sampling Technique

Consecutive sampling of premature neonates admitted to MTRH new born unit was done. Every next study subject meeting the inclusion criteria was recruited until the desired minimal sample size of 175 was attained.

4.6 Outcome measures

The primary outcome measure was the proportion of premature infants who survived to hospital discharge. The secondary outcome was the length of hospital stay.

4.7 Data Collection

Data was collected by the principal investigator using a pretested standard questionnaire and follow up data collection form. The demographic data, neonatal and maternal characteristics were entered in the data collection form at admission. Gestation age was calculated using two

methods; the last menstrual period (LMP) as an entry point and then New Ballard score method for analysis. For most of the infants, there was no significant difference between gestational age by LMP and that by new Ballard score. Infants' anthropometric measurements; weight, length and head circumference were taken by the PI or research assistant. Any missing maternal data was obtained through maternal interview and by checking the ANC attendance booklet.

4.8 Study Execution

The clinicians working in the new born unit were sensitized about the study to enable them inform the principal investigator and research assistant, a NICU nurse, whenever preterm infants were admitted in the new born unit. The research assistant identified infants born at less than 37 completed weeks by LMP and informed the principal investigator. Mothers' of premature infants were identified in the postnatal ward or hostel and informed written consent was obtained from those whose babies met the inclusion criteria.

The gestational age was determined by calculating the number of weeks from the first day of the last menstrual period and confirmed using the new Ballard score within 48 hours of admission (38). The infant's demographic data, maternal antenatal and delivery data and the clinical characteristics were collected by the principal investigator at admission through an interview of the mother and physical examination of the baby.

Information on whether the mother had started attending ANC and their HIV serology status was obtained. Presence of any antenatal and perinatal maternal morbidity was noted.

Anthropometric measurements taken at admission were birth weight in grams (g), length and head circumference in centimeters. Weight was measured using electronic digital weighing scale, SECA model 728 to the nearest 1g.

The diagnosis made and interventions started at admission were recorded. The participants received standard newborn care based on the diagnosis made as per the new born care

protocol. Daily ward rounds were done by the health care providers in NBU and appropriate investigations done to diagnose any new causes of morbidity suspected.

The principal investigator followed up the study subjects and collected information on the significant events; causes of morbidity and interventions received during hospitalization and updated the information in the follow up data collection form until discharge or death. . The length of stay and final outcome were noted.

Discharge was decided by the clinicians taking care of the subjects in the new born unit upon recovery or achieving the recommended weight for discharge.

4.9 Data management, data analysis and presentation

Data collected was coded to maintain confidentiality and then entered into a Microsoft access data base. Data was then checked for consistency by providing validation checks in Microsoft access. Data was then exported to STATA version 10.0 for analysis.

The data was analyzed at 95% level of confidence. Descriptive statistics such as mean and median were used for continuous variables. Frequency listings and percentages were used to describe categorical variables. Survival analysis was done using Cox Proportional Hazards model was used to determine factors associated with survival and Kaplan-Meier Survival curves drawn. Significant correlation was when the confidence interval did not contain 1 and p-value was less than 0.05. Data was presented in prose, tables, figures and curves.

4.10 Ethical Considerations

Approval to conduct the study was granted by Institutional Research and Ethics Committee (IREC) and the management of MTRH. Patients details obtained were handled confidentially by use of computer password known by the principal investigator only. All patients received the necessary standard treatment regardless of their willingness or unwillingness to participate in the study. No incentives or inducements were used to convince mothers to

allow their babies to participate in the study. Informed and written consent was emphasized.

Findings of this study will be shared with MTRH management.

CHAPTER FIVE: RESULTS

A total of 175 preterm infants were studied from December 2012 to August 2013. There were 82 males and 93 female infants giving a male to female ratio of about 1:1.13.

5.1 Infant characteristics

The mean gestation age was 31.94 weeks (± 3.06) and the mean birth weight was 1342g (± 355.5). Among the infants recruited 14.9% (26) were extremely low birth weight, 46.3% (81) were very low birth weight whereas 38.9% (68) were low birth weight.

Table 1: Infant Characteristics

Characteristic		Frequency (n=175)	%
Gender:	Male	82	46.9
	Female	93	53.9
Gestation age:	<28weeks	27	15.4
	28-31weeks	54	30.9
	32-36 weeks	94	53.7
Mode of delivery:			
SVD		138	78.8
EMCS		22	12.6
SBD		15	8.6

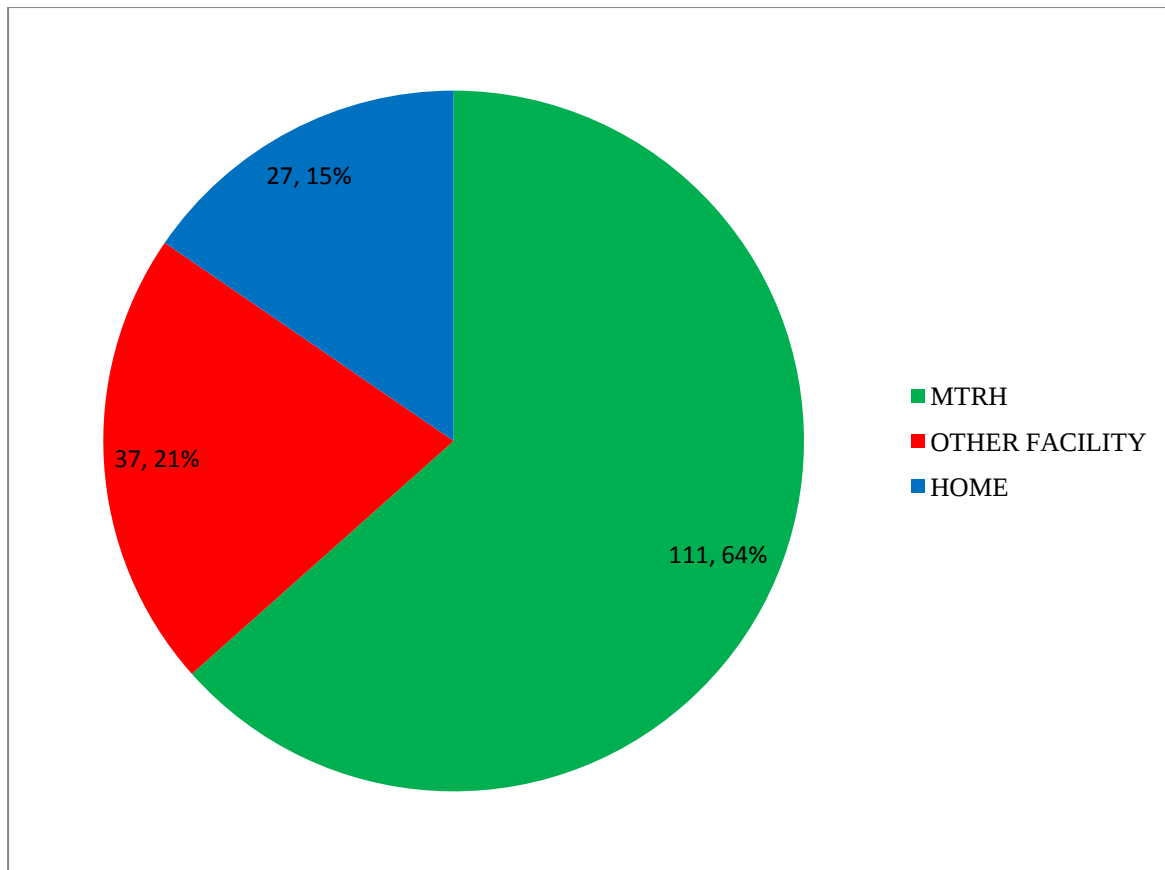


Figure 1: Place of delivery

5.2 Maternal characteristics

The median maternal age was 24 years (range from 14 to 42 years). Twenty percent of the mothers were teenagers. The majority of mothers, 117 (67.2%) were married while 56 (32.2%) were single. Most of the mothers whose infants were studied were primigravidae, 85 (48.6%). Sixty four percent of the mothers had attended antenatal clinic at least once. All mothers had their HIV status known with the most of them, 164 (93.7%) being HIV negative. Sixty nine percent of the mothers reported to have developed spontaneous preterm labour. Mothers who had obstetric complications prior to delivery included 24 with preeclampsia, 13 with Ante partum hemorrhage and 8 with premature rupture of membrane. Most mothers who delivered through caesarian section had antenatal complications with 14 (63.6%) having preeclampsia.

Table 2: Maternal Characteristics

Characteristic	Frequency (n=175)	%
Age (Years):		
<20	36	20.6
20-25	73	41.7
26-30	34	19.4
31-35	15	8.6
>35	17	9.7
Employment status:		
Unemployed	113	64.6
Self employment	49	28.0
Formal employment	13	7.4

5.3 Short term Survival

The overall proportion who survived to hospital discharge was **60.6%** (95% CI 0.53-0.68).

Of the babies who did not survive, 11 (15.9%) died within the first 24 hours with 56 (81.1%) dying by the end of the first week. Only two infants died after the end of the neonatal period.

The mean length of stay for the infants who survived to hospital discharge was 25.8days (± 16.1) whereas for those who died it was 6.2 days (± 7.6).

Table 3: Gestational age specific survival

Gestation age in weeks	Admissions	Survivors at discharge	Survival %
< 28	27	8	29.6
28-31	54	27	50.0
32-36	94	71	75.5
Total	175	106	60.6

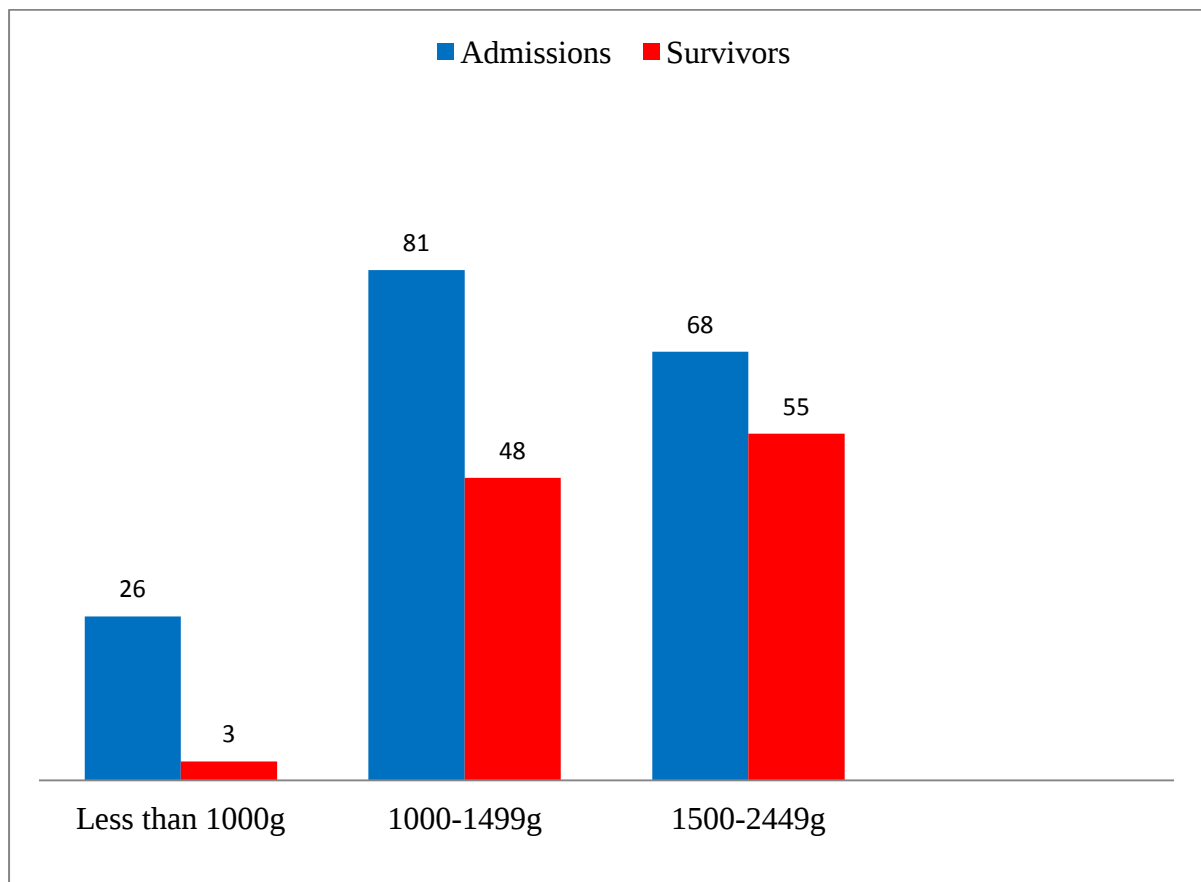


Figure 2: Admissions and Survivors

5.3 Causes of morbidity

The diagnoses made at admission for majority of the study participants were prematurity, low birth weight and respiratory distress syndrome. Various clinical diagnoses made by the clinicians during the infant stay in the new born unit were noted.

Although 155 (88.6%) infants were suspected to have neonatal sepsis, only 24 (15.5%) had blood cultures done. The organisms species that were isolated included: Klebsiella (10), Coagulase negative staphylococcus (4), E. coli (1), Enterococcus (1) and Citrobacter (1). Two cultures had no growth obtained and five had no results back by the time of the patient death or discharge home. Hypothermia (HR 2.87, 95% CI 1.06-7.73, p-value 0.00), apnoea (HR

5.3, 95% CI 2.58-10.98, p-value 0.04) and respiratory distress syndrome (HR 2.92, 95% CI 1.29-6.60, P-value 0.01) were significantly associated with higher hazard of dying.

Table 4: Causes of Morbidity

Diagnosis	Frequency	%
Suspected Neonatal sepsis	155	88.6
Hypothermia	118	67.4
Neonatal jaundice	115	65.7
Respiratory distress syndrome	113	64.6
Apnoea	76	43.4
Anemia	71	40.6
Necrotizing enterocolitis	13	7.4
Hypoglycemia	8	4.6

Table 5: Correlates of Mortality (Causes of morbidity)

Variable	HR	95%CI		p-value
Neonatal Sepsis	0.46	0.15	1.43	0.18
Anemia	0.86	0.51	1.44	0.57
Neonatal Jaundice	0.35	0.21	0.58	0.00
Hypothermia	2.87	1.06	7.73	0.04
Hypoglycemia	2.31	0.88	6.06	0.09
Neonatal Enterocolitis	1.19	0.59	2.37	0.63
Apnoea	5.30	2.58	10.89	0.00
RDS	2.92	1.29	6.60	0.01

5.4 Interventions

All preterm babies were started on IV fluids, intramuscular vitamin K injection and tetracycline eye ointment at admission. Antibiotics were used in 98.9% of the study subjects. The first line antibiotics were Benzyl penicillin and gentamicin, second line was a third generation cephalosporin and amikacin and third line was a fourth generation cephalosporin or meropenem and vancomycin. A total of 71(40.6%) infants were diagnosed to have anemia, 42 (73.2%) of those received blood transfusion.

Babies weighing less than 1500g were nursed in incubators. Eighty infants (45.7%) were nursed in incubator during their stay in the newborn unit.

5.5 Correlates of Mortality

Infant characteristics

The proportion of infants who survived to discharge increased with increasing gestation age and birth weight with those born weighing over 1500g having the highest survival proportion of 80.9%. The hazard of dying was low among low birth weight infants compared to extremely low birth weight infants (HR 0.4, 95% CI 0.20-0.78, p-value 0.003).

The hazard of dying was low for preterm infants born after 31 weeks gestation compared to those born at or less than 28 weeks gestation (HR 0.39, 95% CI 0.18-0.82, p-value=0.013).

The hazard of dying was higher for premature infants born through cesarean section compared to those born via spontaneous vertex delivery (HR 4.25 95% CI 1.875-8.662; p-value=0.001)

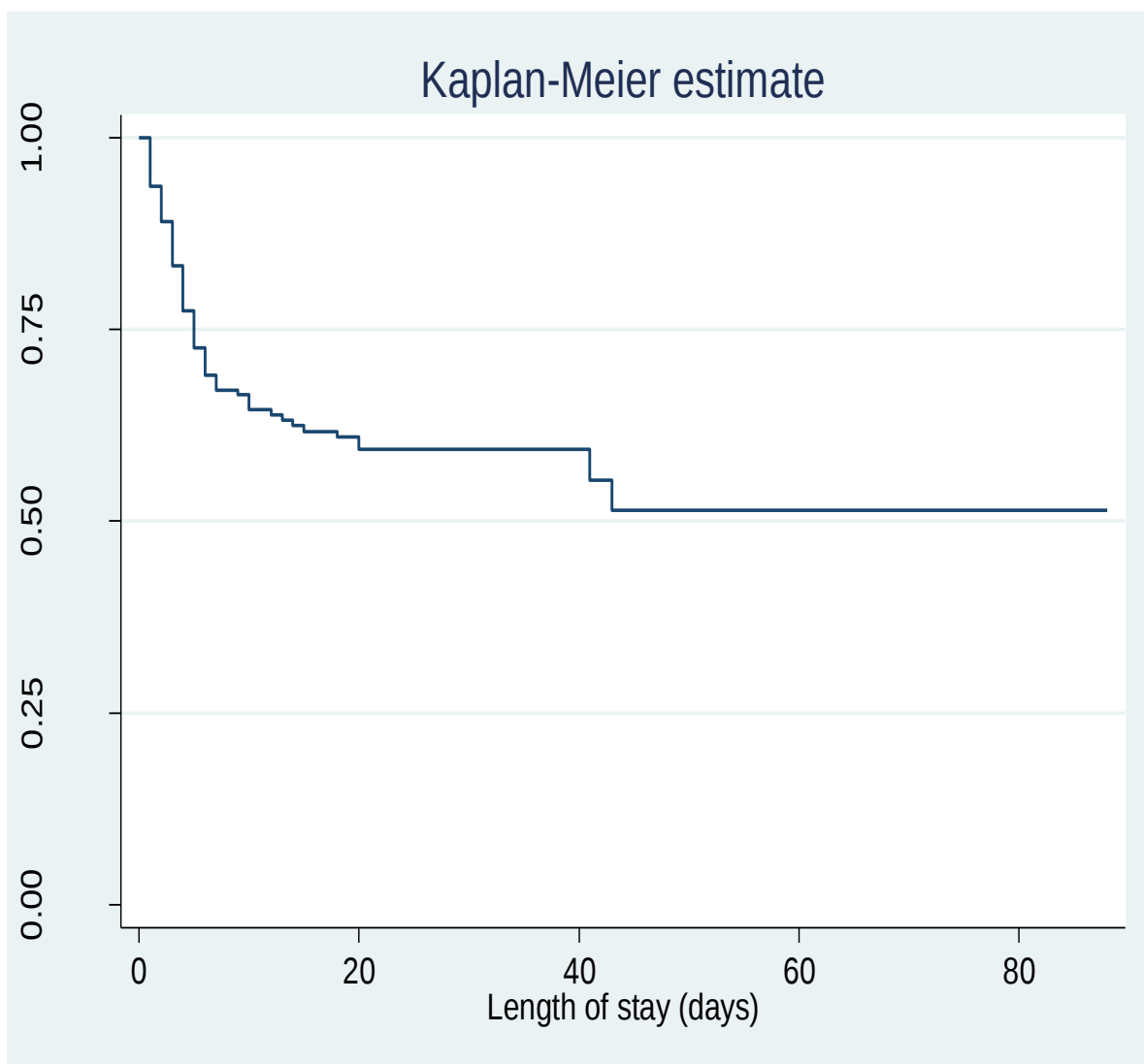


Figure 3: Overall Survival curve

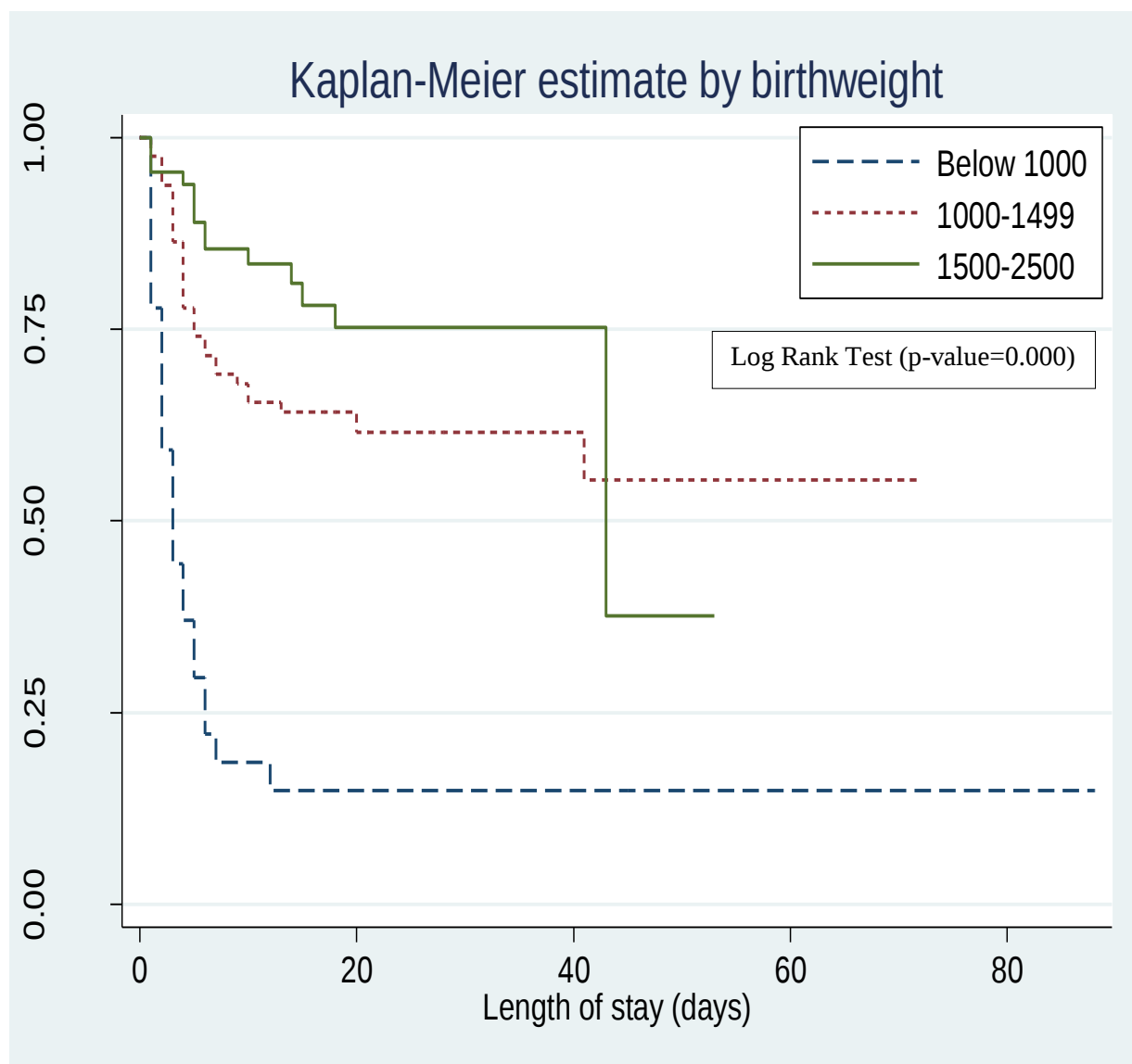


Figure 4: Birth weight specific survival curves

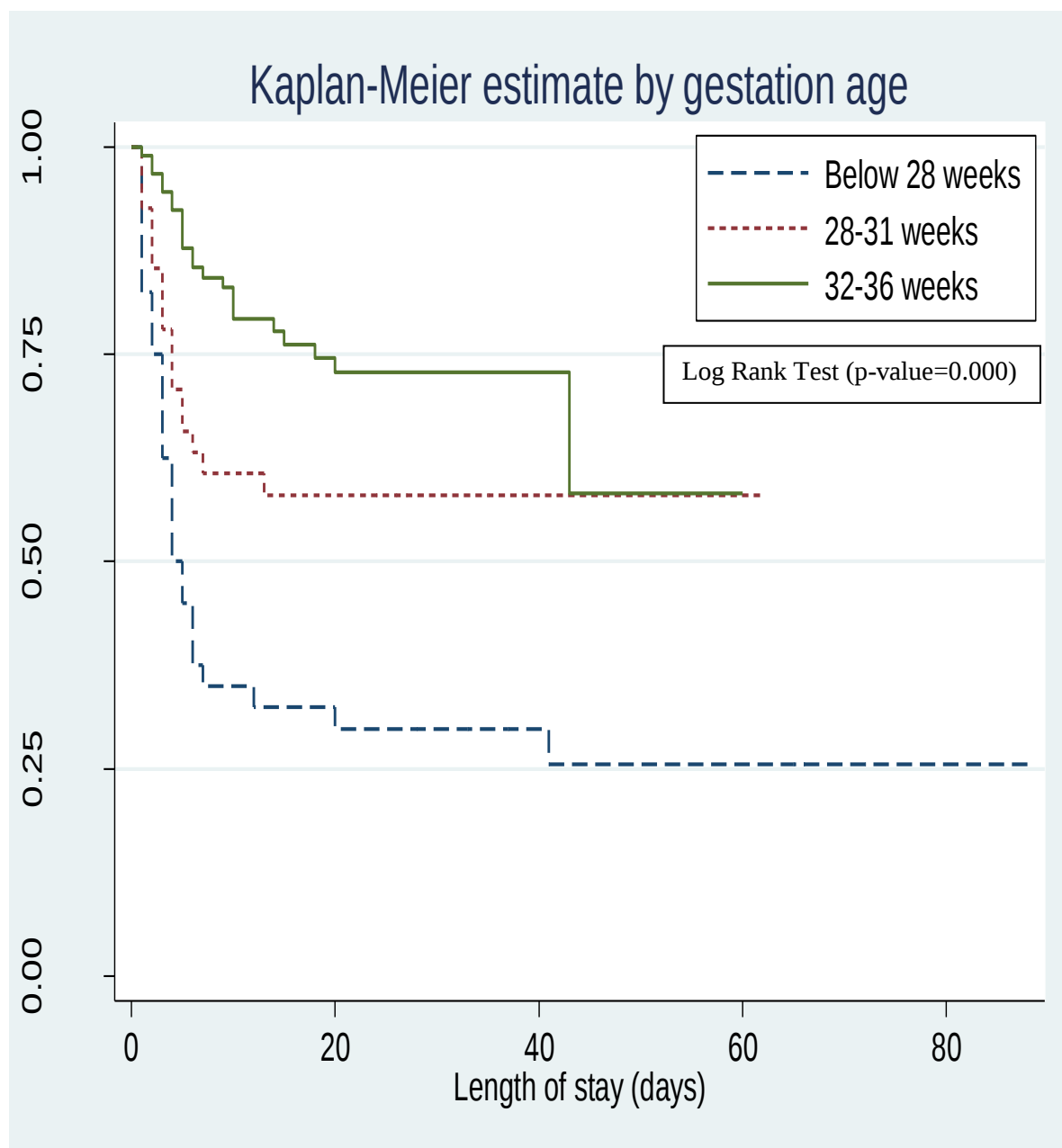


Figure 5: Gestational age specific survival curves

Table 6: Correlates of Mortality (Infant characteristics)

Variable	HR		95%CI	P-value
Place of delivery				
Facility vs MTRH	1.91	0.72	5.10	0.20
Home vs MTRH	2.48	0.87	7.11	0.09
GA in weeks				
28-31 vs <28	0.74	0.37	1.49	0.4
32-36 vs <28	0.39	0.18	0.82	0.013
Sex: Male vs Female	1.50	0.92	2.47	0.108
Mode of delivery				
SBD vs SVD	1.62	0.76	3.45	0.209
EMCS vs SVD	4.26	1.88	9.66	0.001
Birth weight in g				
1000-1499 vs <1000	0.40	0.20	0.78	0.008
1500-2500 vs <1000	0.27	0.11	0.64	0.003
Age at admission in hours				
1-6 vs <=1	0.59	0.24	1.42	0.238
6-12 vs <=1	1.99	0.23	17.22	0.532
12-24 vs <=1	0.87	0.22	3.51	0.849
>24 vs <=2	0.24	0.03	1.93	0.18
Apgar score				
4-5 vs 3	2.29	0.77	6.80	0.137
6-7 vs 3	0.78	0.29	2.15	0.636
8-10 vs 3	0.50	0.24	1.04	0.065

Maternal characteristics

The hazard of dying was lower for premature infants whose mothers attended ANC compared to those whose mothers didn't (HR 0.52 95% CI 0.3-0.9; P-value=0.02).

Maternal age, education level, marital status and HIV status were not significantly associated with short term survival as shown in table 7 below.

Table 7: Correlates of Mortality (Maternal characteristics)

Variable	HR	95% CI		P-value
Age 20-25 vs <20	1.13	0.59	2.17	0.716
25-30 vs <20	1.12	0.50	2.48	0.786
30-35 vs <20	0.99	0.34	2.91	0.981
>35 vs <20	0.32	0.09	1.18	0.087
Education: Post primary vs primary	1.25	0.71	2.20	0.440
Marital status- Married vs Single	0.89	0.48	1.64	0.704
ANC attendance-Yes vs No)	0.52	0.30	0.90	0.020
Parity >0 vs 0	1.18	0.67	2.06	0.571
HIV status- Pos vs Neg	1.57	0.55	4.54	0.403

CHAPTER SIX: DISCUSSION

Demographic data

In this study the male and female subjects were basically the same which is similar to the findings of Kramer in his 1987 meta analysis which found no overall difference in sex distribution in low birth weight infants (39). There was a slight female preponderance among infants surviving to hospital discharge however the difference was not statistically significant. Simiyu in a study done in KNH found a similar gender difference in survival of low birth weight infants which was explained by death of more male newborns but the difference was also not statistically significant (26). A study by Velaphi et al on survival of very low birth weight infants in South Africa showed that male gender was significantly associated with poor neonatal survival (37). The finding in this study suggests that gender has no role in determination of survival; however this question seems not to be conclusively answered because other studies have reported significant difference.

Short term Survival

Preterm newborns are known to have greater risk of both morbidity and mortality compared to term neonates. There are not many studies in Africa that have looked specifically at mortality among preterm infants. Majority of the studies looked at overall neonatal mortality and prematurity was reported a leading cause of neonatal mortality in most of the studies. In this study, two thirds of preterm infants survived to hospital discharge which is similar to findings by Were et al in a prospective study that looked at 163 infants weighing less than 2000g and found a 62.2% survival to hospital discharge (11). The survival rate in this study is slightly higher than what Simiyu in a study done in the year 2000 which reported neonatal mortality low birth weight infants to be 57.4% in the new born unit of KNH (26). That was a retrospective study in a setting where 23 % of the files were missing and hence this could have introduced bias.

Kasirye-Bainda et al reported an overall neonatal mortality rate of 24.6% in KNH and reported that LBW and prematurity accounted for 95.6% of the mortality (40).

In a Tanzanian tertiary referral hospital, neonatal mortality rate of 19% was reported by Klingenberg et al and gestation less than 31 weeks accounted for 67% of the mortality (41). Survival was different for the three birth weight categories with the low birth weight having the best outcome and extremely low birth weight the worst outcome.

This is similar to findings by Kasirye- Bainda et al who reported survival of 48.7% among babies with birth weight less than 1500g while Were et al in the same hospital reported zero survival of newborns less than 1000g and two thirds survival for bigger ones (11, 40).

Increasing survival proportion with increasing birth weight is also true of gestation age as shown in this study finding that the hazard of dying was significantly lower for infants with gestational age 32 to less than 37 weeks compared to those below 28 weeks.

Were et al reported 69% survival among those with gestation 32 to 35 weeks and only 9% for those less than 28weeks gestation (11).

Increasing gestational age and birth weight is associated with better respiratory maturity which enables preterm infants to adapt better to extra-uterine life.

The survival proportion observed in this study is much lower than the one reported in countries with advanced neonatal care. In South Africa, Velaphi et al reported survival to hospital discharge of 32% among premature infants born at gestation below 28 weeks (37). However, the best survival has been reported in the developed countries where survival for newborns with birth weights above 1000g is above 94% (42, 43). In deed research in developed countries is currently concentrating on improving outcome of babies with birth weight 500g to 1000g and they are already reporting good survival as exemplified by survival rates of 55% and 88% for neonates between 501-750 g and 751-1000g surviving respectively reported in the USA (44). Changes in obstetric care and availability of advance neonatal intensive care facilities have led to better outcomes in developed countries.

The risk of developing RDS in infants born less than 28 weeks gestation age is 60-80% (25).

Therefore in a resource limited new born unit without exogenous surfactant and ventilatory support like in this study site, survival of infants born at less than 28 weeks remains low.

It has been shown that 25 – 45% of neonatal mortality occurs within the first 24 hours mainly as a result of birth asphyxia and acute complications of prematurity. Of the infants who did not survive in his study, a tenth died within the first 24 hours while cumulatively four fifths died during the first seven days of life. Other studies reported higher deaths within the first 24 hours, Simiyu (36%), Were et al (28%) and Ezechukwu et al (64.5%) in tertiary hospitals in Kenya and Nigeria respectively (11, 14, 26). Similar findings were reported by Kasirye-Bainda et al where 86.8% of the neonatal deaths in a study done in KNH occurred within the first week of life (40). Notably those studies were done in hospitals without continuous positive airway pressure (CPAP) facilities and in an era where exogenous surfactant and antenatal steroids were not widely used; factors which may explain the current finding of a lower proportion that died in MTRH in the first 24 hours with availability of CPAP and use of antenatal steroids. The higher numbers of preterm infants dying during the first week of life could be due to acute complications of prematurity occurring in a setting with limited neonatal intensive facilities to support the preterm infants especially those with RDS and early onset neonatal sepsis.

Extremely low birth weight infants who survived to hospital discharge had long length of hospital stay. This is similar to findings by Simiyu et al in a study to quantify the morbidity and mortality of low birth infants in KNH (26). This could be attributed to morbidity associated with complications of extreme prematurity and time taken to gain recommended weight before discharge more so in a setting where there is no total parenteral nutrition for these infants for infants who can't tolerate enteral feeds.

This study showed that the limit of viability in MTRH newborn unit was 28 to less than 32 weeks gestation category. Although the WHO has established the upper limit of viability at

37 completed weeks of gestation they have not set the lower limit. The lower limit is defined by fetal organ maturity and advances in high risk obstetrics care and neonatal intensive care. The USA currently defines this lower limit as about 25 weeks or weight above 500g (43). Compared the developed countries, our viability limit is still high, a finding that could be explained by limitation in high risk obstetric care and neonatal intensive care. The mortality rate of preterm infants admitted in MTRH new born unit is still high especially for the very preterm and extremely preterm infants.

Factors associated with survival:

Infant characteristics

In this study, there was a significant improvement in the proportion of premature infants surviving to hospital in the gestation age 32 to 36 weeks category compared to less than 28 weeks or 28 – 31 weeks gestation category. Studies done in KNH and MTRH before reported similar findings, showing a positive correlation between gestation age and survival (11, 13). Indeed it has been stated that the most significant public health intervention to reduce neonatal mortality is reduction in rate of preterm deliveries by prolongation of gestation age whenever possible. This study suggests that efforts should not only aim at reducing preterm births but at increasing gestation age by maximum possible days. This approach is likely to bear more benefit in low resource settings where neonatal intensive care is often inadequate or absent.

The finding that Caesarian section was associated with significant higher hazard of dying was unexpected. This finding was contrary to other studies where caesarian section was associated with better survival (11, 12, 37). In a retrospective audit of births that occurred in MTRH labour ward between 2004 and 2011, Yego et al reported that majority of early neonatal deaths followed vaginal deliveries (45).

We postulated that this finding could partly be explained by the fact that two thirds of mothers who delivered through cesarean section in this study had severe preeclampsia which could have increased the risk of poor outcome. However there could be other reasons and therefore the area needs to be explored in future studies.

Infants born in MTRH had better probability of survival compared to those born either in outside facility or at home, however after adjusting for other factors, difference was not statistically significant. This finding is in agreement with those by Simiyu in KNH, by Welbeck et al in a study done in Accra Ghana. However, it is different from findings from a study done by Udo et al in Nigeria where survival of neonates born in the tertiary hospital facility had better survival than those born in outside the facility (26, 46, 47). The poor outcome in the infants born before arrival in the Ghana study was attributed to delay in transportation of neonates to the tertiary hospital and inappropriate transportation which adversely affected the neonates.

In this study, two thirds of the infants were born in MTRH and whereas those born at lower level facility or at home were fewer likely contributing to statistical insignificance. However studies that look at how babies born outside are transported to our facility and cared for during transport may offer insights into practices that could have improved survival.

Babies with Apgar score above 3 at five minutes were more likely to survive compared to those with lower and in addition this probability was directly proportional to the score with 8 to 10 having the best survival; however the benefit was not statistically significant after adjusting for other factors. In South Africa, Velaphi et al reported that Apgar score less than 6 at 5 minutes was associated with poor survival. Increase in Apgar scores was reported to have better survival to hospital discharge in preterm infants, which is in agreement with findings in our study (37). Birth asphyxia in premature infants worsens the respiratory insufficiency due to RDS and makes short term survival poor.

Maternal characteristics

Two thirds of mothers of the infants who were studied had attended ANC clinic at least once before giving birth. This proportion is lower than 92% reported in KDHS of 2008-09 and could be explained by the fact that a significant number of mothers start attending ANC late in the 2nd and 3rd trimester thus those who had extremely and very preterm deliveries had not yet started attending ANC (16).

Babies whose mothers attended at least one ANC had a lower hazard of dying compared to those whose mothers didn't. This is similar to findings by Velaphi et al in a study where infants whose mothers attended ANC were one and half times more likely to survive (37). Antenatal clinic attendance has been shown to be one of the major contributors to improved neonatal survival in the USA (41). Antenatal care is useful in reducing preterm births by aiding identification of mothers at risk for preterm delivery; offers an opportunity for timely monitoring, intervention and admission to the new born unit. This study did not however look at the optimum number of antenatal visits that were associated with improved survival. It has been estimated that improving the quality of prenatal care would decrease prematurity associated deaths by 75% (2).

Maternal age and parity were not found to be statistically significant in contributing to neonatal survival. This is similar to findings by Welbeck et al in a study done in a tertiary teaching hospital in Accra Ghana where maternal parity and age were not found to significantly contribute to survival of at risk neonates (46). However, Yego et al reported that a significantly higher number of early neonatal deaths occurred for infants whose mothers' were in the age group of 15 to 24 years (45). This finding was due to by high rate of preterm labour and late admission to hospital among young mothers. The difference in findings between this study and our study could be attributed to the sample selection because our study excluded term newborns. Those with preterm labour tend not to delay in seeking care as observed in term labour. Additionally, this could be explained by the fact that after

gestational age and birth weight, the next important determinant of short term survival of preterm infants is the level of neonatal care service in the unit which is independent of maternal demographic characteristics.

Maternal HIV status was not significantly associated with survival to hospital discharge in this study. In studies done in rural Mozambique and South Africa by Ndirangu et al and Nianiche et al respectively, maternal human immunodeficiency virus (HIV) infection was shown to cause small for gestation infants but not preterm births (23, 24). The findings in our study similar to those two studies suggest that HIV infection does not worsen the neonatal survival. This could be attributed to the natural history of vertically transmitted HIV whereby there is no significant immunosuppression in the first month of life and the neonate has maternal antibodies.

It is important to note that in this study the number of HIV positive mothers was few which was comparable to the general prevalence of HIV amongst pregnant women (6.4%) reported in the Rift valley region in the KDHS report (16). Implementation of prevention of mother to child transmission of HIV interventions has also reduced the risk of vertical transmission and hence reduced morbidity and mortality for sero-exposed infants.

Causes of morbidity and Interventions

In this study, respiratory distress syndrome was one of the most common diagnoses made and it was associated with higher hazard of dying. In a study done in KNH new born unit in 1996 to determine birth weight specific survival of infants weighing less than 2000g at birth, 43% developed RDS (11). Another study conducted in the same unit, four years later, to quantify morbidity and mortality of low birth weight infants showed that the leading diagnosis on admission or discharge of low birth weight infants was respiratory distress syndrome at 69% (26). The high rates of respiratory distress syndrome were expected as a consequence of lung

immaturity and perhaps lack of timely prenatal steroid intervention and lack of exogenous surfactant in MTRH new born unit.

This study found that although majority of the infants were suspected to have sepsis and started on antibiotics, most of them did not have blood cultures done. We observed that it was not routine to have all premature infants suspected to have neonatal sepsis have blood cultures done. This was partly due to stock out of blood culture specimen collection bottles and also due to clinicians prioritizing only infants who were very sick and or not responding to initial antibiotic therapy. Simiyu, in two retrospective studies conducted in KNH on newborn babies admitted to the new born unit and the general pediatric wards reported that 37% and 71% had suspected sepsis yet only 14% and 8.4% had confirm sepsis diagnosis respectively (26, 48). One common finding in these studies was use of antibiotics without laboratory confirmation of sepsis. This posed a risk for development of antibiotic resistance. Meticulous infection control and treatment interventions are required to reduce morbidity due to sepsis. It is possible that improvement in newborn intensive care technology will not necessary improve short term outcomes unless there is reduction in the risk of sepsis. In comparison, in the United States, morbidity due to sepsis has decreased remarkably and currently the main causes of morbidity and mortality in preterm infants are respiratory distress syndrome and intraventricular hemorrhage (41). In this study we did not find any diagnosis of intraventricular hemorrhage which could be explained by the low index of suspicion among clinicians and lack of routine IVH screening in MTRH new born unit. Apnoea and hypothermia were associated with increased hazard of dying. These are acute complications of prematurity which occur more often in critically ill infants. This finding was similar to findings by Simiyu in a study done in KNH where apnoea was occurred in 29% of the patients, it was managed with rectal aminophylline but only 12% of these infants survived (26). Lack of conventional drugs such as caffeine citrate in the unit could have contributed to higher mortality in neonates with apnoeic attacks.

Hypothermia occurred in two thirds of the study participants. This proportion is higher than that reported by Simiyu in a KNH study where hypothermia occurred in 27% of the patients (26). The higher incidence could be attributed to the limited number of incubators available in the unit leading to nursing of premature infants in open cots with space heaters where thermal control was poor. Implementation of Kangaroo mother care in the unit was not routinely performed and therefore, from the findings of this study, there is need to scale up and formally implement KMC in the unit. Infants born before arrival were also noted to have hypothermia at admission, especially those transported by private means. Referring health facilities and the general public too need to be sensitized on use of KMC when referring preterm infants to higher level facilities like MTRH new born unit and that could reduce the incidence of hypothermia.

Study Limitations

- Assumption that survival probabilities are the same for study subjects recruited into the study at different times during the study period.
- Estimating the gestational age: use of last menstrual period and New Ballard score, without first trimester ultrasound; each of them is not ideal but combining the two improves accuracy.

CHAPTER SEVEN: CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

- Two thirds of premature infants admitted to MTRH new born unit survived to discharge.
- Majority of the infants died within the first seven days.
- The survival limit was the 28 to less than 32 weeks gestational age category.
- Increasing gestation age, birth weight over 1000g and maternal antenatal care clinic attendance were associated with better survival.
- Caesarean section mode of delivery was associated with poor survival.

RECOMMENDATIONS

1. Whenever possible preterm birth delivery should be delayed until after 28 weeks gestation.
2. More effort should be put in increasing early antenatal care clinic attendance.
3. Further studies are needed to evaluate why caesarean mode of delivery of preterm infants was associated with poor survival and audit the efficacy of current interventions being implemented in the unit.
4. A study that follows premature infants after discharge to determine intermediate and long term survival rates.

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APPENDICES

APPENDIX 1: DATA COLLECTION FORM

Demographic data:

Serial No..... IP No.....
 Date of admission...../...../..... Date of discharge/death.../...../
 Residence district..... Place of delivery: MTRH.....H/Facility... Home....

Infant characteristics

Gestational age-----wks by LMP/-----wks by Ballard Sex: Male....Female.....
 Mode of delivery: SVD.....SBD....AVD.....EMCS.....ELCS.....
 Birth weight.....g Age at the time of admission.....Hrs
 Apgar score at 5min-----/10

Maternal characteristics

Age:.....Years Level of education: None...Primary.....Post primary.....
 Employment status: Unemployed.....Self employment...Formal employment.....
 Parity: PARA.....+..... Interval between this last birth and Conception.....Months
 ANC attendance: Yes/No HIV Serology Neg/Pos
 Antenatal Complications Yes/No, If Yes specify.....

Clinical characteristics

Diagnosis on admission.....

Causes of Morbidity during admission

- ☐ Neonatal Sepsis
- ☐ Anemia
- ☐ Neonatal jaundice
- ☐ Hypothermia
- ☐ Hypoglycemia
- ☐ Necrotizing enterocolitis
- ☐ Apnoea

Interventions on admission

IV fluids
 IV antibiotics
 Blood product transfusion
 Phototherapy
 Anticonvulsants
 Oxygen
 CPAP

Outcome: 1) Discharge home

2) Death

Length of stay.....days

SIGN	SCORE							SIGN SCORE
	-1	0	1	2	3	4	5	
Skin	Sticky, friable, transparent	gelatinous, red, translucent	smooth pink, visible veins	superficial peeling &/or rash, few veins	cracking, pale areas, rare veins	parchment, deep cracking, no vessels	leathery, cracked, wrinkled	
Lanugo	None	sparse	abundant	thinning	bald areas	mostly bald		
Plantar Surface	heel-toe 40-50mm: -1 <40mm: -2	>50 mm no crease	faint red marks	anterior transverse crease only	creases ant. 2/3	creases over entire sole		
Breast	Imperceptible	barely perceptible	flat areola no bud	stippled areola 1-2 mm bud	raised areola 3-4 mm bud	full areola 5-10 mm bud		
Eye / Ear	lids fused loosely: -1 tightly: -2	lids open pinna flat stays folded	sl. curved pinna; soft; slow recoil	well-curved pinna; soft but ready recoil	formed & firm instant recoil	thick cartilage ear stiff		
Genitals (Male)	scrotum flat, smooth	scrotum empty, faint rugae	testes in upper canal, rare rugae	testes descending, few rugae	testes down, good rugae	testes pendulous, deep rugae		
Genitals (Female)	clitoris prominent & labia flat	prominent clitoris & small labia minora	prominent clitoris & enlarging minora	majora & minora equally prominent	majora large, minora small	majora cover clitoris & minora		
TOTAL PHYSICAL MATURITY SCORE								

NEUROMUSCULAR MATURITY

SIGN	SCORE							SIGN SCORE
	-1	0	1	2	3	4	5	
Posture								
Square Window								
Arm Recoil								
Popliteal Angle								
Scarf Sign								
Heel To Ear								
TOTAL NEUROMUSCULAR SCORE								

Maturity Rating

Score	Weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

APPENDIX 4: CONSENT TO PARTICIPATE IN THE STUDY

SERIAL NUMBER

Background

You are being asked to participate in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Read the following information carefully and ask us if there is anything that is not clear or if you would like more information. Please take time to decide whether you want to take part in this study. The

purpose of this study is to determine the proportion of premature infants surviving to discharge at MTRH and the factors that influence their survival. Our study is for research purposes but we hope that the information obtained will be used to inform the hospital and other policy formulators which will result in improved healthcare service delivery.

Study Procedure

The study involves filling out a questionnaire capturing you and your baby's biodata and the presenting symptoms and signs at admission in the NBU. A record will be kept of the anthropometric measurements and causes of morbidity during hospitalization. The findings during subsequent assessments cannot be linked to your baby and are completely anonymous and confidential since we shall be using serial numbers.

Risks

There are no risks involved in this study. This study will be anonymous. The baby will receive treatment as per the diagnosis made based on the hospital and Ministry neonatal protocols.

Benefits

There are no direct medical benefits to your child for participating in this study. A potential benefit of the study will be improved healthcare service delivery based on the recommendations of this study.

Alternative Procedures

You may choose your baby not to participate in this study

Confidentiality

This research will be conducted in accordance with all the Kenyan laws and regulations that protect rights of human research subjects. All records and other information obtained will be kept strictly confidential and your baby's protected health information will not be used without permission. All data collection tools will be identified by number or otherwise coded to protect any information that could be used to identify your baby. Results of this study may be published, but no names or other identifying information will be released.

Person to Contact

If you have questions, complaints or concerns about this study, you can contact the investigator from Moi University, School of Medicine, department of Child Health and Paediatrics, Postgraduate programme ; Dr. Makokha Felicitas Okwako +254722622651 email drmakfelis@gmail.com

Institutional Review Board

This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital. Contact IREC if you have questions

regarding your child's right as a participant, and also if you have complaints or concerns which you do not feel you can discuss with the investigator.

Contact IREC using the address ; The Chairman IREC, Moi Teaching and Referral Hospital, PO BOX 3, Eldoret, Kenya. Tel. 33471/2/3

Voluntary Participation

It is up to you to decide whether your baby takes part in this study. Refusal to participate or the decision to withdraw from this research will involve no penalty or loss of benefits to which your child is otherwise entitled. This will not affect your relationship with the investigators.

Right of investigator to withdraw

The investigator can withdraw your baby from the research without your approval.

Costs and Compensation to participants

There is no cost to you, and there is no compensation to subjects for participation in this study.

Number of Participants: 175 babies

Authorization for use of your protected health information

This study that does not entail the use of your baby's protected health information.

Thank you for your baby's participation in this research and we truly appreciate your help.

CONSENT

By signing this consent form, I confirm I have read the information in this consent form and have had the opportunity to ask questions. I will be given a signed copy of this consent form. I voluntarily agree to take part in this study.

Name of CaregiverSignature/Mark.....

Date.....

Name of InvestigatorSignature.....

Date.....

APPENDIX 5: IREC APPROVAL



MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 334711/2/3

Reference: IREC/2011/160
Approval Number: 000883

Dr. Felicitas Makokha Okwako,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Makokha,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee have reviewed your research proposal titled:

"Survival of Premature Infants Admitted to the New Born Unit at Moi Teaching and Referral Hospital, Kenya."

Your proposal has been granted a Formal Approval Number: **FAN: IREC 000883** on 4th September, 2012. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 3rd September, 2013. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Yours Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc:	Director	-	MTRH
	Principal	-	CHS
	Dean	-	SOM
	Dean	-	SPH
	Dean	-	SON
	Dean	-	SOD



MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 334711/2/3
4th September, 2012



APPENDIX 6: HOSPITAL APPROVAL

**MOI TEACHING AND REFERRAL HOSPITAL**

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke
Ref: ELD/MTRH/R.6/VOL.II/2008

P. O. Box 3
ELDORET

13th September, 2012

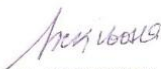
Dr. Makokha Felicitas Okwako,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:

"Survival of Premature Infants Admitted to the New Born Unit at Moi Teaching and Referral Hospital, Kenya."

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.


DR. J. KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD, HRISM