Faculty of Health Science

School of Public Health

***Title:* Factors associated with survival of newborns at hospital discharge at Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa from 01 January 2013 to 30 June 2014.**

By

Johanna Penelao Mufeti

Student no: 886552

A research report submitted to the University of Witwatersrand, Faculty of Health Sciences, School of Public Health, in partial fulfillment of the requirements for the degree of Master of Science Epidemiology in the field of Epidemiology and Biostatistics

Supervisors: Associate Professor T.F. Chirwa (School of Public Health)

Associate Professor D.E. Ballot (School of Clinical Medicine)

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Declaration

I, Johanna Penelao Mufeti, declare that there has not been any prior submission of this research report in part or full for academic or any other purposes. This is my own work, compiled under the supervision of Prof D.E Ballot and Prof T.F Chirwa. The report is being submitted to the School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, in partial fulfillment of the requirements of the degree of MSc in Epidemiology and Biostatistics.

Johanna Penelao Mufeti

25 October 2016 at Windhoek, Namibia

Abstract

Background: Audit for mortality patterns in general is vital as it provides information necessary for health planning and budget allocations. Despite the Millennium Development Goals (MDGs) to reduce mortality in children aged 5 years and younger by two thirds by the year 2015 (1), majority of Sub-Saharan countries are still faced with persistently high levels of neonatal mortality. According to the Perinatal Problem Identification Program (PPIP) (www.ppip.co.za), an audit of perinatal deaths in South Africa, the early neonatal mortality rate has been standing at 9.5 per 1 000 live births over the past few years. However the number could be higher as high numbers of neonatal deaths are unaccounted for.

Aim: The study aims to determine the factors associated with survival at hospital discharge of newborns weighing ≥ 1 500 grams at birth, at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) between 01 January 2013 and 30 June 2014.

Design and setting: This was a retrospective secondary analysis of data from a computerized neonatal database of newborns with a birth weight of ≥ 1 500 grams who were admitted to the neonatal ward at CMJAH between the 1st January 2013 and 30th June 2014.

Methods: The binary response variable took one of the two possible values 1 for survivors and 0 for non-survivors. Survivors were all those newborns who survived up to hospital discharge, while non-survivors refer to all the newborns that died during the period of hospitalization. Independent

variables that were evaluated were gender, place of birth, maternal race, teenage mother, gestational age, birth weight, mode of delivery, major birth defects, multiple births, Initial resuscitation in delivery room, Bacterial sepsis on or before day three, respiratory diagnosis, Oxygen on day 28, Nasal Continuous Positive Airway Pressure (NCPAP) without ETT ventilation, cardiovascular diagnosis, Hypoxic Ischemia Encephalopathy grade (HIE grade), Cerebral cooling, Necrotizing Entero-Colitis (NEC), Sepsis after day three and home oxygen.
Pearson Chi-square test, binary logistic regression model and survival analysis using the Cox proportional Hazards techniques were used for analysis in addressing the research objectives. Graphs and frequency tables were used to summarize the data and present the results.

Results: The data consisted of a total of 1 758 newborns with a birth weight of ≥ 1 500 grams, 57.5 percent were males, 42.1 percent female, 0.1 percent intersex and 0.3 percent with missing information on gender. Overall survival in this group of newborns was 94.1 percent. The total analysis time at risk was 11 903 days, with a median survival time of four days.

The presence of major birth defects was associated with poor newborn survival (HR = 4.25, 95% CI = 2.43: 7.45). Birth weights categories of 2 500 – 4 000 grams and above 4 000 grams were also significantly associated with improved newborn survival (HR = 0.41 and HR = 0.09 respectively) compared to the weight category of less than 2 500 grams. Other factors that were associated with an improved survival were respiratory diagnosis of TTN and Hyaline membrane disease. A gestational age of more than 42 weeks was associated with an increase in hazard (HR = 18.73, 95% CI: 2.09, 167.54) compared to the gestational age of less than 32 weeks. In addition HIE grade two and three, cardiovascular diagnosis of hypotension requiring inotropes and congenital heart disease were all associated with an increase in the risk of the Hazard. While there was significant difference between survivors and non-survivors with regard to whether they were mechanically ventilated, mechanical ventilation was not associated with newborns' outcome at hospital discharge.

Conclusion: Overall survival of newborns weighing 1 500 grams or more was satisfactory high compared to survival of Very Low Birth Weight (VLBW) and Low Birth Weight (LBW) newborns. Even so, more collective efforts still need to be done to further enhance the quality of health care services in improving the outcome of newborns at hospital discharge. Continuing neonatal deaths audit is recommendable in order to determine and decrease deaths and morbidity of newborns from avoidable risk factors.

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Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal care
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
ELBW	Extremely low birth weight
HIE	Hypoxic Ischemia Encephalopathy
HIV	Human Immunodeficiency Virus
IUGR	Intra-Uterine Growth Retardation
MDGs	Millennium Development Goals
MOU	Midwife Obstetric Units
NEC	Necrotizing Entero-Colitis
NCPAP	Nasal Continuous Positive Airway Pressure
NMR	Neonatal Mortality Rate
PPHN	Persistent Pulmonary Hypertension of the Newborn
PDA	Patent Ductus Arteriosus
PPIP	Perinatal Problem Identification Program
LBW	Low Birth Weight
TTN	Transient Tachypnoea of the Newborn
VLBW	Very Low Birth Weight
WHO	World Health Organization

CHAPTER 1: Introduction

1.1. Background

Audit for mortality patterns in general is vital as it provides information necessary for health planning and budget allocations. For targeted interventions to be effective there is a need for reliable statistics pertaining to the intended setting. Neonatal mortality accounts for 37 percent of deaths of all children under the age of 5 years, as such an improvement in maternal and neonatal care is crucial as it will save lives and reduce mortality among newborns.

Despite the Millennium Development Goals (MDGs) to reduce mortality in children aged five years and younger by two thirds by the year 2015 (1), the majority of Sub-Saharan countries are still faced with persistently high levels of neonatal mortality. In South Africa, the National Development Plan also prioritize the reduction of maternal, infant and child mortality (2).

In the past years, the HIV/AIDS pandemic has been increasing and has significantly raised the under-five mortality rates. In South Africa, between 4.4 and 17.0 per 1 000 live-born infants weighing 1 000 grams or more die in the first week of life in different regions, with the highest rate in rural areas (3). According to the Perinatal Problem Identification Program (PPIP) (www.ppip.co.za), an audit of perinatal deaths in South Africa, which covers about forty percent of birth in South Africa, the early neonatal mortality rate has been standing at 9.5 per 1 000 live births over the past few years. This number could be higher due to the high number of neonatal deaths which are unaccounted for, due to incomplete data in hospital record.

The first step in reducing neonatal mortality is by assessing the causes of deaths in neonates and the contributing factors thereof. Subsequently, one can examine the associated factors of survival among newborns and plan intervention strategies. However, with limited resources it is a challenge for health policy makers to decide on the priority intervention, to whom it should be targeted and when.

The aim of this study is to investigate the factors associated with survival of newborns at hospital discharge, in order to inform health policy makers for efficient planning of necessary intervention strategies.

1.2. Statement of the problem

Just like in most developing countries, the situation of neonatal mortality in South Africa is of public health concern. According to the 2013 Global Health Workforce Statistics update, neonatal mortality rate was 14.8 per 1 000 live births (26), which is comparable to the figures resulting from the 2000 - 2002 perinatal care survey of South Africa were the neonatal death rate was highest in the city and town groups (14.5 per 1 000 live births) followed by the rural and metropolitan groups (11.3 and 10.0 per 1 000 live births respectively (4).

Reducing neonatal mortality is one of the requirements and prerequisite to achieving the MDG 4, the target of which is a reduction in child mortality by two-thirds by the year 2015. However, very little progress has been made in the last 15 years towards reducing the number of neonatal deaths (5). In South Africa, neonatal deaths account for approximately 40% of all deaths in children under the age of 5 years (6). Many sub-Saharan countries are faced with this challenge due to socioeconomic status and resources constraints which leads to many babies being delivered at home with limited skilled attendance, which in turn increases the risks for both the mother and the new-born (7,8).

It`s believed that advancement in high-level technology can improve neonatal outcome. This may not however be appropriate in developing countries, other cost effective interventions such as resuscitation at birth, breastfeeding, kangaroo mother care and prevention of hypothermia can drastically reduce the number of deaths in resource limited settings (5).

Preventative measures can be undertaken to strengthen structures at a health facility setting to reduce mortality. One of the many measures that can be undertaken is to evaluate the current methods of caring for the neonates by assessing what interventions works in reducing newborn mortality and strengthening those strategies.

1.3. Justification of the study

Research on neonatal mortality and determinants of survival in Very Low Birth Weight (VLBW) neonates has been well documented (9–11). However, very little research in South Africa has looked at outcome and factors associated with survival up to hospital discharge of newborns weighing 1 500 grams and above.

To bring about a reduction in neonatal mortality and make notable progress towards achieving the MDG 4 for child survival and the South Africa National Development Plan, it is important to recognize the factors contributing to the survival of newborns in order to effectively scale up interventions.

There is however a notable gap in the health sphere in terms of what has been published in the South Africa context in particular, when it comes to survival and predicting factors of low birth weight and normal birth weight neonates. It is equally beneficial if consideration is given to morality in babies over 1 500 grams, as it add significantly to neonatal mortality rates.

The current study aims to fill in the information gap in the public health sphere by outlining the factors associated with survival at hospital discharge of newborns weighing 1 500 grams and above at birth. The study will further contribute to the knowledge sphere by calculating the prevalence of survival among this group of newborns given their underlining characteristics, as a measure of health status. Lastly, the results of the study can potentially aid health policy makers to develop new policies, strengthen and make informed timely interventions to ensure overall neonatal health.

1.4. Literature review

An estimated total of 130 million infants are born worldwide each year, and around 4 million infants die during the first month of life (12). Neonatal deaths account for 40 percent of global under-five mortality (13). In Bangladesh, 57 percent of the under-five mortality in the country are neonatal deaths (14). An analysis of the Neonatal Mortality Rate (NMR) found that while the rate of reduction is slower than for maternal and under-five deaths, the annual rate reduction of NMR globally has accelerated between 2000 and 2010 (2.1% per year) compared with the 1990s (13). There is an urgent need for the global public health community to react to this challenge, through research and other community based projects. Progress statistics for some countries have shown that the NMR can be halved within a decade (13). The countries with the most progress are mainly high and middle-income countries; yet there are a few notable exceptions in low-income country , such as Bangladesh and Nepal (13). Therefore reduction of neonatal mortality has thus been identified as a health priority internationally and in South Africa.

Neonatal mortality rates are high in developing countries especially in sub-Sahara Africa. This is due to limited resources relating to health care, including shortage of skilled health care workers and scarcity of fully equipped health care facilities (6,15).

The NMR in sub-Saharan Africa is persistently high at an estimated rate of 41 per 1 000 live births, translating to around 1.2 million deaths in 2008, which represents one-third of all global neonatal deaths (16). Unlike in developed countries, issues surrounding child birth and care in sub-Saharan Africa are hugely influenced by lack of education, cultural and religious beliefs. Culture influences pregnant mothers' decision to attend antenatal care and whether delivery should be conducted at home or in the hospital setting. This has a direct impact on the survival and well-being of both the mother and newborns (17,18).

Low birth weight, prematurity and Intra-Uterine Growth Retardation (IUGR) were the major determinants of child survival in urban Malawi (19). According to a study conducted in Pakistan, the most common primary obstetric causes of neonatal death were preterm delivery in 34 percent, intra-partum asphyxia in 21 percent and antepartum hemorrhage in 9 percent of the neonates (20). The relative importance of the causal factors is reflected in the distribution of the final causes of neonatal death: immaturity-related in 26 percent, birth asphyxia or hypoxia in 26 percent and infection in 23 percent of the neonates (20). According to Welbeck (21), multiple factors resulting in perinatal mortality and morbidity in developing countries include the high risk nature of the pregnancies resulting in an increased incidence of premature deliveries and asphyxiated babies, delay in transfer of the sick neonate as well as inadequate mode of transfer. Once again, this reflects the problem of resource constraints relating to patients transportation in developing countries (7,8).

Survival of VLBW neonates weighing < 1 500 grams has been well researched and published in South Africa. According to a study done in South Africa at Chris Hani Baragwanath Hospital (CHBH), survival rate is poor (32%) among infants weighing less than 1 000 grams because of severe prematurity and due to the fact that they were not offered mechanical ventilation, as it was only offered to infants weighing > 1 000 grams due to limited resources (22). This situation is alarming and majority of sub-Saharan countries are faced with the same challenges of resource constraints. The health care system in developing countries and South

Africa in particular is hampered by limited health resource and high patients turnover (5,10,23). Health care providers in many cases are faced with a critical decision to make regarding the infants to gain access and receive treatment based on the number of available beds and medical equipment.

According to the study done at CHBH, the factors that were found to be associated with survival in VLBW infants weighing between 500 grams and 1 499 grams were antenatal clinic attendance, delivery by caesarean section, female gender and Apgar of more than 5 at one or five minutes (22). While the study conducted at a public sector hospital in Johannesburg, found the main determinants of survival of VLBW neonates to be birth weight, gender, being born before arrival at the hospital, resuscitation at birth, necrotizing enterocolitis (NEC), NCPAP (Nasal Continuous Positive Airway Pressure) and hypotension (10). Even though the results of the two studies on the determinants of survival showed a deviation in their findings (10,22), they both agree that delivery by caesarean section plays a role in VLBW infants' survival. Although delivery by caesarean section is advantageous, it is not feasible to do elective caesarean sections on all pre-term deliveries due to resource constraints (10).

According to the reviewed literature the most common cause of death in VLBW infants was classified as immaturity, mainly in infants weighing < 1 000 grams and infection as the second common cause of death (22). These results are in close agreement with the findings of Ballot (10). Non-attendance at an antenatal clinic, vaginal delivery, an Apgar score < 6 at one or five minutes, and male gender were associated with lower survival rates (22). The odds of survival to hospital discharge were lower in infants weighing < 1 000 grams as compared to infants above the weight of 1 000 grams (22).

The reviewed literature concentrate mostly on babies with a birth weight of less than 1 500 grams, which is evident that there is a gap since none or very few studies have looked at babies with a birth weight of 1 500 grams or more. Hence the strong need for this study and studies alike to address the issue of the knowledge gap.

1.5. Study Aims and Objectives

1.5.1. Research question

What are the factors associated with survival at hospital discharge of newborns weighing ≥ 1 500 grams at birth, at CMJAH between 01 January 2013 to 30 June 2014?

1.5.2. Aim of the study

The study aims to determine the factors associated with survival at hospital discharge of newborns weighing ≥ 1 500 grams at birth, at CMJAH between 01 January 2013 to 30 June 2014.

1.5.3. Study objectives

1. To compare demographic and clinical characteristics of newborns weighing ≥ 1 500 grams at birth, who have died to those surviving up to hospital discharge, at CMJAH from 01 January 2013 to 30 June 2014.

2. To determine the prevalence of survival among newborns weighing ≥ 1 500 grams at birth, at CMJAH from 01 January 2013 to 30 June 2014.

3. To identify factors associated with survival of newborns weighing ≥ 1 500 grams at birth, at CMJAH form 01 January 2013 to 30 June 2014.

CHAPTER 2: Materials and methods

2.1. Introduction

This chapter gives an outline of the study methodology used in answering the research question and addressing the study objectives. The study design, study site, study population as well as data analysis techniques used are discussed. In addition, possible study limitations of the adopted research methods are explained. The chapter ends with a brief highlight on the issue of ethics clearance.

2.2. Study description

2.2.1 Study design

This is a retrospective secondary analysis of data from a computerized neonatal database of newborns with a birth weight of ≥ 1 500 grams who were admitted to the Neonatal ward at CMJAH between the 1st January 2013 and 30th June 2014.

2.2.2 Study site

The original study is being conducted in the neonatal unit at CMJAH, Johannesburg, South Africa. CMJAH is a central hospital in Johannesburg, South Africa. The hospital has a total of 1 088 beds, it provides tertiary services and more highly specialized services, and functioning as a referral centre for regional clinics and hospitals in its referral chain. CMJAH is one of the main teaching hospitals for the University of the Witwatersrand, Faculty of Health Sciences, by providing the service base for undergraduate and post-graduate trainings in the area of health.

2.2.3 Study population

The study population comprises all the newborns with a birth weight of ≥ 1 500 grams, admitted and treated at CMJAH neonatal ward between 1st January 2013 and 30th June 2014.

Data on newborns weighing ≥ 1 500 grams at birth admitted at the neonatal ward between 1st January 2013 and 30th June 2014 were extracted from the existing CMJAH database, which is gathered from hospital records completed by clinicians as part of a continuing effort on clinical audit. Newborns that were included in the database were all admitted to the neonatal unit for some degree of illness at birth; healthy term newborns that go home with their mothers after birth were not included.

Admission criteria for newborns at birth include; all those with a birth weight below 1 750 grams, babies who are clinically ill (including those who need assisted ventilation), all babies who fail to wean out of supplemental oxygen after 8 hours, babies who cannot feed orally, babies with persistently low blood sugar levels, babies with severe birth asphyxia and those with major congenital abnormalities. A total sample of 1 758 newborns weighing ≥ 1 500 grams at birth was used for analysis.

2.2.3 Study variables

2.2.3.1 Dependent variable

In the current study the response variable "Outcome at discharge" is binary, taking only one of the two possible values; died or survived to hospital discharge. By convention, we coded the presence of the outcome as 1 and the absence as 0. Since the study`s main interest is survival, the dependent variable "Outcome at discharge" takes the value of "1" for all newborns who survived up to hospital discharge (newborns who were discharged home or transferred to other wards or hospitals), and the value "0" for all the newborns who died during the period of hospitalization at CMJAH neonatal ward. Newborns who survived up to hospital discharge were termed into "survivors" and those who died during the period of hospitalization into "non-survivors".

2.2.3.2 Independent variables

The predictor variables were decided on based on previous similar studies in the literature and knowledge of the subject as well as on the available data. All binary independent variables were classified as yes and no. The following independent variables were used in the study;

- **Gender:** refers to the sex of the newborns whether female, male or intersex.
- **Place of birth**: refers to the place where delivery of the newborn took place, and the possible categories were; born at Midwife

Obstetric Units (MOU), born at another hospital, born before arrival, inborn (born at CMJAH) or unknown place of birth.

- **Maternal race:** refers to the racial group of the biological mother, the possible categories were black and others (White, Colored, Indian and Asian).
- **Teenage mother:** this is applicable to newborns that were born by mothers younger than the age of 18 years.
- **Gestational age:** refers to how far along the pregnancy was at the time of delivery, measured in weeks. The categorization was as follow; < 32 weeks, 32-37 weeks, 37-42 weeks, > 42 weeks and unknown.
- **Birth weight:** refers to the weight of the newborn at birth, measured in grams. The categorical variable birth weight has four levels; < 2 500 grams, 2 500 – 4 000 grams, > 4 000 grams and unknown.
- **Mode of delivery:** This refers to the mode in which delivery took place and the possible categories are; assisted vaginal delivery, emergency caesarean section, elective caesarean section, normal vaginal delivery, vaginal breech and unknown.
- **Major birth defects:** whether the newborn was born with any birth deformity.
- **Multiple gestations:** whether the mother gave birth to more than one baby.
- **Initial Resuscitation in delivery room:** This is applicable to all the newborns that were resuscitated at birth and the variable has three levels; none, oxygen (for the newborns that were given oxygen) and resuscitation at birth (these includes newborns that were

resuscitated with face mask ventilation, endotracheal tube ventilation, adrenaline, chest compressions or Nasal CPAP).

- **Bacterial Sepsis on or before Day 3:** refers to a blood infection that occurred in neonates within three days after birth.
- **Respiratory Diagnosis:** refers to whether the newborn was diagnosed with any respiratory conditions classified as; Transient tachypnoea of the newborn (TTN), Congenital pneumonia, Meconium aspiration syndrome, Pneumothorax, Pulmonary hemorrhage, Persistent pulmonary hypertension of the newborn (PPHN), Hyaline membrane disease and none.
- **Oxygen on Day 28:** refers to supplementary oxygen given on the 28th day to babies who were hospitalized for a minimum of 28 days and required supplementary oxygen.
- **NCPAP without ETT ventilation:** this is a yes if Continuous Positive Airway Pressure (NCPAP) without Endotracheal Tracheal Tube (ETT) ventilation was performed
- **Cardiovascular:** refers to whether the newborn has been diagnosed with cardiovascular conditions of; Patent Ductus Arteriosus (PDA), Hypotension requiring inotropes, Cardiac failure, Hypertension, Congenital heart disease and none.
- **HIE Grade:** Hypoxic Ischemic Encephalopathy (HIE), which is a type of brain damage that occurs when an infant's brain does not receive enough oxygen and blood. The Sarnat grading scale (25) of HIE is a scoring system used to grade the severity of an HIE injury. The possible categories were level 1, 2, 3 and none.

- **Cerebral Cooling:** refers to the technique of cooling the newborn`s body to reduce brain temperature to avoid brain damage.
- **NEC** (Necrotizing Entero-Colitis): is a medical condition primarily seen in premature infants, were portions of the bowel undergo necrosis.
- **Sepsis after day three**: refers to the late onset of sepsis which is an infection that occurs in an infant after day three.
- **Home oxygen**: refers to whether the newborn was given home supplementary oxygen.
- **Mechanical ventilation:** the binary variable is applicable to newborns that were mechanically ventilated.

2.3 Data management and analysis

2.3.1 Data management

A dataset in Microsoft-Excel spreadsheet was received from CMJAH neonatal ward. This data included both demographic and clinical information of newborns as well as those of their mothers. Data on newborns weighing ≥ 1 500 grams at birth who were admitted at CMJAH Neonatal Unit between 1st January 2013 and 30th June 2014 were extracted and imported into STATA version 12 for range checking, re-coding, renaming and generation of new variables to suit the study objectives and analysis thereof. Newborns whose date of outcome was missing were excluded from the analysis. When performing survival analysis STATA automatically excludes newborns that have experienced the outcome event on the same day of admission, hence they were also excluded from the analysis.

The main outcome variable "Outcome at discharge" was re-coded into a binary variable, with newborns that have died during hospital admission into "Died" and those who were discharged home, discharged to medical ward or surgical ward or transferred to other hospitals into "survivors".

Continuous predictor variables birth weight and gestational age in weeks were re-coded into categorical variables with four and five range groups respectively. The categorical variable "Mode of delivery" was re-coded and caesarean section emergency and caesarean elective were combined and generalized into caesarean section. Further, the variable maternal race underwent the process of recoding and the categories White, Colored, Indian and Asian were combined into "others", due to small numbers in the specified categories. The time-to-event "Length of hospital stay" was calculated by obtaining the difference between date of outcome and date of admission, and it was recorded in days. Binary variable mechanical ventilation was generated for all the newborns that had duration of ventilation.

2.3.2 Statistical analysis

The main outcome "Outcome at discharge" was coded 1 = Survivors and 0 = Non-survivors, for the purposes of analysis. Maternal predictor variables were maternal race and teenage mother. Predictor variables relating to the newborns were gender, place of birth, gestational age, mode of delivery, major birth defects, multiple gestations, bacterial Sepsis on or before day three, respiratory diagnosis, oxygen on day 28, NCPAP without ETT ventilation, Cardiovascular, HIE Grade, cerebral cooling, NEC, sepsis after day three, home oxygen, mechanical ventilation and NCPAP with or without surfactant. Statistical analyses were done as per each objective, and all the tests were carried out at 5 percent level of significance.

1. To compare demographic and clinical characteristics of newborns weighing ≥ 1 500 grams at birth, who have died to those surviving up to hospital discharge, at CMJAH from 01 January 2013 to 30 June 2014.

To answer the first objective, demographic and clinical characteristics pertaining to newborns were analyzed. Categorical variables were summarized using frequency tables and graphs for graphical illustration. Furthermore, cross-tabulation was carried out for categorical variables using Pearson's chi-square test to compare demographic and clinical factors between the two groups (survivors and non-survivors). In cases where there were 2×2 tables, Fisher exact was used to test for association.

2. To determine the prevalence of survival among newborns weighing ≥ 1 500 grams at birth, at CMJAH from 01 January 2013 to 30 June 2014.

The prevalence of survival among newborns weighing ≥ 1 500 grams was analyzed using frequency tables by birth weight, gestational age and gender. In addition survival rates and mortality rates were also computed to further explain the survival patterns of the study sample, tables were used to present the statistics.

3. To identify factors associated with survival of newborns weighing ≥ 1 500 grams at birth, at CMJAH form 01 January 2013 to 30 June 2014.

With regard to the third objective, the binary outcome variable "Outcome at discharge" was analyzed. This involved statistically significant independent variables at univariate analysis. All the variables which were significant in the bivariate analysis at p-value = 0.2 were included into the multivariable Logistic regression, to determine their effect on newborns survival to hospital discharge. Logistic regression and Cox regression methods were used to determine the factors associated with newborns survival to hospital discharge. Thus, a Cox model and logistic model were built to explore the relationship between survival of newborns and the selected covariates. Overall Kaplan Meier curve on the estimate of the survivor function was graphed and by gender as well, to give a graphical illustration on the shape of the survival curve.

For categorical variables a fairly robust non-parametric test the "log-rank test" of equality across strata was used. The log-rank test is a hypothesis test which compares the survival distributions of two groups, by comparing estimates of the hazard functions of the groups at every observed event time. The null hypothesis (H_0) states that there is no difference between groups, and the alternative hypothesis states the opposite. Explanatory variables with a corresponding p-value of 0.2 or less were considered in the multivariable model.

Possible confounder variables and interactions were also investigated at this stage. Variables found with a p-value < 0.05 were considered statistically significant.

2.4 Limitation of the study

The interpretation and generalizability of the results need to be dealt with caution and in the light of the limitations of the primary study. The study focused on an urban hospital and as a central hospital, CMJAH only sees complicated cases and deliveries which by definition are all high risks cases. Hence, the findings may or may not be applicable to the health care facilities or general population in remote areas due to differentials and advancement in medical care facilities and equipment. Secondly, the study used secondary data from a database obtained from patient's records which are selective in nature. The information is only available for the newborns that were admitted and treated at the neonatal ward, and they may not have similar characteristics to the newborns which were never hospitalized or hospitalized in rural South Africa. Clinical records are in nature hampered with incomplete data and this may serve as a limitation to the study.

2.5 Ethics clearance

Approval to conduct the study was obtained from the University of the Witwatersrand Human Research Ethics Committee (HREC), and an ethics clearance certificate (clearance certificate number: M140929) was issued. Further, the dataset received from CMJAH neonatal unit contained no key identifiers and the researcher adhered to strict rules in keeping the information confidential. The dataset was used only for the intended purpose of addressing the study objectives.

Chapter 3: Results

3.1. Introduction

In this chapter, findings of the statistical analysis are presented. Demographic and clinical characteristics of the study sample are given and their influence on newborns survival at hospital discharge is explored. Further, results of the survival analysis are presented and graphical illustrations of the survival function using Kaplan-Meier techniques were explored.

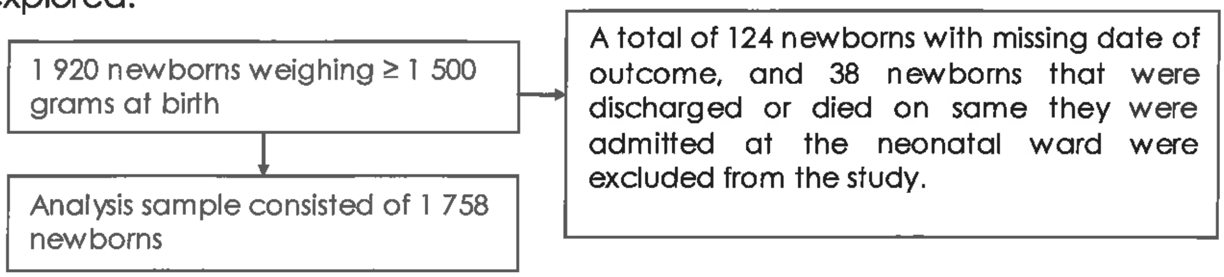

Figure 3.1.1 Flow chart of newborns included in the study to examine factors associated with survival at hospital discharge.

A total of 1 920 newborns were eligible for inclusion into the study, but a total of 162 newborns were excluded from the study. A total of 124 newborns excluded had missing date of outcome and 38 had outcome events occurring on the day they were admitted to the neonatal ward and for survival analysis STATA exclude them automatically, hence they were excluded from all the other analysis to maintain a standardized analysis sample (see Figure 3.1.1).

3.2. Demographic and clinical characteristics of the study sample

3.2.2 Demographic characteristics of the study sample

The analysis sample consisted of a total of 1 758 newborns weighing ≥ 1500 grams at birth, of which a total of 1 654 (94.08%) survived to hospital discharge and 104 (5.92%) died during the period of hospitalization. The study sample comprises of 740 (42.09%) females, 1 011 (57.51%) males, 2 (0.11%) intersex and 5 (0.28%) newborns with missing information on gender (see Figure 3.2.1 below).

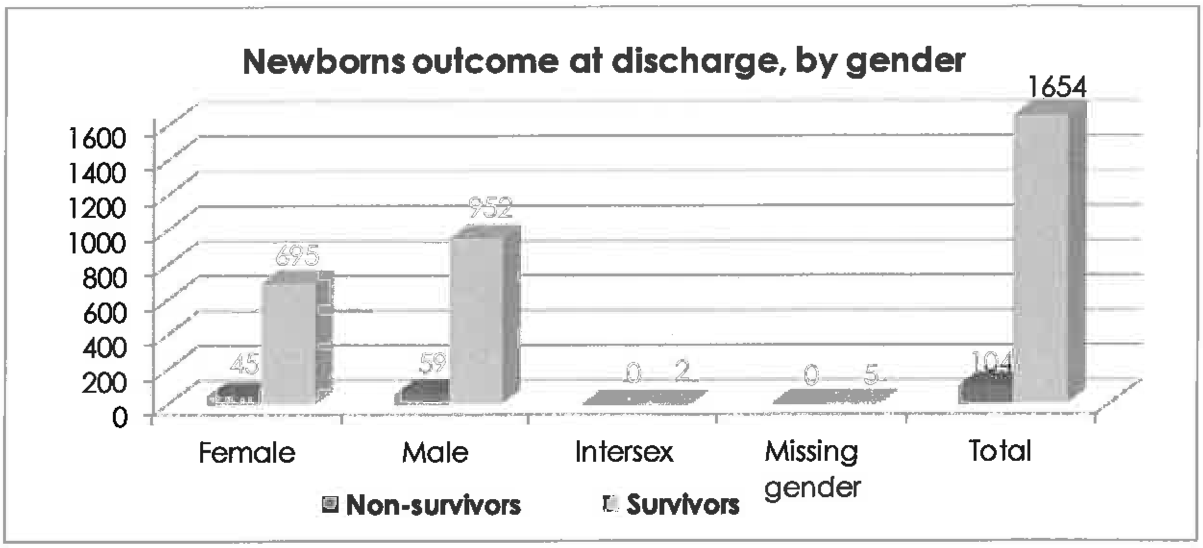

Figure 3.2.2: Survival experience of newborns weighing ≥ 1 500 grams at birth who were admitted to the Neonatal ward at CMJAH between 1st January 2013 and 30th June 2014, by gender.

Table 3.2.2 below summarizes demographic characteristics of the study sample. A bigger proportion of newborns survivors 1 275 (77.09%) and non-survivors 57 (54.81%) were inborn (born at CMJAH), 35 (33.65%) of the newborns non-survivors were born at other hospitals. The majority (95.41%) of newborn survivors were born to black mothers and about 4.6 percent to other South African racial groups (white, colored, Indian, Asian and others).

Table 3.2.2: *Demographic characteristics of newborns weighing ≥ 1500 grams at birth admitted to the neonatal ward at CMJAH between 1st January 2013 and 30th June 2014.*

Predictor variables	Survivors n (%)	Non-survivors n (%)
Place of birth		
Born at MOU	91 (5.50)	9 (8.65)
Born at another hospital	213 (12.88)	35 (33.65)
Born before arrival	43 (2.60)	2 (1.92)
Inborn	1 275 (77.09)	57 (54.81)
Unknown	32 (1.93)	1 (0.96)
Maternal Race		
Black	1 578 (95.41)	98 (94.23)
Others	76 (4.59)	6 (5.77)
Teenage mother <18 years		
Yes	32 (1.93)	2 (1.96)
No	1 448 (87.55)	76 (73.08)
Unknown	174 (10.52)	26 (25.0)
Gestational age in Weeks		
< 32 weeks	272 (16.44)	12 (11.54)
32-37weeks	540 (32.65)	26 (25.0)
37-42weeks	791 (47.82)	60 (57.69)
> 42weeks	4 (0.24)	1 (0.96)
Unknown	47 (2.84)	5 (4.81)

A small proportion of newborns survivors (1.93%) and non-survivors (1.96) were born to teenage mothers (< 18 years of age). Based on the WHO definition on preterm pregnancies (23), about 36.54 percent of the non-surviving newborns were preterm babies, of which 11.54 percent consist of extremely preterm and very preterm babies.

3.2.3 Clinical characteristics of the study sample

In conjunction with demographic characteristic pertaining to newborns, clinical characteristics were also studied to explore the existence of any relationship to newborns survival. Results of the summary statistics are given in Table 3.2.3.

Out of the newborns who died during the period of hospitalization 50.93 percent had birth weights below 2 500 grams, 47.12 percent weighed between 2 500 – 4000 grams and 0.96 percent weighed above 4 000 grams at birth.

A total of 41 (39.42%) newborns out of the total non-survivors, were born with major birth defects. More than half (53.14%) of the newborn who survived to hospital discharge were delivered by Caesarean section. While close to half (49.04%) of non-surviving newborns were delivered by normal vaginal delivery. Vaginal breech and assisted vaginal delivery were the least common mode of delivery in both the survivors and non-survivors.

Table 3.2.3: *Percent distribution of clinical characteristics of newborns weighing ≥ 1500 grams at birth, admitted to the Neonatal ward at CMJAH between 1st January 2013 and 30th June 2014.*

Factors	Survivors n (%)	Non-survivors n (%)
Birth weight (grams)		
< 2500g	774(46.80)	53 (50.93)
2500-4000g	811 (49.05)	49 (47.12)
>4000g	63 (3.81)	1 (0.96)
Unknown	6 (0.36)	1 (0.96)
Major birth defect		
Yes	102 (6.117)	41 (39.42)
No	1 552(93.83)	63 (60.58)
Home oxygen		
Yes	2 (0.12)	1 (0.96)
No	1 652(99.88)	103 (99.04)
Mode Of Delivery		
Assisted vaginal delivery	46 (2.78)	1 (0.96)
Caesarean section	879 (53.14)	39 (37.50)
Normal vaginal delivery	624 (37.73)	51 (49.04)
Vaginal breech	28 (1.69)	1 (0.96)
Unknown	77 (4.66)	12 (11.54)
Multiple Gestation		
Yes	160(9.67)	7 (6.73)
No	1 494(90.33)	97 (93.27)
Bacterial Sepsis on or before Day 3		
Yes	1 610(97.34)	100 (96.15)
No	44 (2.66)	4 (3.85)
Respiratory Diagnosis		
Transient tachypnoea of the newborn	652 (39.42)	5(4.81)
Congenital pneumonia	75 (4.58)	4(3.85)
Meconium aspiration syndrome	76 (4.59)	5(4.81)
Pneumothorax	7 (0.42)	1 (0.96)
Pulmonary hemorrhage	1 (0.06)	2 (1.92)
PPHN	14(0.85)	10 (9.62)
Hyaline membrane disease	314(18.98)	10 (9.62)
None	515(31.14)	67 (64.42)

Factors	Survivors n (%)	Non-survivors n (%)
Oxygen on Day28		
Yes	30 (1.81)	7 (6.73)
No	1 624(98.19)	97 (93.27)
NCPAP without ETT Ventilation		
Yes	203 (12.27)	8 (7.69)
No	1 451(87.73)	96 (92.31)
Cardiovascular		
Patent Ductus Arteriosus	37 (2.24)	2 (1.92)
Hypotension requiring inotropes	13 (0.79)	21 (20.19)
Cardiac failure	1 (0.06)	1 (0.96)
Hypertension	3 (0.18)	1 (0.96)
Congenital heart disease	20 (1.21)	16 (15.38)
None	1 580 (95.53)	63 (60.58)
HIE Grade*		
1	23 (1.39)	1 (0.96)
2	42 (2.54)	6 (5.77)
3	10 (0.60)	12 (11.54)
None	1 579 (95.47)	85 (81.73)
NEC		
Yes	28 (1.69)	11 (10.58)
No	1 626 (98.31)	93 (89.42)
Sepsis After Day3		
Yes	86 (5.20)	19 (18.27)
No	1 568 (94.80)	84 (81.73)
Mechanical ventilation		
Yes	130 (7.86)	38 (36.54)
No	1 524 (92.14)	66 (63.46)
Initial Resuscitation in delivery room		
None	569 (34.40)	47 (45.19)
Oxygen	676 (40.87)	21 (20.19)
Resuscitation at birth	409 (24.73)	36 (34.62)

* Hypoxic Ischaemic Encephalopathy

* The variable Oxygen on day 28 includes only newborns who have survived for a minimum of 28 days

A considerably high number of 47 (45.19%) newborns out of the non-survivors were not resuscitated in the delivery room, and 20.19 percent of those who were resuscitated with oxygen died during the period of admission. A total of 676 (40.87%) of newborns who survived to hospital discharge were resuscitated with oxygen in the delivery room. While a total of 409 (24.73%) newborn survivors were resuscitated with either face mask ventilation, endotracheal tube ventilation, adrenaline, chest compressions or Nasal CPAP. A bigger proportion of 63.46 percent of the newborns non-survivors were not mechanical ventilated.

3.3 Univariate analysis

3.3.1 Introduction

To assess if an association exists between the independent variables and the outcome variable at univariate level, Pearson Chi-square and Fisher Exact test were used.

3.3.2 Comparison of demographic and clinical characteristics of newborns

The first objective of the study was to compare demographic and clinical characteristics of survivors to that of the non-survivors.
Significant statistical difference between survivors and non-survivors could not however be observed for any of these predictor variables; gender, maternal race, teenage mother, birth weight, home oxygen, oxygen on day 28, multiple gestations, bacterial sepsis on or before day three and NCPAP without ETT ventilation at 0.05 level of significance ($P > 0.05$). These results except for home oxygen were excluded from the table.

Differences between survivors and non-survivors are depicted in Table 3.3.2.1. Results of the Pearson's Chi-square showed significant differences between the survivors and non-survivors on a number of newborn characteristics such as; major birth defect, initial resuscitation in delivery room, respiratory diagnosis and mechanical ventilation.

Further, Fisher exact test established a significant association ($P < 0.001$) between outcome at discharge and place of birth, cardiovascular (Patent Ductus Arteriosus, Hypotension requiring inotropes, Cardiac failure, Hypertension and Congenital heart disease), HIE grade, NEC, Sepsis after day three. Gestational age in weeks, modes of delivery and cerebral cooling, were also significantly associated with newborns outcome at hospital discharge at 5 percent level of significance.

Table 3.3.2: *Comparison of demographic and clinical characteristics of newborns weighing ≥ 1 500 grams at birth, who have died during hospitalization to those who survived up to hospital discharge*

Independent variables	**Died n (%)**	**Survivors n (%)**	**P value** [a]
Place of birth			
Born at MOU	9 (8.65)	91 (5.50)	
Born at another hospital	35 (33.65)	213 (12.08)	
Born before arrival	2 (1.92)	43 (2.60)	
Inborn	57 (54.81)	1 275 (77.09)	
Unknown	1 (0.96)	32 (1.93)	< 0.001*b
Gestational age in Weeks			
< 32weeks	12 (11.54)	272 (16.44)	
32-37weeks	26 (25.00)	540 (32.65)	
37-42weeks	60 (57.69)	791 (47.82)	
> 42weeks	1 (0.96)	4 (0.24)	
Unknown	5 (4.81)	47 (2.54)	0.054 b
Clinical characteristics			
Major birth defect			
Yes	41 (39.42)	102 (6.17)	
No	63 (60.58)	1 552 (93.82)	< 0.001*
Home oxygen			
Yes	1 (0.96)	2 (0.12)	
No	103 (99.04)	1 652 (99.88)	0.167 b
Mode Of Delivery			
Assisted vaginal delivery	1 (0.96)	46 (2.78)	
Caesarean section	39 (37.50)	879 (53.14)	
Normal vaginal delivery	51 (49.04)	624 (37.73)	
Vaginal breech	1 (0.96)	28 (1.69)	
Unknown	12 (11.54)	77 (4.66)	0.002 *b

Table 3.3.2 Continues...

Predictor variables	Died n (%)	Survivors n (%)	P value [a]
Initial Resuscitation in delivery room			
None	47 (45.19)	569 (34.40)	
Oxygen	21 (20.19)	676 (40.87)	
Resuscitation at birth	36 (34.62)	409 (24.73)	< 0.001*
Respiratory Diagnosis			
Transient tachypnoea of the newborn	5 (4.81)	652 (39.42)	
Congenital pneumonia	4 (3.85)	75 (4.53)	
Meconium aspiration syndrome	5 (4.81)	76 (4.59)	
Pneumothorax	1 (0.96)	7 (0.42)	
Pulmonary haemorrhage	2 (1.96)	1 (0.06)	
PPHN	10 (9.62)	14 (0.85)	
Hyaline membrane disease	10 (9.62)	314 (18.98)	
None	67 (64.42)	515 (31.14)	< 0.001*
Cardiovascular			
Patent Ductus Arteriosus	2 (1.92)	37 (2.24)	
Hypotension requiring inotropes	21 (20.19)	13 (0.79)	
Cardiac failure	1 (0.96)	1 (0.06)	
Hypertension	1 (0.96)	3 (0.18)	
Congenital heart disease	16 (15.38)	20 (1.21)	
None	63 (60.58)	1 580 (95.53)	< 0.001*[b]
HIE Grade			
1	1 (0.96)	23 (1.39)	
2	6 (5.77)	42 (2.54)	
3	12 (11.54)	10 (0.60)	
None	85 (81.73)	1 579 (95.47)	< 0.001*[b]
NEC			
Yes	11 (10.58)	28 (1.69)	
No	93 (89.42)	1 626 (98.31)	< 0.001*[b]
Sepsis After Day3			
Yes	19 (18.27)	86 (5.20)	
No	85 (81.73)	1 568 (94.80)	< 0.001*[b]
Mechanical ventilation			
Yes	38 (36.54)	130 (7.86)	
No	66 (63.46)	1 524 (92.14)	< 0.001*

*P values < 0.05 are considered statistically significant
[a] Pearson`s Chi-square test
[b] Fisher`s exact test

* The variable Oxygen on day 28 includes only newborns who have survived for a minimum of 28 days

3.4 Multiple Regression analysis

3.4.1 Introduction

In the univariate analysis we assessed the association between a single independent variable and the outcome. Multiple regression analysis allows us the opportunity to explore the influence of numerous factors on the outcome variable at the same time.

Based on Pearson Chi-square and Fischer Exact test results, variables whose corresponding p-values were less than or equal to 0.2 in the univariate analysis were considered in the multiple logistic regression model. These variables were place of birth, gestational age in weeks, major birth defect, home oxygen, mode of delivery, initial resuscitation in delivery room, respiratory diagnosis, cardiovascular, HIE grade, Necrotising Enterocolitis, mechanical ventilation and sepsis after day three.

3.4.2 Logistic regression

In fitting a parsimonious model, a forward selection method was used. Fifteen models were fitted, compared and assessed at each stage using the Likelihood ratio test. A model with eight predictors; place of birth, major birth defect, initial resuscitation in delivery room, respiratory diagnosis, cardiovascular, HIE grade, Necrotising Enterocolitis and mechanical ventilation was chosen as the best fit to the data. The first category of each variable was used as the reference group, except for respiratory diagnosis, cardiovascular and HIE grade were category none was used as the referent group. Results of the final model are presented in Table 3.4.2.

According to the results of the logistic model, the log of the odds of newborns to survive up to hospital discharge was statistically associated with whether they have had major birth defects, diagnosed with NEC and cardiovascular conditions of Hypotension requiring inotropes, Cardiac failure and Congenital heart disease, respiratory diagnosis of TTN and HIE grade levels two and three.

The newborns who were born with major birth defects were less likely to survive up to hospital discharge (OR = 0.12, 95% CI = 0.06: 0.24) compared to normal babies. Similarly, newborns who were diagnosed with NEC presented a worse prognosis (OR = 0.16, 95% CI = 0.06: 0.46). Newborns that were diagnosed with TTN were four times more likely to survive compared to newborns with no known respiratory complications (OR = 3.82, 95% CI = 1.38: 10.61). The presence of cardiovascular conditions of Hypotension requiring inotropes, cardiac failure and congenital heart diseases were associated with a decrease in the odds of survival for newborn sufferers.

With regard to the Hypoxic Ischemic Encephalopathy (HIE), level two and three on HIE grading scale were associated with a worse prognosis for the newborns. The odds of survival for newborns with a level three were 97.8 percent lower than the odds of survival for newborns without any HIE (OR = 0.02, 95% CI = 0.01: 0.06). Mechanical ventilation was marginally associated with newborns outcome at hospital discharge (p-value = 0.06).

Table 3.4.2: *Results of the logistic regression model on survival of newborns weighing ≥ 1 500 grams at birth, admitted to the neonatal ward at CMJAH between 1st January 2013 and 30th June 2014.*

Predictors	Odds ratio	95% Confidence Interval		P>|z|
Constant	26.90	10.06	71.93	< 0.001
Place of birth				
Born at another hospital	1.35	0.50	3.65	0.56
Born before arrival	1.11	0.17	7.17	0.92
Inborn	1.41	0.57	3.50	0.46
Unknown	27.75	1.28	601.47	0.03
Major birth defect	0.12	0.06	0.24	< 0.001
Initial Resuscitation in delivery room				
Oxygen	1.40	0.68	2.87	0.36
Resuscitation at birth	1.11	0.55	2.27	0.77
Respiratory Diagnosis				
Transient tachypnoea of the newborn	3.82	1.38	10.61	0.01
Congenital pneumonia	1.32	0.38	4.52	0.66
Meconium aspiration syndrome	1.69	0.49	5.81	0.41
Pneumothorax	1.35	0.12	15.02	0.81
Pulmonary haemorrhage	0.16	0.01	4.78	0.29
PPHN	0.50	0.14	1.80	0.29
Hyaline membrane disease	1.63	0.67	3.94	0.28
Cardiovascular				
Patent Ductus Arteriosus	2.06	0.37	11.34	0.41
Hypotension requiring inotropes	0.02	0.01	0.06	< 0.001
Cardiac failure	0.02	0.00	0.57	0.02
Hypertension	0.18	0.01	2.89	0.23
Congenital heart disease	0.21	0.08	0.52	0.00
HIE Grade				
1	0.43	0.05	3.51	0.43
2	0.18	0.06	0.52	0.00
3	0.02	0.01	0.06	< 0.001
NEC	0.16	0.06	0.46	0.00
Mechanical Ventilation	0.54	0.29	1.02	0.06
Test	**Chi2**	**Df**		
Overall model evaluation				
Likelihood ratio test	308.30	24		
Goodness of fit test				
Hosmer-Lemeshow	289.16	243		

Predictor variables such as place of birth, initial resuscitation in delivery room and most levels of respiratory diagnosis were not at all significantly associated with outcome of newborns at hospital discharge, as their corresponding p-values were greater than 0.05. But the Likelihood test proved that the model which includes these variables to be a superior fit than the model without them, therefore they were kept in the model.

The overall model was significant, with a corresponding Likelihood ratio Chi-square value of 308.3 and a p-value of < 0.001. According to the Hosmer-Lemeshow goodness of fit test, there is no evidence of a lack of fit in our model ($p > 0.05$).

3.5 Survival Analysis

3.5.1 Introduction

With regard to the current study the earliest date of outcome was 3rd January 2013, and the latest was the 30th June 2014. The outcome at discharge was either newborns were discharged from the CMJAH neonatal ward or died during the period of hospital admission. Newborns who were discharged from the neonatal ward where characterized into survivors and those who died into non-survivors. The failure event in the current study is "Died" which represents all the newborns who have died during hospitalization.

The total analysis time at risk was 11 903 days, with a median time of four days. The maximum length of hospitalization was 78 days.

3.5.2 Mortality rates

To assess the variation or the rate at which death occurred for males and females, and between different weight categories, mortality rates were computed by gender and by birth weight.

According to Table 3.5.2 below, there were no major difference in mortality rates between males and females, but the rates were slightly high for females (8.91 per 1 000 live births) than for male newborns (8.67 per 1 000 live births). Mortality rate for intersex was zero since all the two intersex babies survived up to hospital discharge, but either way the number was too small for comparisons. The results shows that newborn mortality is differential by birth weight, as the rates are high among newborns with a birth weight of 2 500 – 4 000 grams (11.57 per 1 000 live births) when compared with newborns weighing above 4 000 grams (4.07 per 1 000 live births) and under 2 500 grams (7.18 per 1 000 live births) respectively.

Table 3.5.2 *Mortality rates of newborns weighing ≥ 1 500 grams at birth, admitted to the neonatal ward at CMJAH between 1st January 2013 and 30th June 2014, by gender and birth weight.*

Predictor variables	Deaths	Person years	Mortality rate (s)	95 % Confidence interval	
Gender					
Female	45	5.06	8.91	6.64	11.92
Male	59	6.81	8.67	6.71	11.18
Intersex	0	0.01	0	-	-
Unknown	0	0.02	0	-	-
Birth weight (grams)					
< 2500g	53	7.38	7.18	5.49	9.40
2500-4000g	49	4.24	11.57	8.74	15.31
> 4000g	1	0.25	4.07	0.57	28.86
Unknown	1	0.04	23.26	3.28	0.00

3.5.3 Prevalence of survival

The prevalence of survival among newborns in this case will be the proportion of newborns who have survived up to hospital discharge. Newborns survival rates in terms of gender, birth weight and gestational age given in Table 3.5.3 below.

The results show that survival rates are associated with birth weight, showing that the high the newborns birth weight the high their rates of survival. With regard to gestational age, a gestational age of less than 32 weeks was associated with high survival rate of close to 85.0 percent, and newborns with a gestational age of more than 42 weeks had the lowest survival rate of 16.0 percent.

Table 3.5.3: *Prevalence and survival rates of newborns weighing ≥ 1 500 grams at birth, who have died during hospitalization to those surviving up to hospital discharge*

Predictors	Survivors n(%)	Survival rate	95% Confidence Interval	
Gender				
Female	695 (39.5)	0.14	0.13	0.15
Male	952 (54.2)	0.14	0.13	0.15
Intersex	2 (0.1)	0.14	0.04	0.57
Missing	5 (0.3)	0.23	0.09	0.55
Birth weight (grams)				
< 2500g	774 (44.0)	0.10	0.10	0.11
2500-4000g	811 (46.1)	0.19	0.18	0.21
> 4000g	63 (3.6)	0.26	0.20	0.33
Unknown	4 (0.2)	0.14	0.06	0.31
Gestational age (weeks)				
< 32 weeks	272 (15.5)	0.85	0.08	0.10
32-37weeks	540 (30.7)	0.13	0.12	0.14
37-42weeks	791 (45.0)	0.20	0.18	0.21
> 42weeks	4 (0.2)	0.16	0.06	0.43
Unknown	47 (2.7)	0.10	0.08	0.13

3.5.4 Kaplain-Meier survival function

The Kaplain-Meier survival function plots the survival experience of the cohort as a function of time and they are useful in determining whether the survival functions are parallel in evaluating the proportional hazard assumption.

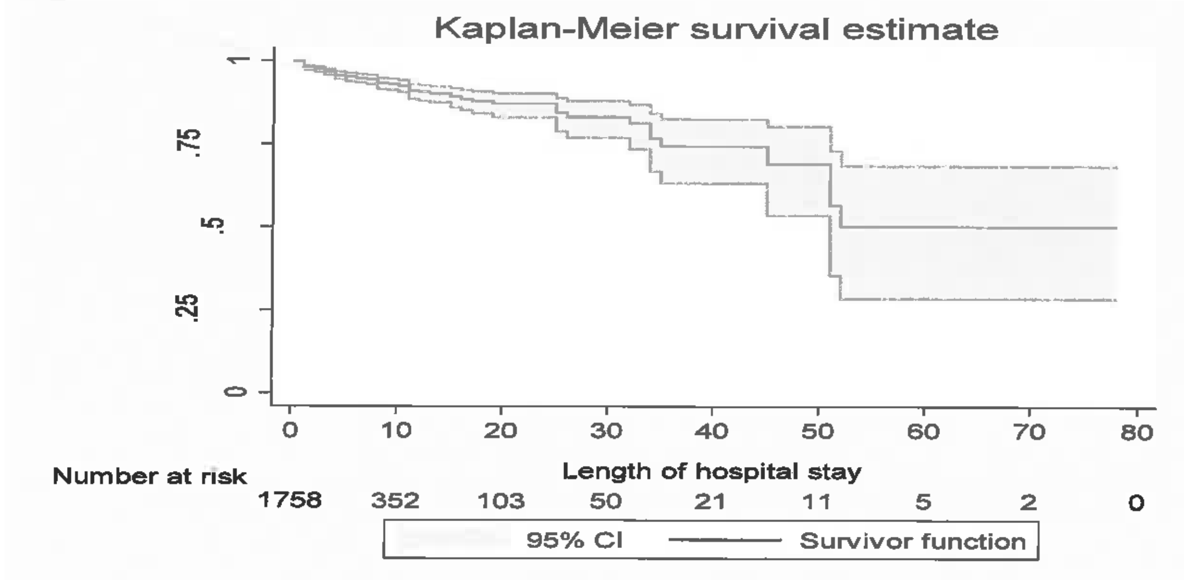

Figure 3.5.4.1 Kaplain-Meier estimates of the survivor function, of newborns weighing ≥ 1 500 grams at birth, who were admitted to the neonatal ward at CMJAH between 1st January 2013 and 30th June 2014.

Figure 3.5.4.1 above is characterized by a high probability of survival at admission and the subsequent few days. About 80.0 percent of the total study sample was at risk from time zero to the 10th day of hospitalization, and only a small proportion (20.02 %) was at risk beyond the 10th day (hospitalized for more than 10 days). The key note from the figure is that, newborns survival probability to hospital discharge decreases with an increasing length of hospitalization.

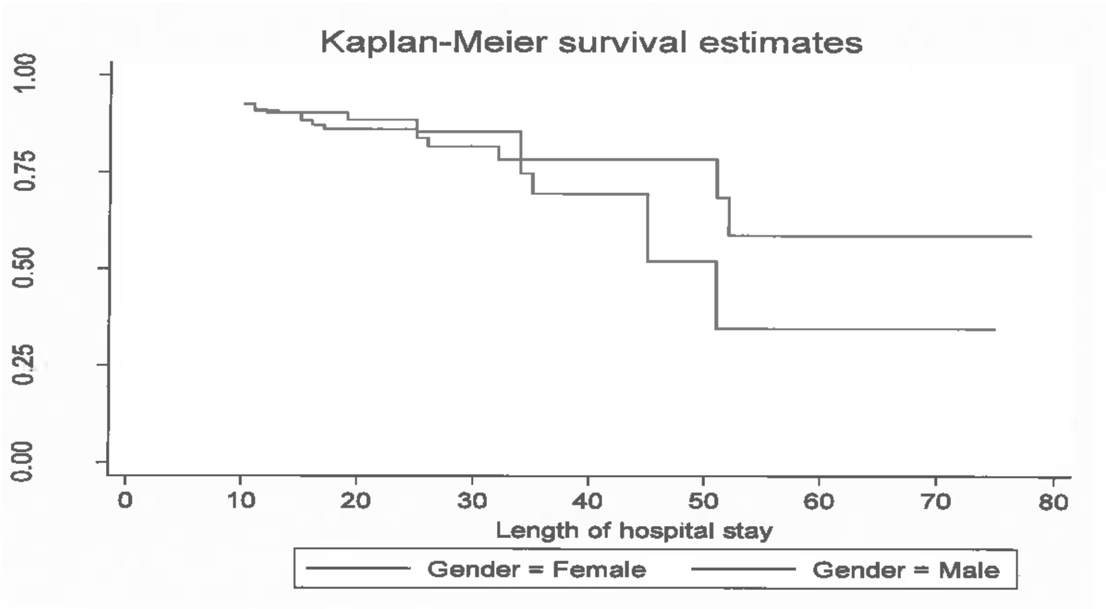

Figure 3.5.4.2 Kaplain-Meier estimates of the survivor function, of newborns weighing ≥ 1 500 grams at birth, admitted to the neonatal ward at CMJAH between 1st January 2013 and 30th June 2014, by gender.

According to Figure 3.5.4.2 above, the probability of survival is slightly higher for females than for males during the first few days of admission. But at around the 35th day, the survival probability of female gradually dropped below that of the male newborns.

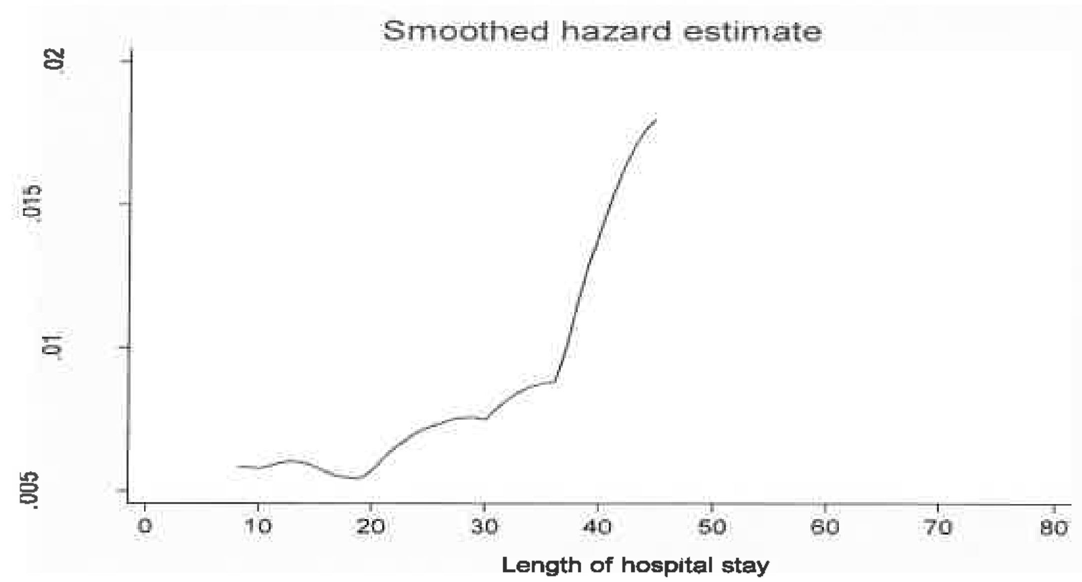

Figure 3.5.4.3 Smoothed hazard estimates of newborns weighing ≥ 1 500 grams at birth, who were admitted to the Neonatal ward at CMJAH between 1st January 2013 and 30th June 2014

Figure 3.5.4.3 shows that mortality is considerably low for newborns at around the first few days of hospitalizations, and it increases with increasing length of hospital stay. The hazard rate is considerably high for the newborns who were admitted for more than 20 days when compared to those who were discharged earlier.

3.5.6 Univariate analysis

In any statistical data analysis it is fundamental to do some univariate analysis before proceeding to more complex multiple regression models. Univariate analysis is useful in determining the predictor variables to be considered in the multivariable model.

3.5.6.1 Log-rank test for equality of survivor functions

The table below (Table 3.5.6.1) shows the results of predictor variables with a p-value of less than or equal to 0.2, in terms of the observed and expected death events. These variables were place of birth, birth weight, gestational age in weeks, major birth defect, mode of delivery, initial resuscitation in delivery room, bacterial sepsis on or before day three, cerebral cooling, HIE grade, Sepsis after day three, NEC, cardiovascular, NCPAP without ETT Ventilation, NJRP and respiratory diagnosis.

There was a significant (corresponding p-values were less than 0.05) differences between the survivor functions of the two groups with regard to their place of birth, whether they had major birth defects, resuscitation in delivery room, respiratory and cardiovascular diagnosis, NCPAP without ETT ventilation, HIE grade, cerebral cooling, NEC, and NJRP.

Table 3.5.6.1 *Results of the log-rank test of equality across strata of newborns weighing ≥ 1 500 grams at birth, who were admitted to the Neonatal ward at CMJAH between 1st January 2013 and 30th June 2014.*

Predictor variables	Events Observed	Events expected	chi2(2)	Pr>chi2
Place of birth				
Born at MOU	9	7		
Born at another hospital	35	19		
Born before arrival	2	5		
Inborn	57	71		
Unknown	1	2	19.75	0.001*
Birth weight (grams)				
< 2500g	53	61		
2500-4000g	49	40		
>4000g	1	2		
Unknown	1	0	4.94	0.176
Gestational age (weeks)				
< 32weeks	12	26		
32-37weeks	26	35		
37-42weeks	60	39		
> 42weeks	1	0		
Unknown	5	4	25.86	< 0.001*
Major birth defect				
Yes	41	14		
No	63	90	63.16	< 0.001*
Mode Of Delivery				
Assisted vaginal delivery	1	2		
Caesarean section	39	50		
Normal vaginal delivery	51	44		
Vaginal breech	1	2		
Unknown	12	7	8.52	0.074
Initial Resuscitation in delivery room				
None	47	38		
Oxygen	21	39		
Resuscitation at birth	36	27	13.88	0.001*

Table 3.5.6.1 Continues...

Predictor variables	Events Observed	Events expected	chi2(2)	Pr>chi2
Respiratory Diagnosis				
Transient tachypnoea of the newborn	5	27		
Congenital pneumonia	5	4		
Meconium aspiration syndrome	5	5		
Pneumothorax	1	1		
Pulmonary haemorrhage	2	0		
PPHN	10	2		
Hyaline membrane disease	10	28		
None	67	35	113.86	< 0.001*
NCPAP without ETT Ventilation				
Yes	8	16		
No	96	88	5.31	0.021*
Cardiovascular				
Patent Ductus Arteriosus	2	6		
Hypotension requiring inotropes	21	3		
Cardiac failure	1	0		
Hypertension	1	1		
Congenital heart disease	16	5		
None	63	90	160.64	< 0.001*
HIE Grade				
1	1	1		
2	6	3		
3	12	1		
None	85	99	98.29	0.001*
Mechanical ventilation				
Yes	38	17		
No	66	87	34.73	< 0.001*
Necrotising Enterocolitis				
Yes	11	6		
No	93	98	4.86	0.028*
NJRP				
Yes	9	25		
No	86	70	14.18	0.001*

*P values < 0.05 are considered statistically significant

[a]Pearson`s Chi-square test

The above cited predictors were all probable candidates for the multivariable Cox model, as their corresponding p-values were less than or equal to 0.2.

3.5.7 Multivariable Survival analysis

Multivariate analysis unlike univariate analysis allows us to observe and analyze more than one predictor variable at a time in relation to the outcome of interest.

3.5.7.1 Cox Proportional Hazard model

A semi-parametric Cox Proportional Hazard model which expresses the relationship between the hazard function and a set of covariates was used to determine factors associated with survival of newborns at hospital discharge.

A forward selection model building technique was used, by first considering a model with the outcome variable only and thereafter adding significant predictor variables one at a time starting with the most significant variables. The significance and superiority of the models was ascertained at each level using the Likelihood test. Categorical variables with more than one level where included in the model using dummy variables by making use of the xi command, the first category of each variable was taken as the reference group and is omitted from the result table. Except for respiratory diagnosis, cardiovascular and HIE grade, were category none was used as the reference group.

The multivariable Cox regression model (see Table 3.5.7.1) revealed that the variables most strongly associated with newborn outcome at discharge was the presence major birth defects ($P < 0.001$). Newborns who had major birth defects at birth had 4.3 times increased risk of dying compared to normal babies (HR = 4.25, 95% CI: 2.43, 7.45).

Birth weights of 2 500 – 4 000 grams and above 4 000 grams where significantly associated with survival (p-values < 0.05). Newborns whose birth weight was between 2 500 – 4 000 grams presented a 58.7 percent high chances of survival than newborns with a birth weight of below 2 500 grams at birth (HR = 0.41, 95% CI: 0.28: 0.69), while those with a birth weight of above 4000 grams showed an even better survival chances (HR = 0.09, CI = 0.01; 0.82).

In addition, gestational age of 37-42 and above 42 weeks were significant predictors of newborns outcome at hospital discharge (P=0.043 and P=0.009 respectively). Newborns whose gestational age was more than 42 weeks had close to 19 folds increase in hazard (HR = 18.73, 95% CI: 2.09, 167.54) compared to newborns whose gestational age was less than 32 weeks. The risk in the hazard rate increased with an increasing HIE grades. Newborns who ranked grade three (which is considered as severe Hypoxic-Ischemic Encephalopathy) on the HIE grading were close to 17 times more likely to die compared to those with no diagnosed Hypoxic-Ischemic Encephalopathy (HR = 16.85, 95% CI: 8.19, 34.66).

Respiratory diagnosis of Transient tachypnoea of the newborn and Hyaline membrane disease were positively associated with survival of newborns outcome at hospital discharge.

Table 3.5.7.1 *Results of the multivariable Cox proportional hazard model of newborns weighing ≥ 1 500 grams at birth, who were admitted to the Neonatal ward at CMJAH between 1st January 2013 and 30th June 2014.*

Predictor variables	Hazard ratio	Standard errors	95% Confidence Interval		P>z
Birth weight (grams)					
2500-4000g	0.41	0.11	0.25	0.69	0.00
> 4000g	0.09	0.10	0.01	0.82	0.03
Unknown	0.15	0.24	0.01	3.36	0.23
Gestational age (weeks)					
32-37weeks	1.07	0.41	0.51	2.25	0.86
37-42weeks	2.27	0.92	1.03	5.04	0.04
> 42weeks	18.73	20.94	2.09	167.54	0.01
Unknown	1.70	1.00	0.54	5.39	0.37
Major birth defect					
Yes	4.25	1.22	2.43	7.45	< 0.001
Respiratory Diagnosis					
Transient tachypnoea of the newborn	0.24	0.12	0.09	0.62	0.00
Congenital pneumonia	0.94	0.52	0.32	2.79	0.91
Meconium aspiration syndrome	0.71	0.36	0.26	1.94	0.51
Pneumothorax	0.56	0.64	0.06	5.23	0.61
Pulmonary haemorrhage	1.97	1.57	0.41	9.42	0.40
PPHN	1.50	0.66	0.64	3.55	0.35
Hyaline membrane disease	0.35	0.14	0.15	0.78	0.01
HIE Grade					
1	2.68	2.75	0.36	20.12	0.34
2	3.58	1.71	1.40	9.12	0.01
3	16.85	6.20	8.19	34.66	< 0.001
Cardiovascular					
Patent Ductus Arteriosus	0.31	0.23	0.07	1.33	0.11
Hypotension requiring inotropes	14.58	5.01	7.44	28.59	< 0.001
Cardiac failure	23.95	39.45	0.95	604.44	0.05
Hypertension	2.73	3.18	0.28	26.92	0.39
Congenital heart disease	2.23	0.77	1.13	4.40	0.02

Generally, newborns who were diagnosed with cardiovascular conditions (apart from Patent Ductus Arteriosus) presented an increased hazard rate, predicting a worse prognosis for the newborns. Hypotension requiring inotropes, and Congenital heart disease were significantly associated with survival (p-value < 0.05), newborns who were diagnosed with Hypotension requiring inotropes showed an increased risk of dying (HR = 15.72, CI = 8.08:30.57). These results are supported by Figure 3.6.1.1 below, which shows the survival experience of newborns that were diagnosed with hypotension.

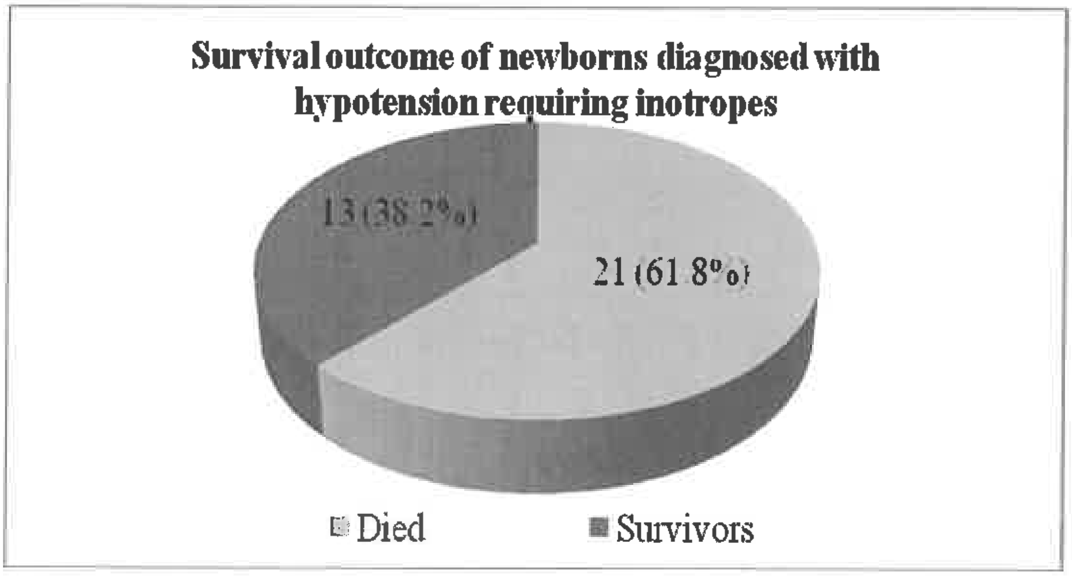

Figure 3.5.7.1 Survival experience of newborns weighing ≥ 1 500 grams at birth, which were diagnosed with hypotension requiring inotropes.

A total of 34 newborns were diagnosed with this cardiovascular condition (Hypotension requiring inotropes) and out of that total, more than half 21 (61.8 %) of the newborns died during hospitalization (see Figure 3.5.7.1).

3.5.7.2 Proportional Hazard Assumption investigation

One of the fundamental key assumptions of the Cox model fitted above is that of the proportional hazards. Cox proportional hazard model assumes that the hazard ratios are constant over time; this means that two strata should have hazards that are proportional over time.

STATA can compute the Schoenfeld residuals, which are the differences between the values of an individual's covariates at failure and the risk-weighted mean covariates for those at risk, and use these to construct a test of proportionality of hazards. To test for proportionality in the hazard ratios, STATA compute two tests; the global test and a more detailed test for each covariate, based on the scaled Schoenfeld residuals.

The null hypothesis (H_0) state that the log hazard ratio function is constant over time (zero slopes), while the alternative hypothesis (H_1) condition that the log hazard ratio function is not constant over time. Rejecting the null hypothesis indicates a violation of the assumption.

Table 3.5.7.2 below gives the results of the proportional hazard assumption based on the Schoenfeld residuals. The global test yield a Chi-squared value of 11.08 with a p-value of 0.98 where $p > 0.05$, hence globally there is no evidence that the proportional hazards assumption has been violated. Looking at specific covariates, it is also apparent that there is lack of evidence against the proportional hazards assumption since the covariates corresponding p-values were all not significant at 5 percent level of significance.

Table 3.5.7.2 *Results of the Proportional-hazards assumption test based on the Schoenfeld residuals.*

Predictors	Rho	chi2	Degree of freedom	Prob > Chi2
Gestational age (weeks)				
32-37weeks	0.05	0.22	1	0.64
37-42weeks	0.01	0.01	1	0.90
> 42weeks	0.06	0.36	1	0.55
Unknown	-0.01	0.02	1	0.89
Respiratory Diagnosis				
Congenital pneumonia	0.05	0.30	1	0.58
Meconium aspiration syndrome	0.01	0.00	1	0.95
Pneumothorax	-0.12	1.72	1	0.19
Pulmonary haemorrhage	-0.11	1.84	1	0.18
PPHN	-0.01	0.01	1	0.91
Hyaline membrane disease	-0.03	0.17	1	0.68
None	0.09	0.93	1	0.33
Major birth defect				
Yes	0.02	0.03	1	0.86
Cardiovascular				
Patent Ductus Arteriosus	0.04	0.13	1	0.72
Hypotension requiring inotropes	-0.02	0.04	1	0.85
Cardiac failure	0.01	0.00	1	0.95
Hypertension	0.05	0.38	1	0.54
Congenital heart disease	-0.12	1.61	1	0.20
HIE Grade				
1	-0.01	0.01	1	0.92
2	-0.06	0.37	1	0.54
3	-0.01	0.02	1	0.89
Birth weight (grams)				
2 500 – 4 000g	-0.05	0.27	1	0.60
> 4 000g	-0.03	0.12	1	0.73
Unknown	-0.02	0.01	1	0.93
Global test		**11.08**	**23**	**0.9824**

Chapter 4: Discussion

4.1. Introduction

This chapter gives a summary of the main findings of the study, by discussing the characteristics of the study group, prevalence of survival among the study group as well as a detailed discussion on significant predictors of survival. Similarities between the current study findings and other similar research in the literature are explored. Possible study flaws and potential areas of study which could be pursued to build on or to better this study are discussed.

The present study gives insight in the survival and the predicting factors pertaining to newborns of a defined birth weight group during the period of hospitalization, at an urban neonatal ward setting in Johannesburg. The first hours and subsequent few days following child birth are the most critical with regard to the survival and wellbeing of both the mother and the newborn. Likewise, the medical care and attention provided during this period is of great importance, because it and in combination with other clinical, demographic and biological factors determines the health outcome of both the mother her newborn.

4.2 Newborns survival experience and comparison between the survivors and the non-survivors

The prevalence of survival among newborns weighing ≥ 1 500 grams at birth was quite high, as more than ninety percent (94.1%) newborns survived up to hospital discharge. As anticipated, the prevalence of survival was high compared to the 70.5 percent survival of VLBW neonates reported at the same unit from 2006 - 2007 (10). Mortality was reasonable low in this sub group, as there were only 5.9 percent deaths. But more efforts can still be done to reduce newborn mortality, especially for deaths resulting from avoidable causes such as birth asphyxia, diarrhoea, pneumonia, measles, malaria, HIV/AIDS and the underlying cause of under nutrition (24).

The study sample was predominated by males (57.5%), and 42.1 percent were females. Survival rates for males and females were similar, although slightly high for males (14.0%) than for females (13.7%). However, the absolute differences were small and the log rank test has not shown any significant difference in the survivor functions between different gender groups. This is contrarily to known knowledge of the male disadvantage with regard to neonatal mortality at birth and consequent few days (9,25–27). In the current study, higher survival for males can be potentially attributed to the fact that there were more male babies.

A bigger proportion of 1 359 (75.8%) newborns were born at CMJAH, contributing 54.8 percent to the total deaths. Both Chi-square and the log-rank test found there to be a highly significant difference between the survivors and the non-survivors with regards to their place of birth.

Majority of newborns were in the weight categories of 2 500 - 4 000 grams (49.3%) and less than 2 500 grams (46.7%) at birth. Mortality was most predominant among newborns with a birth weight of less than 2 500 grams, as out of all deaths more than half (50.4%) newborns were in that weight group. However` both Pearson chi-square and Log-rank tests found no statistically significant difference between the survivors and non-survivors given their birth weight.

With regards to gestational age, a total of 876 (48.8%) had a gestational age of 37 – 42 weeks with 48.2 percent of these newborns surviving, 288 (16.1%) newborns had a gestational age of less than 32 weeks contributing close to 13.0 percent to the total deaths (see Table 3.3.2).

The most common mode of delivery was caesarean section, with more than half 935 (52.1%) newborns being delivered through elective or emergency caesarean and 95.2 percent of them survived to hospital discharge. Caesarean section can be very risky, but if done well by a careful skilled professional it can be very safe, and more and more women nowadays are opting for elective caesarean section to avoid labor pain. Mortality was most high among a total of 689 newborns who were delivered through normal vaginal delivery, contributing 46.2 percent to the total deaths.

A total of 146 (8.1%) newborns were born with major birth defects of a given severity and out of those, a total of 44 (30.1%) died during the period of hospitalization. A highly significant p-value of less than 0.001 was observed, implying a significant difference between the survivor and non-survivors for newborns born with birth defects.

A total of 708 (39.4%) newborns were resuscitated in the delivery room with oxygen and 456 (25.4%) with other methods (face mask, endotracheal tube ventilation, adrenaline, chest compression or nasal CPAP). The statistical analysis revealed that the survivor functions of newborns who were resuscitated at birth differ significantly between the survivors and non- survivors. A total of 168 (9.56%) newborns were mechanically ventilated, both Pearson`s chi-square and Log rank test results showed highly significant differences in the outcome of survivors and non-survivors ($p < 0.001$). There was however no significant difference in the survivor functions of the survivors and non-survivors with regards to whether they were given supplementary oxygen on day 28, for newborns who were hospitalized for a minimum of 28 days.

A total of 657 (37.4%) newborns were diagnosed with Transient Tachypnoea of the newborn, which is a respiratory problem that is observed in newborns soon after delivery. The other common respiratory diagnosis was the Hyaline membrane disease, affecting a total of 324 (18.4%) newborns. Both the Chi-square and Log-rank test results showed a highly significant difference between survivors and non-survivors ($p < 0.001$), relating to whether newborns were diagnosed with any respiratory condition. Similarly, there were significant differences between newborns survivors and non-survivors with reference to whether they were diagnosed with cardiovascular complications, p-value < 0.001.

With regard to HIE grade, a total of 48 (2.73%) newborns had a grade 2 which refers to mild Hypoxic Ischaemic Encephalopathy, and a total of 22 (1.25%) had a grade three (severe Hypoxic Ischaemic Encephalopathy). Hypoxic Ischaemic

Encephalopathy in this study group was fortunately not so common; however significant difference between survivor and non-survivors existed.

4.3 Predictors of newborns survival

The aim of the present study is to determine factors associated with survival at hospital discharge of newborns weighing ≥ 1 500 grams at birth. In quest to determine significant predictors of newborns survival at hospital discharge, two statistical methods were carried out, the Logistic regression and the Cox regression. Although slightly different, the results of the two resulting models were similar. The most significant predictors of survival identified with the logistic regression model are major birth defects and NEC. Other partially significant categorical variables are respiratory diagnosis of TTN, HIE grades two and three, and cardiovascular diagnosis of hypotension requiring inotropes, cardiac failure and congenital heart disease. In addition to these variables, birth weights of 2 500 and above, gestational ages of 37 to 42 weeks and above, and Hyaline membrane disease were also statistically associated with survival in the Cox regression analysis. Even though NEC emerged as one of the most significant predictors of newborns outcome at hospital discharge in the logistic regression, it was however not a candidate in the final Cox regression model.

The survival times in our dataset are highly skewed due to outliers arising from the presence of newborns that were hospitalized much longer than the others. The skewed distribution is typical of survival data, as newborns were admitted and experienced the outcome at different time intervals. Based on the reasons cited above and the goodness of fit test, the Cox model emerged as the superior model and was chosen as the best fit to our data. Consequently its results will be discussed here.

The primary purpose of neonatal death audits is to determine those contributing factors which are implicated in deaths that could be avoided if fundamental interventions and practices are implemented. To my knowledge this is the first study done in South Africa so far looking specifically at the predictors of survival at hospital discharge of newborns with a birth weight of ≥ 1 500 grams. Prior researches have mostly looked at the outcomes and predictors of survival in VLBW, LBW (Low Birth Weight) babies and babies born before arrival to hospital (1,10,11). Identifying causes of deaths and factors contributing to improved outcome of normal birth weight newborns can also be of great importance and beneficial in making progress towards reaching the MDGs as well as the National Development Plan. However minimal the statistics are currently, deaths of newborns weighing 1 500 grams and above at birth contribute significantly to the country`s overall child mortality and if overlooked can escalate dramatically.

Having said that, according to the results of the Cox proportional model the most significant determinant of newborns survival at hospital discharge was major birth defect ($p < 0.001$). Other factors which emerged as strong predictors of survival (although all levels were not significant) were respiratory diagnosis of TTN and Hyline membrane disease, Cardiovascular diagnosis of hypotension requiring inotropes cardiac failure and congenital heart disease, birth weight of 2 500 – 4 000 grams and above, gestational ages of 37 – 42 weeks and above, and HIE grade two and three.

Newborns who were born with major birth defects had a hazard ratio of 4.25 (95% CI = 2.4253: 7.4515), predicting a worse prognosis for newborns sufferers. The findings compares well with causes of perinatal deaths reported by Statistic South Africa (27). More lives may be saved, if newborns with birth deformities are diagnosed well in advance and offered the medical care and therapeutic support they deserve. This can however only be achieved if all deliveries were done in a hospital setting with adequate resources and by a skilled birth attendant.

Birth weight is an important factor when studying neonatal deaths, and the role it plays when it comes to survival of newborns is well documented in the literature (10,11,20). In a study done in urban Pakistan a birth weight of < 2 000 was associated with neonatal mortality (20). On the contrary in the current study birth weight was associated with improved newborns survival, this could be attributed to the differences in birth weights with respect to the two studies. A birth weights of 2 500 – 4 000 grams and above 4 000 grams were significantly associated with survival, with corresponding p-values of 0.001 and 0.032 respectively. Newborns whose birth weight were above 4 000 grams at birth had a reduced risks of dying by 91.0 percent (HR = 0.0897, 95% CI = 0.0098: 0.8225). A 58.7 percent (HR = 0.4128, 95% CI = 0.2465: 0.6913) reduction in the mortality risk for newborn weighing 2 500 – 4 000 grams at birth, compared to those with a birth weight of below 2 500 grams was observed. The findings are not surprising and are similar to the findings of the study done among VLBW babies in the same setting at CMJAH neonatal unit (10).

Further, gestational ages of 37- 42 and above 42 weeks were significant predictors of survival. Newborns whose gestational age in weeks were more than 42 weeks had a notably increase in hazard (HR = 18.7319, 95% CI: 2.0943, 197.5441) compared to newborns whose gestational ages were less than 32 weeks. These results compares favorably with that of a study done among extremely preterm neonates in Canada, which also found gestational age as a predicting factor of neonatal outcome (22,28). In agreement with the findings of the current study, other studies have also revealed that post term pregnancies can pose great risks for both the mother and the newborns which at times contributes to increased still births and neonatal deaths (29,30).

Respiratory condition of TTN was associated with an increased newborn survival (HR = 0.24, 95% CI = 0.09: 0.62) and prevalence of survival among this group of newborns was considerably high (99.2 %). This is because TTN usually eases after few days with treatment and majority of newborns sufferers usually make a full recovery. Surprisingly, hyaline membrane disease was also associated with improved survival among the group of newborn sufferers (HR = 0.35, 95% CI = 0.15: 0.78).

The presence cardiovascular conditions of Hypotension requiring inotropes and congenital heart disease were significantly associated with increased risk of the hazard ($P<0.05$). Newborns who were diagnosed with Hypotension had close to 15 folds increased risk of death (HR = 14.58, 95% CI = 7.44: 28.59), while newborns with congenital heart disease experienced twice the risk of death (HR = 2.23, 95% CI = 1.13: 4.40) as opposed to newborns with no cardiovascular condition. Other cardiovascular conditions of cardiac failure and Hypertension predicted a worse prognosis for newborns diagnosed with these conditions. According to the perinatal death audits for 2011 to 2013, cardiovascular disorder was among the leading causes of early neonatal deaths for the period of the consecutive three years from 2011 to 2013 (27).

Level two and three on the HIE grading system, which are characterized as mild and severe HIE respectively emerged as significant predictors of survival ($p < 0.05$). The odds of survival decreases with an increase in the HIE grade. Newborns with severe HIE (level three) experienced close to 17 times increased risk of hazard (HR = 16.85, 95% CI = 8.19: 34.66) when compared to babies without Hypoxic Ischaemic Encephalopathy.

The Kaplain-Meier survival curve has illustrated that newborns survival probability to hospital discharge decreases with an increasing length of admission. Early discharge of newborns will not only help resolve the problem of over crowdedness in short-staffed hospitals, but it will also help in achieving positive outcomes of newborns. Studies have found out that longer stay in hospital would also expose these infants to nosocomial infections that increase morbidity and mortality, especially in low birth weight babies (31,32).

Place of birth in our study did not reach statistical significance for our final model as a predictor of newborn survival. Nonetheless, both Chi-square and the Log-rank test results found highly significant differences between newborns survivors and non-survivors with regard to their place of birth. Based on the statistical release on perinatal deaths by Statistics South Africa, a significant number of perinatal deaths can be prevented because they occur due to the type of place of delivery and the quality of care received during delivery (27). This goes to show that place of birth plays an important role in improving neonatal survival rates and consequently preventing deaths from avoidable causes.

Although mechanical ventilation did not achieve statistical significance in this study and was not an entrant in the final Cox model as a predictor of survival, significant differences existed between newborns survivors and non-survivors. Mechanical ventilation was however marginally associated with newborns outcome at hospital discharge in the logistic regression model (p-value = 0.058).

The major limitation of our study analysis could be attributed to the small number of newborns case experiencing and diagnosed with a certain condition. For example only a total of two newborns out of the total study sample have experience cardiac failure. Differences in the quality and nature of the treatment given to newborns with different conditions might have influenced their outcome. For example newborns of a low birth weight may have been monitored closely than newborns of much high birth weights, or newborns with severe HIE may have been treated more aggressively compared to newborns with mild HIE and this often is attributable to inadequate resources and understaffing.

Another possible limitation of the study is the retrospective design, which is inevitably complicated by incomplete data obtained from hospital records. An example relating to the current study is that of a total of 124 eligible newborns with missing date of outcome, which were consequently excluded from the analysis.
A possible area of study to further strengthen or build on the findings of this study would be to do a matched case control study between newborns survivors and non-survivors who have suffered major birth defects. As we have gathered that the presence of birth defects hampered the survival of newborns greatly, it will be interesting to evaluate the characteristics of newborns by birth defect types and understand the underlying preventable causes of birth deformity in newborns and hopefully come up with preventative and therapeutic interventions.

Chapter 5: Conclusion and recommendations

5.1 Introduction

This chapter gives a conclusion and recommendations following from the discussion of the results in the previous chapter. The chapter highlights major resulting recommendations and areas for future research.

5.2 Conclusion and recommendations

Overall, the survival to hospital discharge rate of newborns weighing ≥ 1 500 grams at birth was reasonably better compared to the survival of VLBW and LBW. Even so, more collective efforts still need to be done to further enhance the quality and delivery of health care services, in order to decrease deaths and morbidity of newborns from avoidable risk and causing factors.

Based on our study findings, the predictor variable major birth defects emerged as the most significant predictor of survival. Other predictor variables that were also significantly associated with survival even though all levels did not reach significance, were birth weight, gestational age, TTN, hyaline membrane disease, HIE grade two and three, Hypotension and congenital heart disease. Our study has shown that high birth weight is associated with positive newborns prognosis. Although our results failed to show any statistically significant association between gender and newborns survival, it has been well documented in previous studies as a strong predictor of survival, especially the female gender (9,22,25).

The presence of major birth defects has hampered the prognosis and survival of newborns thereof. That being said, there is a need to employ effective measures to persuade and educate expectant mothers on the importance of regular Antenatal care (ANC) attendance as a way for early detection of pregnancy related complications. Secondly, regular visit to the hospitals coupled with expectant mothers' knowledge of the early signs of pregnancy related complications will potentially limit the birth of extreme and premature births which can results in birth deformities and other associated complications to the newborns. Ensuring that all deliveries are done at the hospital, improved neonatal resuscitation, improving therapeutic strategies to prevent or treat birth defects, effective treatment of respiratory and cardiovascular related conditions are some of the strategies which can aid in improving survival rates of newborns.

Resources constraints and staffing are among the many challenges faced by the policy makers, clinicians and researchers in addressing issues related to neonatal deaths and under five years mortality. But it is also the absence of reliable data on births, deaths and their causes that makes it difficult to track progress toward the MDGs (33). In order to monitor and track progress towards achieving goals of reducing child mortality and improve overall maternal health, we need information that will enable us to see the magnitude of the problem (27). The availability of reliable data on deaths and their causes aids in formulating informed, relevant and well articulated policies in addressing the problems from the grass roots. It also helps researchers to study mortality trends, the risks factors and causes, in order to narrow down to specific causes in coming up with possible long term solutions. CMAJH is among the hospitals that regularly submit data to the PPIP which covers about 40 percent of births in South Africa, however` the majority of neonatal deaths remain unaudited and the national figure is thus probably higher (10). Perinatal deaths audit serves as an indicator of the quality of prenatal, obstetric and neonatal care, by providing the information required to improve health care for both expectant mothers and newborns (27).

WHO has developed guidelines with recommendations on improving outcomes of preterm babies (34). So far, much emphasis has been made on the care and interventions on how to improve survival rates of VLBW and LBW babies which is commendable. But it`s about time we look at normal weight newborns as well and solve these problems parallel, if we neglect them and focus only on VLBW and LBW births, the problem is going to escalate and before we know it the death rates for normal weight babies have bypassed that of VLBW and LBW babies.

The finding of the study provides policy makers, pediatricians and clinicians with evidence-based information that may be useful in decision making with regarding to improving newborns survival by strengthen the associated factors. The study also contributes to the knowledge sphere with efforts to close the knowledge gap when it comes to factors associated with survival in this group of newborns.

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6. Appendices

6.1 APPENDIX ONE: Plagiarism declaration form

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I ***Johanna Penelao Mufeti (Student number: 886552)*** am a student registered for the degree of ***Master of Science in Epidemiology in the field of Epidemiology and Biostatistics*** in the academic year 2014.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

Signature: ____________ Date: *13/10/2016*

6.2 APPENDIX TWO: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Ms Johanna Penelao Mufeti and Prof DE Ballot

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140929

NAME: (Principal Investigator)	Ms Johanna Penelao Mufeti and Prof DE Ballot
DEPARTMENT:	School of Public Health Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Factors Associated with Survival of New-Borns at Hospital Discharge at Charlotte Maxeke Johannesburg Academic Hospital SA from 1 January 2013 to 30 June 2014
DATE CONSIDERED:	03/10/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof TF Chirwa
APPROVED BY:	Professor Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	12/12/2014

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.**

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES