UNIVERSITY of RWANDA

PREVALENCE AND FACTORS ASSOCIATED WITH INTRAHOSPITAL POST-NATAL GROWTH FAILURE UP TO THE POINT OF DISCHARGE AT KIGALI UNIVERSITY TEACHING HOSPITAL/NEONATOLOGY UNIT

Investigator: MUNYENGABE François, MD

College of Medicine and Health Sciences

School of Medicine

Master of Pediatric and child health

2018-03-28

UNIVERSITY of RWANDA

PREVALENCE AND FACTORS ASSOCIATED WITH INTRAHOSPITAL POST-NATAL GROWTH FAILURE UP TO THE POINT OF DISCHARGE AT KIGALI UNIVERSITY TEACHING HOSPITAL/ NEONATOLOGY UNIT.

By

MUNYENGABE Francois, MD

A dissertation submitted in partial fulfilment of the requirements for the degree of

MASTER OF MEDICINE IN PEDIATRICS AND CHILD HEALTH

In the College of Medicine and Health Sciences

Supervisors: 1. Dr Faustine AGABA Neonatologist, CHUK

2. Dr Peter Cartledge, Paediatrician, CHUK

3. Dr James Webb, Imperial College London.

2018-03-28

DECLARATION

I declare that this memoire contains my own work except where acknowledged.

Dr MUNYENGABE François, RMDC: 2188

Signature…….

Date: March 28th, 2019

ACKNOWLEDGEMENTS

I cordially thank my Almighty God for being with me all the time.

My sincerely grateful to the government of Rwanda for the sponsorship of my studies.

My respectful thanks goes to AGABA Faustine, PETER Cartledge and JAMES Webb my supervisors, for their support, guidance and encouragement for this achieved work.

Many thanks to my family for their love, support and encouragements.

I thank neonatology team at CHUK for their support.

Finally I would like to thank the residents in Pediatrics for their support during the past 4 years.

May God bless everyone who contributed for my training and for all my achievements, nothing could have been done without you.

DEDICATION

To The Almighty God

To my parents GAKWERERE Felecien and MUKANTAGARA Francine for your love, support and encouragement.

To my wife UWINGABIRE Joselyne for your love and encouragement.

To my children IZERE TETA M Ella and INEZA Jolie Diella.

To my sisters and brothers for your encouragement.

I dedicate this work.

GLOSSARY OF TERMS

AAP- American Academy of Pediatrics

AGA- Appropriate for Gestational age

CGA-Correct Gestational Age

EGA- Estimated Gestational Age

ELBW- Extremely Low Birth Weight

ESPGHAN- European society of gastroenterology, hepatology, and nutrition

G- Gram

HIE-Hypoxic Ischemic encephalopathy

HRH- Human Resources for Health

IRB-Institutional Review Board

LBW- low birth weight

NEC- Necrotising Enterocolitis

NICHD- National Institute of Child and Human Development

NICU-Neonatal Intensive Care Unit

PN- parenteral nutrition

PNGF – Postnatal Growth Failure (also called Extra-uterine growth failure in the literature)

RDS-Respiratory Distress Syndrome

SGA-Small for gestational Age

SPSS- Statistical Package for the Social Sciences

SSA- sub-Saharan Africa

US-Ultrasound

CHUK– Centre Hospitalier Universitaire de Kigali

VLBW-very low birth weight

WHO-world health organization

LIST OF TABLES

LIST OF FIGURE

LIST OF APPENDICES

TABLE OF CONTENTS

ABSTRACT

Background: Post-natal growth failure (PNGF) remains a big challenge globally; despite many remarkable advances in neonatal care, many studies show that there are many independent variables contributing to poor post-natal growth.

Aims: The aim of the project was to provide an up-to-date overview of the prevalence of PNGF for LBW neonates and all the factors contributing to PNGF for LBW neonates admitted at the neonatology unit of a tertiary hospital in Kigali.

Methodology: A prospective cross sectional study was conducted and the data collected was entered into Excel and was statistically analyzed using the Statistical Package for the Social Sciences SPSS 21.0. Categorical variables (nominal) were described using frequency and percentages and statistically analyzed using the Chi Square test. Multivariate logistic regression analysis was carried out to determine which factors are independently associated with PNGF. For continuous data, the mean and standard deviation were used, and a Student T-test and/or ANOVA was also conducted depending on the number of groups. A P-value of < 0.05 was considered as statistically significant.

Results: 122 neonates meeting inclusion criteria were enrolled in the study, females' neonates represented 57% of all participants, 63.1% among enrolled neonates were born AGA, 111 neonates survived to discharge, 11 neonates died during study period, infants with PNGF at discharge were 72.1%, growth velocity was 14.9g/kg/day.
The study showed that there are many variables with non-significant association with PNGF, Neonates who are small for gestation age at birth have significant risk to develop PNGF for weight at discharge with adjusted odd ratio of 8.756 (CI: 1.59 to 48.22), and p=0.013 .

Conclusion: Postnatal growth failure is common in low birth weight neonates especially those who are small for gestational age at birth, and there is non- significant correlation with different morbidities.

CHAPTER I. INTRODUCTION

1.1 GENERAL INTRODUCTION

It has been previously found that there are many factors contributing to the development of post-natal growth failure (PNGF); low birth weight (LBW) is one of the reported factors (1).

PNGF remains a big problem globally, with a lot of research conducted in order to reduce its incidence, but despite many advancements in the area of neonatology, globally , incidence of neonates suffering from post- natal growth failure still persists, and this remains high in neonates who are small for gestational age as well as the neonates with morbidities (1).

This is despite evidence that normal growth patterns can be established with robust implementation of feeding guidelines, Johnson et al (2017) proved improvements in nutrient intake and weight gain in their study evaluating the effects of new guideline implementation by measuring objective changes in nutrition intake (2).

1.1.1 Definition

The Vermont Oxford Network defines PNGF as discharge weight that is lower than the 10th percentile for postmenstrual age (3,4).

PNGF is considered a marker of nutrition deficit for which many strategies have been developed to provide adequate nutrition to neonates born with LBW. Poor post-natal nutrition, not using evidence-based feeding strategies, remain an important contributing factor (5)

Fenton and Kim curves, which are post natal growth curves that have recently become available (6), are used to assess the growth velocity of neonates during hospitalization till the day of hospital discharge (7,8).

1.1.2 Which neonates at high risk of getting PNGF?

Many studies found that PNGF occurs most commonly in neonates of VLBW and ELBW. In 2001, the National Institute of Child and Human Development (NICHD) Neonatal Research Network found that 97% of all VLBW and 99% of all ELBW neonates included in the study experienced PNGF by 36 weeks corrected gestational age (9).

Clark et al (2003) have reported the relationship between PNGF and both EGA and birth weight. They found that as EGA and birth weight decreased, the incidence of EGR increased. Clark. showed significant PNGF for weight (28%), length (34%), and head circumference (16%) in preterm infants during hospitalization (10). Prematurity and associated critical illness were among the factors which contributed a lot to the delay in starting minimal enteral feeds and this results in nutritional deficits. Morbidities that affect premature infants, such as hyaline membrane disease, prolonged respiratory support, neonatal sepsis, broncho-pulmonary dysplasia, anemia, intra-ventricular hemorrhage, and exposure to post-natal steroids all contribute highly to poor postnatal growth (11).

Nangia et al (2017), identified that optimal nutrition is the fundamental factor for reducing mortality and long term morbidities like PNGF and poor neurodevelopmental outcomes in preterm neonates with LBW (12) .

1.1.3 Target postnatal growth and calorific goal

Ayotollah and colleagues (2015) state that anthropometric measurements serve as significant indices to predict infant health and future outcome. Weight, height and head circumference of neonates are the most common parameters for measuring the physical growth of neonates (13).

Preterm as well as term neonates lose weight during their 1st week of life, and once they are back at their birth weight, they should gain 15-20g/kg/day up until term when they gain 20-30g/day for the initial term period (14,15).

The American academy of pediatrics (AAP) and the European society of gastroenterology, hepatology , and nutrition (ESPGHAN) committees recommend an energy intake of 105-130kcal/kg/day and 110-135 kcal/kg/day for preterm neonates respectively (16).

1.1.4 LBW neonates

LBW is defined by World Health Organization as the first weight recorded after birth that is less than 2500g, regardless of gestational age. This birth weight is further categorized into very low birth weight (VLBW < 1500g) and extremely low birth weight (ELBW< 1000g) (17).

Globally, it is estimated that 15-20% of all births, or > 20 million newborns annually are LBW neonates, 97% being born in developing countries (18). Badshab et al, found that neonates with LBW have a >20 times greater risk of dying than neonates with a birth weight of >2500 g (17).

According to the WHO, there are marked global and regional variations in LBW rates. An estimated 6% of infants are born LBW in East Asia and the Pacific, 13% in Sub-Saharan Africa, and 28% in South Asia (17).

1.2 PROBLEM STATEMENT

PNGF remains a significant challenge globally despite many remarkable advances in neonatal care. Many studies show that there are many independent variables contributing to poor post-natal growth, but there is limited data for the Sub-Saharan region, and specifically in our region**.** In Rwanda. no single study has been conducted to demonstrate how we stand in terms of post neonatal growth velocity, frequency of PNGF. Even though the main variables that contribute to PNGF are known, it's still obscure which ones contribute more to PNGF in our setting; such knowledge would allow us to prevent its incidence.

This prospective cross-sectional study was conducted to clarify this in our setting, as the information gained from the study will help health professionals to prevent PNGF.

1.3 AIMS AND OBJECTIVES

1.3.1 Research aims

The aim of the project is to provide a current overview on the prevalence of PNGF for LBW neonates as well as of all the factors contributing to PNGF; this was based on evaluation of LBW neonates admitted at the neonatology unit of a tertiary hospital in Kigali.

1.3.2 Research objectives

The specific objectives of this research project were to:

Assess the prevalence and risk factors for PNGF in LBW neonates,
Assess the post-natal growth velocity in LBW,
Evaluate the feeding variables contributing to PNGF in LBW neonates.

2.1.1 Neonates affected by PNGF

Many studies identify that the neonates that are most affected are those in developing countries, especially those born prematurely with LBW and who are small for gestational age (7). There is limited data regarding postnatal growth of LBW infants in sub-Saharan Africa. Several observational studies have confirmed the strong influence of nutritional practices on growth (19).

Ruth and colleagues found in their study that most affected neonates have a birth weight that is average for gestational age, but by the time of hospital discharge, their weight is lower than the 10th percentile for corrected gestational age (20).

Radmacher and associates found in their study that hospitalized neonates with extremely LBW and those who were born before 29 weeks had birth weights that were average for gestational age but at the time of hospital discharge from the NICU, 59% had PNGF. PNGF is more common in infants <2500g and it is for this reason that this study will focus on this cohort of neonates (20).

According to the Vermont Oxford network in 2015, in study done on 362 833 infants weighing 501 to 1500 g without major birth defects born from 2000 to 2013 and who were hospitalized for 15 to 175 days at 736 North American hospitals in the Vermont Oxford Network, it was found that the incidence of PNGF was decreasing from 64.5%to 50.3% and severe PNGF was 27.5% (4).

2.1.2 Risk factors associated with PNGF

Studies show that in order to decrease the incidence of PNGF, the first consideration has to be identification of all contributing factors (19).

Embleton and colleagues, in their cross-sectional studies of PNGF, found that poor growth was associated with feeding problems, and respiratory problems, as well as other clinical findings and demographic factors (21).

Ehrenkranz et al found other independent contributing factors such as IUGR, the male gender, a need for assisted ventilation on the 1st day of life and prolonged need for respiratory support, length of hospital stay, and the development of neonatal morbidities such as BPD, NEC and late onset sepsis (22).

2.1.3 Consequences of PNGF

2.1.3.1 Short term consequences

Length of stay: Marinkovi et al. found that poor postnatal weight gain in LBW neonates is associated with a prolonged hospital stay, increased cost of care and an increased risk of nosocomial infection (23).

Infection rates: it has been found in study done by S. Lee et al. that the group of infants with PNGF, compared to the non-PNGF group, the PNGF group had a higher incidence of

sepsis and NEC during the admission period (3), many studies demonstrated that infection is one of the comorbidities contributing to the PNGF with (3,24).

Survival from the neonatal unit:

The increased survival rate of very LBW neonates (VLBW; <1500 g) in recent decades has focused attention on the importance of growth and nutrition to improve health and developmental outcomes (25). It has been found in study done by Lima et al, that increased hospital stay by adding one day of hospitalization increased the chance of growth restriction at discharge by 3%, and being SGA at birth increased the risk by 2.1 times (10).

2.1.3.2 Neurodevelopmental consequences

PNGF remains a big problem worldwide despite advancement in the area of neonatology. Studies have found an association between PNGF, developmental outcome, and long-term morbidity.

Clark et al. 2003 found that postnatal growth lag is associated with neurological and sensory handicaps and poor school performance (26).

In two longitudinal studies done by Ruth and colleagues comparing 242 VLBW infants to 233 normal birth weight infants at 20 years of age, VLBW infants scored significantly lower on measures of academic achievement, and fewer graduated from high school (20).

PNGF in preterm neonates, secondary to suboptimal nutrition, is a major problem in neonatal intensive care units. Evidence is emerging that early growth deficits have long-term adverse effects, including short stature and poor neurodevelopmental outcomes.

2.1.4 Prevention of PNGF

Nevertheless, in study done by Yu et al. early initiation of enteral feeding in a sub-nutritional trophic quantity is vital for promoting gut motility and bile secretion, inducing lactase activity, and reducing sepsis and cholestasis jaundice (27).

Trophic feeds: B. Su et al(2014) found that trophic feeds reduce the cumulative caloric and protein deficits in acute stage to minimal degree and this contribute to the prevention of PNGF and associated abnormal cognitive and neurodevelopmental outcomes (5)

***Advancement of feeds*:** many studies showed that in clinically stable VLBW infants, early introduction of progressive feeds and advancement of feeds at a faster rate (30–35 mL/kg/d) is safe and does not increase the incidence of NEC (28).

***Fortifying feeds**:* V.Gupta et al (2019), found in their prospective, randomized controlled trial in the neonatal unit of a tertiary care hospital in South India that fortification with infant milk powder achieves better growth parameters than unfortified human milk and can be a useful alternative for feeding preterm VLBW infants in low resource settings (25,).

CHAPTER III. METHODOLOGY

1.2 STUDY DESIGN

Prospective cross-sectional study

1.3 SETTINGS

The study was done at CHUK, Kigali University teaching hospital, Neonatology Unit. CHUK is the main public hospital, located in the Centre of Kigali - the capital city of Rwanda with a population of 1.2 million and it serves as a tertiary hospital. The hospital conducts approximately 2000 deliveries annually, the neonatology unit holds 20-30 babies each day, their care is assured by 3-5 nurses and 3-5 residents supervised by 2 pediatricians.

After approval from the IRB, recruitment of data was initiated until the required sample size was achieved. Data collection required six months. The data was prospectively collected, by the principal investigator (PI) from patient case-files and ranged from admission up to the point of discharge or death - whichever came first. No post-discharge outcomes/variables were assessed.

1.4 PARTICIPANTS

All neonates with birth weight of <2500 grams that were admitted to the neonatology unit within 24 hours of birth were included. Neonates with congenital anomalies (e.g. gastroschisis) ,neonates who were transferred during hospitalization and those who had not completed their inpatient stay (i.e still inpatients) were excluded from the study.

Recruitment and enrolment: a convenience sampling methodology was used to select the participants.

1.5 OUTCOMES

The following definitions for variables were employed,

Post-natal growth failure (PNGF): Was defined as weight at discharge which is less than the 10^{th} percentile.

Time to regain birth weight: The day when the neonate's attained weight equaled or surpassed the initial birth weight, or defined as the day birth weight was regained and sustained (or exceeded) for 2 consecutive days.

The length of stay: defined as the number of days from the date of admission to the date of discharge or death.

How were outcomes defined? SGA neonates were defined as those with birth weight less than 10th percentile by sex using the Fenton growth chart. The length of stay was defined as the number of days from the date of admission to the date of discharge or death.

Growth rate (g/kg/day) was defined as the weight gained or lost from the date of admission to the date of discharge or death divided by the length of stay and the birth weight of the neonate.

Time to reach full feeds: Defined as the number of days required for the infant to receive all nutritional intake (enteral). Full enteral feeds will be defined as total enteral feeds of 150 ml/kg/day, which gives a total calorie of 100 kcal/ kg/day, estimated from breast milk intake, which gives 67 kcal/100 ml (14).

Mortality rate: the number of deaths per thousand population per year: in effect the incidence of death in a population.

Exploratory Variables

SGA: Defined as weight at birth which is less than 10^{th} percentile by sex, using the Alexander reference population US national reference (30).

Gestational age: Was assessed by the last menstrual period and first trimester ultra-sonogram. If the information on obstetric echography and last menstrual periods are unknown, the gestational age was calculated by the method of clinical examination via the new Ballard score.

Birth weight: Neonates were classified as LBW (1500-2500g), Very Low-birth Weight (VLBW 1000-1500g) and Extremely LBW (<1000g).

Type of feed: was defined as the predominant feed received in the first 4 weeks.

Feeding intolerance: Feeding intolerance is defined by difficulty in ingestion or digestion of the milk that causes a disruption in the enteral feeding plan due to the manifestation of clinical symptoms. These symptoms include increased gastric residuals (>50%) of the previous feeding, emesis, abdominal distention, visible bowel loops, and change in the character of stool (31).

Chronic lung disease: CLD is defined as a need for increased oxygen: Infants < 32 weeks gestation: oxygen requirement at 36 weeks gestational age (GA) or at discharge (whichever comes first).Infants ≥ 32 weeks GA: oxygen requirement at age > 28 d or at discharge (whichever comes first).

Demographics: Name; gender; social class

Co-morbidities: e.g. RDS, sepsi

1.6 DATA COLLECTION TOOLS

A questionnaire was designed specifically for this study (Appendix 1), including prenatal, natal, and post-natal conditions, infant sex and gestational age, birth weight, feeding methods, date of birth, time of initiation of enteral feeding, time to reach full enteral feeds, comorbidities related to prematurity, time to regain birth weight, duration of hospital stay, and the mother's medical illnesses during pregnancy were recorded.

After approval from the academic team, three cases were collected to pilot the questionnaire. These data sets were not used in the final analysis and were destroyed. This was to ensure feasibility of the questionnaire and to build the excel spreadsheet.

The questionnaire was verified using the Core Outcome Set created by Imperial College in London to ensure relevant outcomes (32).

1.7 LIMITATION AND BIAS

Data was collected from patient files which were not always complete. There is a risk of confounding (e.g. gestation) which was addressed in the statistical analysis.

1.8 SAMPLE SIZE CALCULATION

Sample size required for determining the frequency of a factor in a population was determined using the Kelsey formula (http://www.openepi.com/SampleSize/SSPropor.htm):

$$n = \mathbf{deff} \times \frac{\mathbf{N\hat{p}\hat{q}}}{\frac{\mathbf{d^2}}{\mathbf{1.96^2}}(\mathbf{N}-\mathbf{1}) + \mathbf{\hat{p}\hat{q}}}$$

Where:

deff = design effect = 1.0

N = population size = CHUK receives approximately 50 cases per month; a four month population is therefore 200

$\hat{p}$ =the estimated proportion = The recent study of a large multicenter by Vermont Oxford Network reported that the prevalence of PNGF was 27.5% (24).

$\hat{q} = 1 - \hat{p}$

p = desired absolute precision or absolute level of precision = 95% confidence interval

n = sample size = **122**

Therefore 122 cases were recruited for this study, with cases being recruited from the point of ethics clearance until the sample size was achieved.

1.9 STATISTICAL METHODS

All collected data was entered into Excel and was statistically analyzed using Statistical Package for the Social Sciences SPSS 24.0.

Excel was used to determine which neonates were SGA and PNGF by Fenton growth reference (8), weight velocities (g/kg/day), weight at birth and at discharge (8).

Categorical variables (nominal) were described using frequency and percentage and statistically analyzed using the Chi-Squared (X) test (Fischer exact if less than 5 cases).

Factors with p value < 0.2, were included in multivariate logistic regression analysis, with descriptions of adjusted odds ratios (AOR), were carried out to determine which factors are independently associated with PNGF.

For continuous data, the mean and standard deviation (or median if non-normally distributed) were used, and the Student T-test and/or ANOVA was also calculated depending on the number of groups. A p-value of < 0.05 was considered as statistically significant.

1.10 ETHICAL STUDY/OVERSIGHT

Funding & Sponsors: No funding has been sought for this project.

Potential conflict of interest: No conflict of interest

Confidentiality: The information collected was protected with a password and the names were not on the questionnaire. A unique patient identifier was used to protect the data. Identifiers were kept in a separate password protected spreadsheet.

Informed Consent: As no contact was made with the patients and/or caregivers, with no experimentation on subjects and only review of cases files, consent was not necessary.

Incentives for subjects: No incentives received by subjects for this study

Risk to subject: The only significant risk of the study was related to confidentiality. However, based on the methodology and procedure used in the study; no physical, social, emotional, legal and/or financial risks associated to the subjects during this study.

Ethical approval: This research project was approved by Institutional Review Board (IRB) College of Medicine and Health Sciences (CMHS.

Academic integrity: The study protocol was approved by the University of Rwanda academic team on September 7th, 2018.

Institutional review board (IRB):

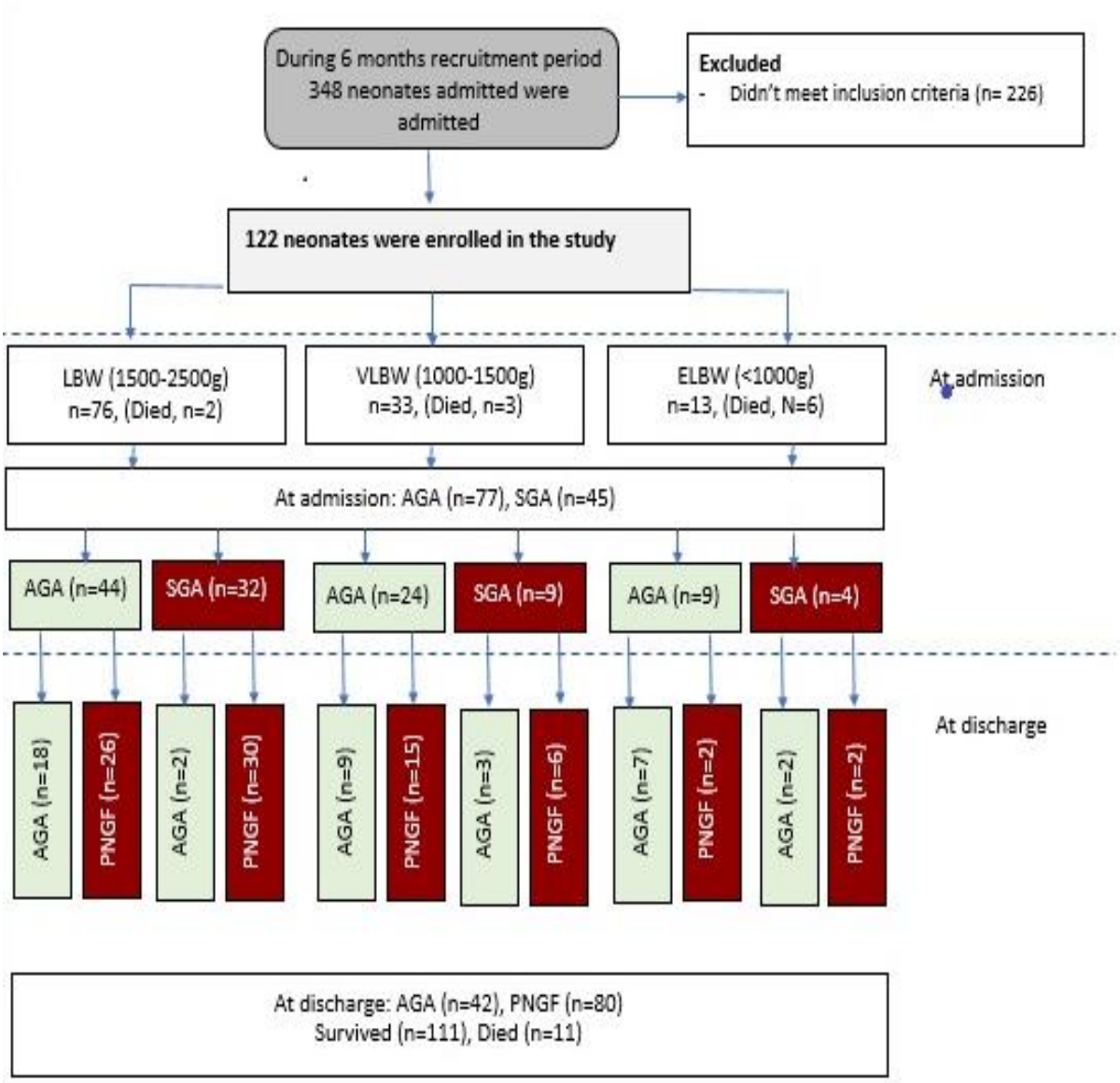
The study protocol was reviewed and approved by the University of Rwanda , College of Medicine and Health Science IRB; Ref: No 358/CMHS IRB/2018

CHAPTER IV: RESULTS

4.1 Demographics:

A total of 348 neonates were admitted to the neonatal unit. Of these, we enrolled 122 neonates that met our inclusion criteria (Figure 1). The sample population consisted of 57% females, and the participants were categorized as either LBW (62%), VLBW (27%) or ELBW (11%). Of these, 63% were AGA at birth upon admission, 9% neonates died during the study period, and the PNGF among the survived neonates was 80 (72.1%).

Figure 1: Consort diagram



4.2 Characteristics of LBW neonates and their mothers:

The majority of neonates in the study were AGA (77 neonates; 63.1%) and female neonates represented 57% of our sample. 78% of the neonates were born between 32-37 weeks GA, and 111 survived up till discharge. What is most notable is that 82% of our participants were from a moderate social economic status group (Table 1).

Table 1: Characteristics of LBW neonates and their mothers

Variables	**N (%)**
Gender	
Female	69 (56.6)
Male	53 (43.4)
Gestational groups	
Term (>37 weeks)	7 (5.7%)
32-37 weeks	78 (63.9)
28-32 weeks	29 (23.8)
<28 weeks	8 (6.6%)
Categories by birth weight	
AGA	77 (63.1%)
Maternal age	
Old (>25years)	98 (80.3%)
Social status	
Low (Ubudehe category 1 and 2)	20 (18.3 %)
Moderate (ubudehe category 3)	91 (82 %)
Problem during pregnancy:	
GD	
HBP	3 (2.5%)
Maternal infection	43 (35.2 %)
Maternal HIV positive	20 (16.4%)
	2 (1.6 %)
Mortality	
Dead	11(9%)
Alive	111(91%)
Exposure to Antenatal steroids	80 (65.6%)

4. 3 Anthropometric demographic characteristics at birth and at discharge

The mean birth weight was 1611 ± 422 g, whilst mean gestational age was 32.7 ± 3.1 weeks at admission. The mean weight at discharge was 1793.5 ± 341.5 g, at an average gestational age of 35 ± 2.9 weeks, the mean z-score for weight decreased during the hospitalization period (-1.1 to -1.9) (table 2) which mean that our babies had mild postnatal growth failure.

Table 2: Anthropometric demographic characteristics at birth and at discharge

	Birth	***Discharge***
Variables	Mean ±SD	Mean ± SD
Weight (g)	1611 (SD ±422)	1793.5 (SD±341.5)
	Min=540,Max=2490	Min=540,Max=2660
Weight Z score	-1.1 (SD± 1.003)	-1.9(SD±1.16)
	Min= -4.2, Max= 1.0	Min=-5.9,Max=1.0
HC (cm)	30.2 (SD ±2.5)	32.1 (SD ± 1.6)
	Min=23, Max=36	Min=27, Max=36
Length (cm)	40.7 (SD ± 3.6)	42.7 (SD ± 2.3)
	Min= 29, Max= 48	Min= 32, Max= 48
Gestational	32.7 (SD± 3.1)	35 (SD ± 2.9)
age(weeks)	Min= 24, Max=40	Min= 24,Max=45

GA, gestational age; HC, head circumference; SD, standard deviation.

4.4 Growth and other characteristics of LBW neonates

The mean growth velocity for neonates was 14.9 g/kg/day, which is comparable to the 15g/kg/day found in various studies and recommended by the American Academy of Pediatrics. Median APGAR at 5 minutes was 7 (range 3 to10), the mean volume of feed when IV fluids were discontinued was 122.6 ml/kg/day and the mean number of days it took to achieve maximum feed was 15 days, the mean hospital stay was 20.62 days (Table 3).

Table 3: *Growth and other characteristics of LBW neonates*

Variable	Mean (SD)
APGAR score at 5 min **Median (range)**	7.4 (SD± 1.4) Min = 3, Max = 10
Number of fully days(after birth) receiving any IVF	4.34 (SD±3.289) Min =0, Max =16
Number of fully days (after birth) receiving Full IVF	1.39 (SD±0.991) Min = 0, Max = 7
Volume of feeds when IV fluids discontinued (ml/kg/day)	122.6 (SD±17.04) Min = 80, Max = 168
Days maximum feeds achieved	15.26 (±13.80) Min = 3, Max = 66
Number of days for weight gain	16.66 (±14.01) Min = 0, Max = 61
Duration of hospital stays in days	20.62 (SD±16.25) Min =1.0, Max = 71
Growth velocity	14.93 (SD±8.41) Min = 0.00, Max = 40.3

4.5 Comparative data of an outcome

Sixty-two percent of participants were born with LBW (1500-2500g); ELBW and VLBW neonates took more days to reach maximum feeds with means of 27.97 (SD±14.65) vs 8.31 (SD±6.41) for LBW (Table 4).

Table 4: *Comparative data of an outcome*

Variables		ELBW and VLBW (n=46, 38%)	LBW (n=76, 62%)
Feed volume (ml/kg/day)	**Day 1**	4.49 (SD±9.06)	18.3 (SD±25.33)
	Day 2	16.95 (SD±21.7)	56.66 (SD±39.73)
	Day 3	41.10 (SD±35.42)	92.78 (SD±41.49)
	Day 4	67.47 (SD±41.41)	124.05 (SD±43.77)
	Day 5	87.61 (SD±48.77)	137.01 (SD±41.95)
	Day 6	112.16 (SD±50.66)	152.42 (SD±53.27)
	Day 7	129.85 (SD±57.09)	166 (SD±20.71)
Day max feed achieved		27.97 (SD±14.65)	8.31 (SD±6.41)
Day of life fortification started		16.31 (SD±12.62)	11.33 (SD±3.08)
Weight change (g/kg/day)		23.65 (SD±42.17)	15.17(SD±20.74)
Lowest weight on day		7.19 (SD±8.27)	5.88 (SD±5.04)

ELBW = extremely low birth weight (≤1000g); VLBW = very low birth weight (1000-1500g); LBW = low birth weight (1500-2500g)

4.6 Maternal factors associated with SGA at birth

The table below showed that there were no factors that were significantly associated with SGA at birth - this may be due to the fact that the sample size was low as there was a significant association in other studies where the sample size was bigger than that presented in this study, and some of maternal risks factors were not recorded. The negative association noted was confounding. Notably maternal hypertension and the female sex were negatively associated with SGA at birth with odd ratios of 0.721 and p=value =0.401, and 0.80 and p-value =0.558, respectively (Table 6).

Table 5: Maternal factors for SGA at birth

		Prevalence	Unadjusted Odds ratio for SGA (df=1)	ΔAdjusted Odds Ratio (AOR)* (df=1)
Sex	Male	18/53 (33.9%)		
	Female	27/69 (39.1 %)	OR: 0.80 (CI: 0.38 to 1.69) p=0.558Δ	NA
Gravidity	Primparous	10/40 (25 %)		
	Multiparous	35/82 (42.7 %)	OR: 2.234 (CI: 0.96 to 5.17) p=0.057Δ	AOR: 2.36 (CI: 0.94 to 5.92) p=0.066
Maternal age	<25 years	6/24 (25 %)		
	>25 years	39/98 (39.8 %)	OR: 1.983 (CI: 0.723 to 5.44) p=0.178Δ	AOR: 1.482 (CI: 0.50 to 4.40) p=0.479Δ
Birth weight group	ELBW and VLBW	13/46 (28.2 %)		
	LBW	32/76 (42.1 %)	OR: 1.846 (CI: 0.84 to 4.055) p=0.125Δ	AOR: 2.22 (CI: 0.98 to 5.04) p=0.057Δ
Economic status (Ubehehe group)	Low (1&2)	8/22 (36.3 %)		
	High (3)	37/100 (37 %)	OR: 1.028 (CI: 0.394 to 2.681) p=0.955Δ	NA
Gestational diabetes	Yes	1/3 (33.3 %)		
	No	44/119 (36.9 %)	OR: 1.173 (CI: 010 to 13.32) p=0.694F	NA
Maternal Hypertension	Yes	18/43 (41.8 %)		
	No	27/79 (34.1 %)	OR: 0.721 (CI: 0.336 to 1.55) p=0.401Δ	NA

4.7 Variables associated with PNGF in surviving neonates

Neonates who are small for gestation age at birth have a significant risk to develop PNGF at discharge for weights with adjusted odd ratio of 8.756 (CI: 1.59 to 48.22), and p=0.013. However, RDS, CLD, and early neonatal clinical sepsis have non-significant risks for PNGF at discharge (Table 6).

Table 6: Variables associated with PNGF in surviving neonates

		Percentage of PNGF (%)	Unadjusted Odds ratio for PNGF (df=1)	ΔAdjusted Odds Ratio (AOR)* (df=1)
SGA	Yes	37/39 (94.9%)		
	No	43/72 (59.7%)	OR: 12.477 (CI: 2.787 to 55.85) p<0.001Δ	AOR: 8.756 (CI: 1.59 to 48.22) p=0.013
Sex	Male	33/45 (73.3 %)		
	Female	47/66 (71.2 %)	OR: 1.112 (CI: 0.476 to 2.598) p=0.807Δ	
Gravidity	Primiparous	26/38 (68.4 %)		
	Multiparous	54/73 (73.9 %)	OR:1.312 (CI: 0.555 to 3.103 p=0.536Δ	
Maternal age	≤25 years	16/23 (50 %)		
	>25 years	64/88 (72.7 %)	OR: 1.167 (CI: 0.427 to 3.186) p=0.763Δ	
Birth weight group	ELBW and VLBW	24/37 (64.8 %)		
	LBW	56/74 (75.6 %)	OR: 1.685 (CI: 0.714 to 3.978) p=0.231Δ	
Economic status (Ubedehe group)	Low (1&2)	14/20 (60 %)		
	Moderate (3)	66/91 (72.5 %)	OR:1.131 (CI: 0.39 to 3.27) p= 0.820Δ	
Length of hospital stay	>7 days	66/92 (71.7 %)		
	≤7 days	14/19 (73.6 %)	OR: 1.103 (CI: 0.361 to 3.372) p=0.863Δ	
RDS	Yes	44/70 (62.8 %)		
	No	36/41 (87.8 %)	OR: 4.255 (CI: 1.483 to 12.202) p=0.005 Δ	AOR: 1.433 (CI: 0.37 to 5.52) p=0.601
CLD	Yes	5/10 (50 %)		
	No	75/101 (74.2 %)	OR: 2.885 (CI: 0.773 to 10.770) p=0.103 Δ	AOR: 3.62 (CI: 0.59 to 22.35) p=0.165
Early neonatal sepsis, clinical	Yes	53/79 (67.1 %)		
	No	27/32 (84.3 %)	OR: 2.649 (CI: 0.915 to 7.672) p=0.066 Δ	AOR: 2.23 (CI: 0.66 to 7.54) p=0.197
Anemia requiring Transfusion	Yes	7/12 (58.3 %)		
	No	73/98 (74.5 %)	OR: 2.086 CI: 0.607 to 7.166 p= 0.236Δ	
Nosocomial infection	Yes	17/20 (85 %)		
	No	63/91 (69.2 %)	OR: 0.397 (CI: 0.108 to 1.465) p= 0.123 F	AOR: 0.198 (CI: 0.036 to 1.104) p=0.065
NEC	Yes	3/4 (75 %)		
	No	77/107 (71.9%)	OR: 0.856 (CI: 0.086 to8.552) p=1.000Δ	

ΔPearson Chi-squared; F Fischer, CI = 95% confidence interval; df = degree of freedom; Multivariate analysis was used for variables with p value < 0.2

4.8 Therapeutic variables associated with PNGF

In univariate analysis, the table below showed that use of respiratory support, KMC use, trophic feeds, colostrum and feeding intolerance have a non-significant statistical correlation with PNGF and only the use of respiratory support was analyzed in multivariate analysis and remained not-significant with odds ratio = 1.022, p-value = 0.092.(Table7)

Table 7: Therapeutic variables associated with PNGF

Variables		Percentage of PNGF (%)	Unadjusted Odds ratio for PNGF (df=1)	ΔAdjusted Odds Ratio (AOR)* (df=1)
Use of respiratory support (CPAP)	Yes	40/61 (65.5 %)		
	No	40/50 (80 %)	OR: 2.10 (CI: 0.879 to 5.02) p= 0.092Δ	AOR: 1.022 (CI: 0.34 to 3.09) p=0.969
KMC used	Yes	65/88 (73.8 %)		
	No	15/23 (65.2 %)	OR: 1.507 (CI: 0.565 to 4.02) p= 0.411Δ	
Trophic feeds in 1st 24 hours	Yes	54/73 (73.9 %)		
	No	25/36 (69.4 %)	OR: 1.25 (CI: 0.518 to 3.02) p= 0.619Δ	
Time of initiation of feeding	≥48hours	13/20 (65 %)		
	≤ 48hours	66/90 (73.3 %)	OR:1.48 (CI: 0.528 to 4.15) p= 0.454Δ	
Antenatal steroids	Yes	54/74 (72.9 %)		
	No	19/26 (73.1 %)	OR: 0.995 (CI: 0.363 to 2.723) p=0.992Δ	
Colostrum given	Yes	11/13 (84.6 %)		
	No	66/95 (69.5 %)	OR: 2.417 (CI: 0.503 to 11.60) p=0.258Δ	
Feeding intolerance	Yes	8/13 (61.5%)		
	No	70/96 (72.9%)	OR: 1.683 (CI: 0.504 to5.61) p=0.393Δ	
Fortification	No	52/68 (76.5 %)		
	Yes	27/41 (65.8 %)	OR: 0.593 CI: 0.252 to 1.395 p= 0.230Δ	
Supplements	Yes	14/20 (70 %)		
	No	65/89 (73 %)	OR: 1.161 (CI: 0.4 to 3.3366) p= 0.784Δ	

ΔPearson Chi-squared; CI = 95% confidence interval; df = degrees of freedom; 1 variable was analyzed in multivariate analysis

CHAPTER V: DISCUSSION

The aim of this study was to provide a current overview on the prevalence of PNGF for LBW neonates as well as all the factors contributing to PNGF; this was based on evaluation of LBW neonates admitted at the neonatology unit of a tertiary hospital in Kigali. 122 babies were included in the study and only 111 were followed up to discharge.

The majority of them female (57%), 63% of them were AGA at birth, among the SGA 94.9% (37/39) demonstrated postnatal growth failure. The mean postnatal growth velocity was 14.9 g/kg/day which almost similar to the 15 g/kg/day recommended by the American Academy of Pediatrics, but also the Z- score for weight both at admission and discharge were -1.1 and -1.9 respectively, this means that our babies have mild growth failure.

5.1 Demographic characteristics of participants

In our study we found that 57% (69/122) of neonates were female and 63.1% of them were AGA, our findings were different from the study done by Mudahemuka et al. which reported 73% (33) as AGA, and the study done by Lima et al AGA were 67% (1). The majority of mothers (82%) were from moderate socioeconomics (ubudehe categoty 3). Comparing ubudehe category and babies who are born appropriate for gestational age doesn't explain why many of our babies (37%) are born small for gestational age, further research is recommended to find out the cause. Of this problem.

5.2 Prevalence of postnatal growth failure

This study revealed that among the neonates that survived to discharge (n=111) those with PNGF were 80 (72.1 %). Our findings were much higher than the studies done by Fenton et al (34) and Mudahemuka et al (33) that reported 65% and 56.4% respectively.

Kavurt et al showed in their study done in 2018 that, among 144 neonates that fulfilled the inclusion criteria, PNGF for weight was detected in 46 babies (37%) (24). Lima et al found that PNGF for weight was observed in 26% (149/570) neonates at discharge (10).

In 2015, according to the study done at 736 North American hospitals in the Vermont Oxford Network (VON), on 362,833 infants weighing 501 to 1500 g without major birth defects born from 2000 to 2013 and who were hospitalized for 15 to 175 days, PNGF and severe PNGF (defined as discharge weights less than the 10th and third percentiles for postmenstrual age, respectively) decreased from 64.5% to 50.3%, and from 39.8% to 27.5% respectively.

The observed potential reasons why most of our babies had high postnatal growth failure compared to other studies were due to the different methodologies used to define and calculate PNGF, sample size, the different characteristics of participants, advances in neonatal care, different nutritional practices as well as the use of TPN which was not used in our study settings.

5.3 Variables associates with PNGF

Many studies done previously in different regions showed that there are many variables associated with PNGF. Our study, showed that RDS, CLD, early onset clinical sepsis, use of trophic feeds in first 24 hours, colostrum, and time of initiation of feeds, feeding intolerance, supplements, nosocomial infection, anemia requiring transfusion, KMC use and respiratory support use all have non-significant association with PNGF. Notably, being small for gestation age at birth was positively associated with PNGF; among neonates who were SGA at birth, 37/39 (94.9%) developed PNGF at discharge, with unadjusted odds ratio of 12.477 and p=0.001 and 8.756 with p=0.013 for adjusted odds ratio.

There is a small difference between our study and the study done by De Freitas et al in 2016, where 85% of infants who were SGA developed PNGF at discharge (7). This also was comparable to the study done by K.Marks et al in 2006 which showed that IUGR was a major predictive marker of PNGF as in their study all neonates who were SGA (< 10 percentile) at birth developed PNGF at discharge (35).

Any observed difference reported in prevalence among the studies was due to the different growth charts used, different demographic characteristics of the participants and sample size as well as nutritional practices, such as use of parental nutritional in some settings and methods used to fortify expressed breast milk.

5.4 Postnatal growth velocity

During our study, the mean growth velocity was 14.9g/kg/day. This was comparable to the currently recommended growth velocity of 15g/kg/day by the American Academy of Pediatrics and was higher than that reported by Mudahemuka et al (2014) of 13.2 g/kg/day (33). Lango et al in 2018 reported a mean GV of 14.0 g/kg/day (14). In general we expected to have much lower postnatal growth velocity which was not the case with the findings we got, we think the major reasons why we got higher postnatal growth velocity were due to different methods used to

calculate the growth velocity for low birth weight neonates, technical errors in weighing babies, and lack of standardization methods in calculation of growth velocity might have contributed to the difference observed.

5.5 Feeding variables contributing to PNGF

The current study showed that many feeding variables have a non-significant correlation with PNGF such as giving trophic feed for the 1st 24 hours, time of initiation of feeds, colostrum, feeding intolerance. Even expressed breast milk fortification didn't show any improvement in weight gain. However, the study done by Kuschel et al in 2009 demonstrated that there's a statistically significant impact of fortification on postnatal growth parameters in neonates with prolonged hospital stays (37), the reason was that the methods used in our unit to fortify is completely different from other methods used to fortify expressed breast milk, also use of TPN in those other units might have contributed a lot.

Many studies showed that trophic feeding to promote intestinal maturation reduced time for initiation of feeds, enhanced feeding tolerance and decreased the time to reach full feeding independently of parenteral feeds and length of hospital stays (5,27).

5.5 Study limitation/strengths

Limitation: There's no previous research done in our country on postnatal growth failure so that our results can be compared to a similar population. This study was done in only one hospital in Rwanda, so it can't be generalized to the whole country.

Strength: The study is the 1st one done in Rwanda.

CHAPTER VI: CONCLUSION AND RECOMMENDATION

6.1 Conclusion

Our study found that there is high prevalence 72% of postnatal growth failure among the low birth weight neonates survived up discharge and the study showed that postnatal growth failure is common in low birth weight neonates especially those who are small for gestational age at birth, and there is non- significant correlation with many other morbidities, so new neonatal feeding strategies and care are highly needed for better growth of low birth weight neonates, as poor postnatal growth is associated with poor neurological outcomes.

6.2 Recommendations

To the Ministry of health

Further research are needed in other hospitals to get representative sample.

To conduct further research on the long-term outcomes of those neonates with postnatal growth failure.

Introduction of total parenteral nutrition in our setting.

Emphasize on improving antenatal care for all pregnant women.

Emphasize on the use of appropriate methods of fortification.

To the hospital

Close follow up of those neonates who are discharged with poor postnatal growth

Implementation of new standardize feeding protocols.

Regular training of medical staff on the new updated standardized guidelines.

.

REFERENCES

1. Azara P, Lima T, Carvalho M De, Carolina A. Variables associated with extra uterine growth restriction in very. J Pediatr (Versão em Port [Internet]. 2014;90(1):22–7. Available from: http://dx.doi.org/10.1016/j.jpedp.2013.05.007
2. Johnson MJ, Leaf AA, Pearson F, Clark HW, Dimitrov BD, Pope C, et al. Successfully implementing and embedding guidelines to improve the nutrition and growth of preterm infants in neonatal intensive care : a prospective interventional study. 2017;
3. Lee SM, Kim N, Namgung R, Park M, Park K, Jeon J. Prediction of Postnatal Growth Failure among Very Low Birth Weight Infants. Sci Rep [Internet]. 2018;(February):1–8. Available from: http://dx.doi.org/10.1038/s41598-018-21647-9
4. Horbar JD, Ehrenkranz RA, Badger GJ, Edwards EM, Morrow KA. Weight Growth Velocity and Postnatal Growth Failure in Infants 501 to 1500 Grams : 2000 – 2013. 2018;136(1).
5. Su B. ScienceDirect Optimizing Nutrition in Preterm Infants. Pediatr Neonatol [Internet]. 2014;55(1):5–13. Available from: http://dx.doi.org/10.1016/j.pedneo.2013.07.003
6. Fenton TR, Chan HT, Madhu A, Griffi J. Preterm Infant Growth Velocity Calculations : A Systematic Review. 2018;139(3).
7. De Freitas BAC, Priore SE, Lima LM, Franceschini S do CC. Extrauterine growth restriction: Universal problem among premature infants. Rev Nutr. 2016;29(1):53–64.
8. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatr. 2013;13(1).
9. Horbar JD, Ehrenkranz RA, Badger GJ, Edwards EM, Morrow KA, Soll RF, et al. Weight Growth Velocity and Postnatal Growth Failure in Infants 501 to 1500 Grams: 2000-2013. Pediatrics [Internet]. 2015;136(1):e84–92. Available from: http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.2015-0129
10. Lima PAT, De Carvalho M, Da Costa ACC, Moreira MEL. Variables associated with extra uterine growth restriction in very low birth weight infants. J Pediatr (Rio J) [Internet]. 2014;90(1):22–7. Available from: http://dx.doi.org/10.1016/j.jped.2013.05.007
11. Coverston CR, Schwartz R. Extrauterine Growth. 2004;101–6.
12. Nangia S, Bishnoi A, Goel A, Mandal P, Tiwari S, Saili A. Early Total Enteral Feeding in Stable Very Low Birth Weight Infants: A Before and After Study. J Trop Pediatr [Internet]. 2017;1–7. Available from: https://academic.oup.com/tropej/article-lookup/doi/10.1093/tropej/fmx023
13. Ayatollahi SMT, Haem E, Sharafi Z. Growth Velocity of Infants From Birth to 5 Years Born in Maku, Iran. Glob J Health Sci [Internet]. 2015;8(2):56–63. Available from: http://www.ccsenet.org/journal/index.php/gjhs/article/view/44121
14. Lango O, Horn AR, Harrison MC. Growth Velocity of Extremely Low Birth Weight Preterms at a Tertiary Neonatal Unit in South Africa. 2018;59(2):79–83.

15. Anchieta LM, Xavier CC, Colosimo EA, Souza MF, Valadares O, Federal U, et al. Weight of preterm newborns during the first twelve weeks of life. 2003;36:761–70.

16. Health H, Ormond G, Hospital S, Health C. Nutrition : enteral nutrition for the preterm infant Definitions relating to prematurity and birthweight. 2017;1–29.

17. Cutland CL, Lackritz EM, Mallett-moore T, Bardají A, Chandrasekaran R, Lahariya C, et al. Low birth weight : Case definition & guidelines for data collection , analysis , and presentation of maternal immunization safety data. Vaccine [Internet]. 2017;35(48):6492–500. Available from: https://doi.org/10.1016/j.vaccine.2017.01.049

18. World Health Organization. Guidelines on optimal feeding of low birth-weight infants in low-and middle-income countries. Geneva WHO [Internet]. 2011;16–45. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Guidelines+on+Optimal+feeding+of+low+birth-+weight+infants+in+low-and+middle-income+countries#0

19. Medi T. Defining the Nutritional Needs of Preterm Infants. 2014;(May).

20. Ruth VA. Extrauterine Growth Restriction : A Review of the Literature. 2007;(July):177–84.

21. Embleton NE, Pang N, Cooke RJ. Postnatal Malnutrition and Growth Retardation: An Inevitable Consequence of Current Recommendations in Preterm Infants? Pediatrics [Internet]. 2001;107(2):270–3. Available from: http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.107.2.270

22. Ehrenkranz RA. Extrauterine growth restriction : is it preventable ? ☹ , ☹☹ ¸ ão do crescimento extrauterino : é possível evitar ? J Pediatr (Rio J) [Internet]. 2014;90(1):1–3. Available from: http://dx.doi.org/10.1016/j.jped.2013.10.003

23. Marinkovi V, Bo N, Rankovi M. Original Article / Оригинални рад ISSN Online 2406-0895 Effect of Early Introduction of Minimal Enteral Feeding on Growth and Rate of Achieving Optimal Nutritive Intake in Very Low Birthweight Preterm Infants Утицај ране минималне ентералне исхране на рас. 2017;1–7.

24. Kavurt S, Celik K. Incidence and risk factors of postnatal growth restriction in preterm infants. J Matern Neonatal Med [Internet]. 2018;0(0):1105–7. Available from: https://doi.org/10.1080/14767058.2017.1306512

25. Shakeel F, Napolitano A, Newkirk M, Harris JE, Ghazarian SR. Improving Clinical Outcomes of Very Low Birth Weight Infants by Early Standardized Nutritional Management. Ican. 2015;(December):328–37.

26. Clark RH, Wagner CL, Merritt RJ, Bloom BT, Neu J, Young TE, et al. Nutrition in the neonatal intensive care unit: How do we reduce the incidence of extrauterine growth restriction? J Perinatol. 2003;23(4):337–44.

27. Yu VYH. Extrauterine growth restriction in preterm infants: importance of optimizing nutrition in neonatal intensive care units. Croat Med J. 2005;46(5):737–43.

28. Ramani M, Ambalavanan N. Feeding Practices and Necrotizing Enterocolitis. Clin Perinatol [Internet]. 2013;40(1):1–10. Available from:

http://dx.doi.org/10.1016/j.clp.2012.12.001

29. Gupta V, Rebekah G, Sudhakar Y, Santhanam S, Thomas N. A randomized controlled trial comparing the effect of fortification of human milk with an infant formula powder versus unfortified human milk on the growth of preterm very low birth weight infants. J Matern Neonatal Med [Internet]. 2019;0(0):1–9. Available from: https://doi.org/10.1080/14767058.2018.1554046

30. Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. Obs Gynecol. 1996;87(2 \t):163–8.

31. Khashana A, Moussa R. Incidence of feeding intolerance in preterm neonates in neonatal intensive care units, Port Said, Egypt. J Clin Neonatol [Internet]. 2016;5(4):230. Available from: http://www.jcnonweb.com/text.asp?2016/5/4/230/194165

32. Webbe J, Brunton G, Ali S, Duffy JM, Modi N, Gale C. Developing, implementing and disseminating a core outcome set for neonatal medicine. BMJ Paediatr Open [Internet]. 2017;1(1):e000048. Available from: http://bmjpaedsopen.bmj.com/lookup/doi/10.1136/bmjpo-2017-000048

33. Mudahemuka JC, Chb MB, Ballot DE, Chb MB, Sa F. Birth weight recovery among very low birth weight infants surviving to discharge from Charlotte Maxeke Johannesburg Academic Hospital. 2014;8(4).

34. Fenton TR, Nasser R, Eliasziw M, Kim JH, Bilan D, Sauve R. Validating the weight gain of preterm infants between the reference growth curve of the fetus and the term infant. BMC Pediatr [Internet]. 2013;13(1):1. Available from: BMC Pediatrics

35. Marks K, Reichman B, Lusky A, Zmora E. Fetal growth and postnatal growth failure in very-low-birthweight infants. 2006;(May 2005):236–42.

36. Ca K, Je H. Multicomponent fortified human milk for promoting growth in preterm infants (Review). 2009;(1).

APPENDICES

Appendix : Questionnaire

Data collector (initials):	
Hospital site: CHUK ☐ Infant DOB: dd/mm/yyyy Sex: M -3 ☐ F -2 ☐. DNA -0 ☐ Unique Patient Identifier:	
Maternal Date of birth	dd/mm/yyyy
Maternal Medical insurance	Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐
Maternal Social status (Ubudehe)	Category 1 ☐ Category 2 ☐ Category 3 ☐Category 4 ☐ DNA (99) ☐
Gravida / Parity/ Abortion	Gr_____ Par_____ Ab _____
Due date	LMP dd/mm/yyyy DNA ☐ (Excel will calculate EDD). EDD: dd/mm/yyyy DNA ☐
Problems during Pregnancy	**GD - Gestational diabetes** No – 3 ☐ Yes - 2 ☐ NA – 1 DNA - 0 ☐ **HBP - High blood pressure** No – 3 ☐ Yes - 2 ☐ NA – 1 DNA - 0 ☐ **MI - Infection** No – 3 ☐ Yes - 2 ☐ NA – 1 DNA - 0 ☐ **O - Other** No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐

Maternal HIV status	Positive -1 ☐ Not tested -2 ☐ Negative – 3 ☐ DNA – 0 ☐ In PMTCT programme: Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐		
Serology	**Torch screen performed** Yes -2 ☐ No - 1☐ DNA - 0 ☐ **Hepatitis B (HB)** Negative – 3 ☐ Positive - 2 ☐ NA – 1 ☐ DNA - 0 ☐ **Toxoplasma (T)** Negative – 3 ☐ Positive - 2 ☐ NA – 1 ☐ DNA - 0 ☐ **Rubella (R)** Negative – 3 ☐ Positive - 2 ☐ NA – 1 ☐ DNA - 0 ☐ **Other:** Negative – 3 ☐ Positive - 2 ☐ NA – 1 ☐ DNA - 0 ☐		
Onset of labour	Date: dd/mm/yyyy Time: DNA ☐		
Was thick meconium present?	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐		
Antenatal steroids	Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐ How many doses? 1 ☐ 2☐ 3☐ 4☐ NA ☐ DNA ☐		
Maternal fever (temp ≥ 38°C)	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐	Foul smelling amniotic fluid	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
PROM ≥18 hours	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐	Chorioamnionitis	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Maternal UTI	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐	Meconium staining	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Prematurity (<37 weeks)	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐	Other	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Any antibiotics?	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐	OTHER…….. DESCRIBE	
Place of birth	Home (H) ☐ on-route to hospital (OR) ☐ HC ☐ Clinic (C) ☐ D H ☐ Tertiary hospital (TH) ☐ DNA ☐DNA (99) ☐		
APGAR	/1 min DNA (99) ☐. / 5 min DNA (99) ☐. /10 min DNA (99) ☐		
Resuscitation required?	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐ **BMV** No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐ **Chest compressions (CC)** No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐		
Gestation at birth	……. Weeks ……. Days DNA ☐ Based on : USS ☐ LMP ☐ Ballard score (BS) ☐ DNA ☐		
Growth chart in the medical records	Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐		
Was growth chart plotted with birth parameters	**Weight** Yes -3 ☐ No - 2 ☐ ☐DNA -0 ☐ **HC** Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐ **Length** Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐		
Was growth chart plotted with future parameters	**Weight** Yes -3 ☐ No - 2 ☐ ☐DNA -0 ☐ **HC** Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐ **Length** Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐		

Co-morbidities	
Respiratory distress syndrome (RDS)	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Use of respiratory support (CPAP)	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Chronic lung disease CLD	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
patent ductus arteriosus (PDA),	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Anemia requiring transfusion (packed cells)	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Jaundice requiring phototherapy	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Early Onset Sepsis (<72 hours) – Culture or CRP positive	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Early Onset Sepsis (<72 hours) - Clinical sepsis	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Number of FULL days antibiotics given after birth	_____ days DNA (99) ☐ NA (99) ☐
Late Onset Sepsis (>72 hours) – Culture or CRP positive	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Late Onset Sepsis (>72 hours) - Clinical sepsis	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐

Necrotizing enterocolitis (NEC)	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Nosocomial infection	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐ OTHERS ? DESCRIBE:
Variables associated to feeding practices	
Colostrum given	Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐
Trophic feeds in first 24 hours	Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐
Time of initiation of feeds	<48 hours ☐ >48 hours ☐ DNA (99) ☐
Date achieving full feeds (150mls/kg/day) (which day of life)	__ /__/_____
Volume of feeds when IV fluids discontinued	…….ml/kg/day
Feeding intolerance,	No – 3 ☐ Yes - 2 ☐ NA – 1 ☐ DNA - 0 ☐
Number of "episodes" of feeding intolerance where feeds withheld	
Total number of days feeds withheld	
Feeding type	
Number of FULL days (after birth) receiving FULL IV fluids	
Number of FULL days (after birth) receiving ANY IV fluids	
Exclusive Breast milk	Exclusive Breast milk ☐ Exclusive Formula☐ Mixed formula and breast milk☐ DNA (99) ☐
Volumes of milk (**mls/day)**	Day 1: ____ mls/day DNA ☐ Day 2: ____ mls/day DNA ☐ Day 3:_____ mls/day DNA ☐
	Day 4: _____ mls/day DNA ☐ Day 5: _____ mls/day DNA ☐
	Day 6: _____ mls/day DNA ☐ Day 7: _____ mls/day DNA ☐
Maximum feed volume	_____mls/day Day achieved_____
Fortification — Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐	Date started __ /__/_____ **Type:** Formula powder ☐ oil ☐ DNA (99) ☐ Maximum fortification kcal/ml _____ DNA ☐
Supplements (Iron, Vitamin D or multivitamins)	Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐
Discharge anthropometrics	
Discharge weight	Kg DNA ☐ Percentile: Discharge date:
Discharge Head circumference	cm DNA ☐ Percentile:
Discharge Length	cm DNA ☐ Percentile
Appropriateness of weight at CGA at discharge (> 10percentile)	Yes ☐ No ☐ DNA (99) ☐
KMC used	Yes -3 ☐ No - 2 ☐ NA – 1 ☐DNA -0 ☐

Baby's measurements (DNA if not available)	Birth	1	2	3	4	5	6	7	8	9	10	11	12
Date													
Weight (gms)													
HC													
Length													

Appendix 1: IRB Ethical approval

UNIVERSITY OF RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 26th /10/2018

Dr Munyengabe Francois
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 358/CMHS IRB/2018

Your Project Title *"Prevalence And Factors Associated With Intra-hospital Post-Natal Growth Failure Up To The Point Of Discharge At Kigali University Teaching Hospital/ NICU – A Cross-Sectional Study"* Has been evaluated by CMHS Institutional Review Board.

		Involved in the decision		
		Yes	No (Reason)	
Name of Members	**Institute**		**Absent**	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS	X		
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS	X		
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 16th October 2018, **Approval has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months**.
You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 26th October 2018

Expiration date: The 26th October 2019

Professor Kato J. NJUNWA
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR