

**A STUDY TO DETERMINE THE ASSOCIATION BETWEEN 5 MINUTE
APGAR SCORES IN TERM NEWBORNS AND MORTALITY,
NEONATAL ENCEPHALOPATHY AND NEURODEVELOPMENT AT
EIGHT WEEKS POSTNATAL AGE, AT THE UNIVERSITY TEACHING
HOSPITAL**

BY

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Master of Medicine in Pediatrics

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DECLARATION

I hereby declare that this dissertation represents my own work and has not been presented either wholly or in part for a degree at the University of Zambia or any other University.

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APPROVAL

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ABSTRACT

Background

In 1952, Virginia Apgar devised a system of scores as a means of evaluating the physical condition of the newborn immediately after birth. The Apgar score has since been accepted for use to assess newborns in almost all labour wards worldwide.

While infant mortality is reducing worldwide, neonatal morbidity is increasing. Improved resuscitation techniques have improved neonatal survival, what is not yet known is how many of these babies survive without sequelae.

This study sought to validate the association between 5 minute Apgar scores and mortality, neonatal encephalopathy and adverse neurodevelopment at 8 weeks postnatal age at the University Teaching Hospital, Zambia.

Methods

A total of 140 study subjects, meeting the inclusion criteria and consenting parents took part in the study to determine the association between 5 minute Apgar scores in term newborns and neonatal mortality, neonatal encephalopathy and neurodevelopment at 8 weeks postnatal age. The study subjects had their 5 minute Apgar scores taken by specially retrained midwives equipped with stop watches. Neonatal encephalopathy at 6-12 hours was assessed with a clinical neurological examination by the PI. At eight weeks postnatal age, their mental and motor development was assessed by the PI with the Bayley Scale of Infant Development II. Cross-tabulations and chi-square calculations in SPSS 20.0 windows version were used to assess the relationships between the Apgar scores and mortality, encephalopathy at age 6-12 hours, mental and motor development at eight weeks.

Results

Very low 5 minute Apgar scores (0-3) were associated with 73.3 % (22/30, OR 30.9) neonatal mortality. Very low Apgar scores (0-3) were associated with significant (moderate to severe) encephalopathy at 6 to 12 hours of age (83.3%, OR 25.6).

Infants with very low 5 minute scores were 9.2 and 8 times more likely have delayed mental (OR 9.2) and motor (OR 7.7) development respectively, at eight weeks postnatal age.

High mortality (22.1%) and high follow up loss (38.6%) in the very low Apgar group made the later part of the study not statistically significant, thus needing further larger long term research.

Conclusion

The results of this study underscores the evidence, as reported from other studies, that Apgar scores can be used to identify infants at increased risk of neonatal encephalopathy and death, needing greater and immediate attention. Furthermore, the study has demonstrated the ability of Apgar scores to identify children who need further neurodevelopmental follow-up.

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TABLE OF CONTENTS

	Page
Declaration	ii
Copyright.....	iii
Approval	iv
Abstract.....	iv
Acknowledgements	vi
Table of contents.....	vii
List of tables	ix
List of figures.....	x
List of abbreviations.....	xi
CHAPTER ONE	
1.0 Introduction.....	1
1.1 Statement of the problem and justification of the study	2
1.2 Study Question/Hypothesis.....	3
1.2.1 Main Objectives.....	3
1.2.2 Specific Objectives.....	3
CHAPTER TWO	
2.0 Literature review	4
CHAPTER THREE	
3.0 Methodology	6
3.1 Study design.....	6
3.2 Study site.....	6
3.3 Study period.....	6
3.4 Study population.....	6
3.5 Inclusion criteria	6
3.6 Exclusion criteria.....	6
3.7 Sample size calculations.....	6
3.8 Study Tools.....	7
3.9 Procedure	8
3.10 Data analysis	8
3.11 Ethical Issues.....	9
CHAPTER FOUR	
4.0 Results	10

CHAPTER FIVE

5.0 Discussion18

CHAPTER SIX

6.0 Conclusion.....23

6.1 Study limitations.....23

6.2 Recommendations.....24

References.....25

Appendices.....28

LIST OF TABLES

Table 4.1	Infant attributes of the sampling distribution
Table 4.2	Maternal attributes of the sampling distribution
Table 4.3	Infant health and development
Table 4.4	Infant related factors associated with Apgar scores
Table 4.5	Maternal related factors associated with Apgar scores
Table 4.6	Measure of association between mortality and 5 minute Apgar scores
Table 4.7	Measure of association between encephalopathy and 5 minute Apgar score
Table 4.8	Measure of association between delayed neurodevelopment (motor) and 5minute Apgar scores
Table 4.9	Measure of association between delayed neurodevelopment (mental) and 5 minute Apgar scores

LIST OF FIGURES

- Figure 4.1 Frequency of Apgar scores at 5 minutes in term infants
- Figure 4.2 Grades for neonatal neurological Examination
- Figure 4.3 Bayley scale of infant development II

LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
BSID II	Bayley Scale of Infant Development II
CP	Cerebral Palsy
HIV	Human Immunodeficiency Virus
Mo.	Month
NICU	Neonatal Intensive Care Unit
NNE	Neonatal Neurological Examination (protocol)
OFC	Occipital Frontal Circumference
OR	Odds Ratio
PI	Principal Investigator
SD	Standard deviation
STD	Sexually Transmitted Disease
UTH	University Teaching Hospital
Vs	Versus
WHO	World Health Organization

Chapter One

1.0 Introduction

Estimates from 2000 of the distribution of direct causes of (neonatal) death indicate that preterm birth (28%), severe infections (36%, including sepsis and pneumonia [26%], tetanus [7%], and diarrhoea [3%]), and complications of asphyxia (23%) account for most neonatal deaths. Of the remaining 14%, 7% of deaths were related to congenital abnormalities (Lawn et al; The Lancet, 2005).

Survivors of perinatal asphyxia have a high rate of mental retardation, cerebral palsy (CP) and other developmental disorders. Perinatal asphyxia accounts for one million of the five million neonatal deaths estimated for each year worldwide (Adamson et al, 1995).

Many studies using meta-analyses concluded that early intervention programmes prevent or minimize cognitive impairment in high- risk infants (Knippenberg et al, 2005, Damstadt et al, 2005). These interventions are usually cost effective and affordable to most resource constrained countries including Zambia; if measures and tools are put in place for early recognition of the at-risk infant.

The Apgar Scores, is a simple statistical model of five physiological signs, devised by Dr. Virginia Apgar in 1952 to decipher immediate neonatal wellbeing as recently reviewed by Casey et al (Casey, 2001). Using this clinical assessment tool, newborn infants are evaluated based on five variables: heart rate, respiratory effort, muscle tone, reflex irritability, and color. A numerical score of 0–2 is assigned in each category for a maximum score of 10.

Low Apgar scores (defined as Apgar score ≤ 3 at 1 minute or <7 at 5 minutes) have been used as an indicator of ‘a baby with a problem’ ever since Virginia Apgar devised the tool in 1952 as ‘-a means of evaluating the physical condition of the newborn immediately after birth-’ (Basket, 2000; Papile, 2001; Apgar, 1953).

With improved resuscitation techniques more babies are surviving the neonatal period. What is not certain is, are they doing so without sequelae? This study attempts to provide a cost effective method/tool of identifying the at risk infant requiring follow up for adverse neurodevelopmental outcomes.

The study also evaluates the association between Apgar scores and neonatal encephalopathy and neurodevelopmental delay in term infants at eight postnatal weeks; born at the University Teaching Hospital (UTH) in Lusaka, Zambia.

1.1 Statement of the problem and justification of the study

Perinatal/neonatal problems are the leading causes of perinatal and neonatal mortality in the developing world and accounts for about one million of the five million neonatal deaths that occur each year worldwide (WHO, 1994). In a multicentre prospective study in eighteen countries, in eastern, central and southern Africa, neonatal mortality was 38 per 1000 live births (Kinoti 1993).

Perinatal asphyxia was singled out as the commonest cause of long-term morbidity leading to mental retardation, CP, and other neurodevelopmental disorders (WHO 1994). Mortality and morbidity from perinatal asphyxia disproportionately affect more infants in developing countries, particularly infants from the lowest socio-economic groups. The rate of deaths due to perinatal asphyxia is approximately 10 times that of developed countries. Though accurate estimates of neurodevelopmental sequelae from asphyxia in sub-Sahara Africa are not available; it is likely that these sequelae are many times more prevalent in developing countries than in developed countries (Carlo & Chomba, 2005; Collins & Paneth, 2001).

Neonates with asphyxia are apnoeic at birth and require resuscitation to survive the immediate new born period. Six to ten percent of these infants require assistance with breathing at birth. Once spontaneous breathing is established, they may no longer require further support (Perlman & Risser, 1995), but many of them are at high risk for neurological impairment, (Carlo & Chomba, 2005). A study in Zimbabwe found that there was a significant association between a very low Apgar score (<4) after 5 minutes and neurological outcome at 4 months (Wolf et al 1985).

At UTH, all newborns with 5 minute Apgar scores 0-3 are taken to NICU for continued resuscitation. Despite these mostly timely interventions, those who survive have prolonged hospital stays and their long term neurodevelopmental outcomes are uncertain. High impact interventions (e.g. resuscitation) instituted in the intrapartum and immediate postpartum periods have improved the survival chances of these neonates, but, their long term development has not been well followed up.

Nelson and Ellenberg had shown that an Apgar score of less than three at 5 minutes in term babies is an ominous finding, with 44% of the infants dying and a 21-fold increased risk of CP in the survivors (Nelson & Ellenberg, 1981).

This study has been undertaken in part to validate these findings from other countries at UTH; to set up future longer term research in the association of low Apgar scores with adverse neurodevelopment not only with CP, but other impairments as well and to follow up these children in the long term for appropriate and timely intervention; to influence policy in better child development monitoring and follow up. No similar study has been done at UTH before.

1.2 Study Question/Hypothesis

- Are very low/low 5 minute Apgar scores in term newborns associated with neonatal encephalopathy and neurodevelopmental delay at eight weeks postnatal age at UTH?

1.2.1 General objective

- To determine the association between very low/ low 5 minute Apgar scores in term newborns and neonatal encephalopathy and neurodevelopment at eight weeks postnatal age at UTH.

1.2.2 Specific objectives

- To calculate the Prevalence/proportion of newborns who present with very low/ low 5 minute Apgar scores at UTH.
- To estimate the Prevalence of neonatal encephalopathy and neurodevelopment delay in term infants with very low/low 5 minute Apgar scores at eight weeks postnatal age at UTH.
- To determine the association between mortality and very low/low 5 minute Apgar scores in term newborns at UTH.
- To determine the association between neonatal encephalopathy and very low/ low 5 minute Apgar scores in term newborns at UTH.

Chapter Two

2.0 Literature review

Virginia Apgar's newborn score is used in labour wards almost universally. Her main reason for developing this method of early appraisal of the neonate was to redirect some of the attention (of birth attendants) from the mother to the newborn at a very critical stage when, if required, resuscitation efforts would yield great(est) benefit (Baskett, 2000). In 1952, Apgar reported that neonatal survival through 28 days of age was related to the condition of the infant in the delivery room (Apgar V, 1953).

In a study in Norwegian neonates, Mostal et al showed the relationship between poor Apgar scores and adverse outcomes; that low Apgar scores at 5 minutes were associated with subsequent death or cerebral palsy (CP). Children who recovered from a low 1-minute to a normal 5-minute score also had a 17-fold increased risk for CP compared with infants with two normal scores (i.e. at 1 and 5 minutes) (Moster et al, 2001).

In *The Continuing Value of the Apgar score for the Assessment of Newborn Infants*, Brian M. Casey et al concluded that the five-minute Apgar score was a better predictor of neonatal outcome than was measurement of umbilical-artery blood pH, even for newborn infants with severe acidemia. However, the combination of five-minute Apgar scores of 0 to 3 and umbilical-artery blood pH values of 7.0 or less increased the relative risk of death in both preterm and term infants (Casey B et al, 2001).

Many studies have indicated that newborns with low Apgar scores are associated with a high mortality and morbidity. The question is what the high morbidity leads to (i.e. outcome) in each particular case (Casey, 2001; Dijxhoorn et al, 1986; Nelson & Ellenberg, 1981; Ellis, 1999; Collins & Paneth, 2001).

The Apgar score is affected by gestational age, maternal medications, resuscitation, and cardio-respiratory and neurologic conditions. Low 1- and 5-minute Apgar scores alone are not conclusive markers of an acute intrapartum hypoxic event. Resuscitative interventions modify the components of the Apgar score (AAP Committee on Fetus and Newborn, 2005–2006).

There is an ongoing debate on the use of Apgar scores in predicting long term outcomes. Montgomery argues that there is little scientific evidence to support [the Apgar score's] use in predicting long-term outcomes (Montgomery, 2000).

The American Academy of Pediatrics' Committee on Fetus and Newborn and the American College of Obstetricians and Gynecologists' Committee on Obstetric Practice (1996), cautioned that the Apgar score should not be used as the *only* measure to evaluate the possibility that neurological damage occurred during the birthing process.

However, many researchers have attempted to correlate Apgar scores with various outcomes including development (Behnke et al, 1989; Blackman, 1988; Riehn et al, 1998), later delinquency (Gibson & Tibbetts, 1998), intelligence (Nelson & Ellenberg, 1981), and neurological development (Sommerfelt et al, 1996; Wolf et al, 1997; Moster et al 1987).

Ehrenstein et al found that most newborns with Apgar scores below 7 grow up healthy, but risks of neurodevelopmental disability among them are greater than among those with higher Apgar scores, particularly in the short term. Increased risks have been reported for neonatal seizures; neonatal intracranial hemorrhage; cerebral palsy; mental retardation; and epilepsy. There are also reports of association between five-minute Apgar scores below 7 and risk of motor and developmental impairments at school age, including symptoms of attention deficit and speech and language problems (Ehrenstein et al; 2009).

Moster et al in a study in Norway found a close relationship between severe (Apgar 0–3) and moderate (Apgar 4–6) depression of Apgar scores and mortality (Moster et al 2001).

Efforts at mitigating the rise in neonatal morbidity and mortality should be directed at reduction in the risk factors and much more care for expectant mothers exhibiting signs and symptoms of these factors (Martines, 2005, WHO, 1999).

In a 'Short-term outcome of infants born with low Apgar scores at the University Teaching Hospital,' Nalubamba (2003) observed that there was a significantly high mortality associated with an Apgar score of 4 and below at 5 minutes, in babies born at UTH and admitted to the Neonatal Intensive Care Unit. Almost half (49.7%) of the newborns born with low Apgar scores enrolled to this study died within the neonatal period (Nalubamba, 2003).

Chapter Three

3.0 Methodology

3.1 Study design: A cohort prospective study.

3.2 Study site: University Teaching Hospital.

3.4 Study period: 6 months, (April to October 2007).

3.5 Study population: Estimated 1200.

3.6 Inclusion criteria

- Term infants (Birth weight: 2 500g and above or ≥ 37 weeks gestation age).

3.7 Exclusion criteria

- Preterm infants. (<2.500 kg birth weight or < 37 weeks gestation)
- Small for gestation age.
- Infants with obvious life threatening congenital abnormalities.

3.8 Sample size calculation

The following sample size formula for cohort studies was used

$$n = \frac{[Z_{\alpha}\sqrt{(1 + 1/w)P^*(1-P^*)} + Z_{\beta}\sqrt{P_0(1-P_0)/w + P_1(1-P_1)}]^2}{(P_0 - P_1)^2}$$

The formula makes comparison of those with very low/ low and normal Apgar scores and those who had encephalopathy and neuro developmental delay at 8 weeks.

Where $Z_{\alpha} = 1.96$ standard normal variate at 95% Confidence level

$W =$ number of control subjects per experimental subjects = 1 (where experimental subjects are those with very low and low 5 minute Apgar scores and control are those with normal Apgar scores)

$Z_{\beta} = 0.84$ standard normal variate for power or type II errors at 80% power

P_0 is the probability of having encephalopathy or delayed neurodevelopment in the experimental group (those with very low and low Apgar scores) = 50% =0.5 which is an estimate because the proportion is not from other studies.

P_1 is the probability of having encephalopathy or delayed neurodevelopment in the control group (those with normal Apgar scores) = 30% =0.3 which is an estimate given that of the experimental group has been estimated at 50%

$$P^* = \frac{P_0 + wP_1}{w+1} = \frac{0.5 + 0.3}{1+1} = 0.4$$

Therefore sample size

$$n = \frac{[1.96\sqrt{(2 \times 0.4) \times (1-0.4)} + 0.84\sqrt{0.5 \times (1-0.5)} + 0.3(1-0.3)]^2}{(0.5 - 0.3)^2}$$

$$= \frac{[1.96\sqrt{0.8 \times 0.6} + 0.84\sqrt{0.5 \times 0.5} + 0.3 \times 0.7]^2}{(0.2)^2} = 61 \text{ in each of the 2 groups}$$

Thus 61 for the very low and low Apgar scores and 61 for the group with normal Apgar scores

Total sample size = $61 \times 2 = 122$.

3.9 Study Tools

- Apgar score chart.
- The Neonatal Neurological Examination (NNE) adapted from Precht, a tool this study used to determine encephalopathy was proved to be very accurate in evaluating neonatal encephalopathy (94% accuracy) (Wolf et al, 1985) in a study in Zimbabwe. This tool uses 7 signs that may be present or absent in the neonate and assigns scores of normal 0, mild 1, moderate 2, and severe 3. Scores 2 to 3 are considered significant encephalopathy in the study.
- The Bayley Scale of Infant Development II (BSID II, 1995) developed by the American Psychological Association is a tool used to determine mental and motor

development and behaviour ratings (BRS) appropriate for ages 1 to 42 months. In this study, the mental and motor scales adequately covered the BRS at 2 months of age.

3.10 Procedure

Four midwives were recruited, equipped with stop watches and retrained to record Apgar scores at 5 minutes. Apgar scores of all newborns meeting the inclusion criteria were recorded on scoring charts. Study subject recruitment was done on week days. Names of postnatal mothers (of study subjects) and wards were communicated to the Principal investigator (PI) to follow up within 6-12 hours. Scored Apgar score charts were not availed to the PI when conducting the NNE, this provided a blind. After explaining the purpose of the study, the PI obtained a signed written consent to the study with information for future tracking.

The PI then conducted the NNE and graded the newborns accordingly: 0, normal; 1, mild; 2, moderate and 3, severe.

At 8 weeks postnatal age, a series of tests and observations were conducted using a BSID II manual and index scores were assigned to each baby. These scores were then converted to raw scores equivalent to age, in terms of motor and mental development. The behavior rating scale (BRS) was not done because, at 8 weeks, the motor and mental scales were considered adequate.

Results were recorded as <1, 1, 2 or 3 months. The PI did not refer to Apgar scores or the NNE of the infants being assessed before completing the BSID II, for blinding.

3.11 Data analysis

Data analysis was done using SPSS 20 software. Descriptive statistics in form of frequency tables, pie chart and bar graphs were obtained. Chi-square tests of association was done to test the association between Apgar scores (very low, low, normal) with the categorical variables; sex (male/female), mortality (yes/no), Grades for Neonatal Neurological Examination (Normal/mild/moderate/severe), encephalopathy (yes/no), delayed motor neurodevelopment (yes/no), delayed mental neurodevelopment (yes/no), mothers age (<20/20-29/≥30), Parity (≤1/2-5/>5) and lost to follow up (yes/no). One way analysis of

variance was done to compare the means of the continuous variables weight at birth, weight at 8 weeks, Head circumference at birth and head circumference at 8 weeks. The equality of means within very low, low and normal scores was tested for these continuous variables.

To obtain odds ratios the categories low and normal for the Apgar scores were collapsed and combined and compared with very low scores. The categories became two (very low, low or normal). These two categories were tested for associations with the variables mortality, encephalopathy, delayed neurodevelopment (motor) and delayed neurodevelopment (mental). The 2x2 tables contingency tables were obtained for each of these variables and odds ratios were produced.

3.12 Ethical issues

Ethical approval to conduct the study was given by the Research and Ethics Committee of the University of Zambia. The study was observational, and had no intrusive procedures on the study subjects. Those study subjects observed to have medical problems, were referred for appropriate medical attention. Permission was obtained from the Head of Department, Obstetrics and Gynaecology to conduct the study in labour wards. Written informed consents were obtained from mothers of study subjects.

Chapter Four

4.0 Results

A total of 140 full term infants were sampled from the University Teaching Hospital. The Apgar scores collected were for these infants at 5 minutes. Twenty nine (21%) had very low Apgar scores (0-3), 28 (20%) had low Apgar scores (4-6) while 83 (58%) had normal scores (7-10) (Figure 4. 1 and table 4.3).

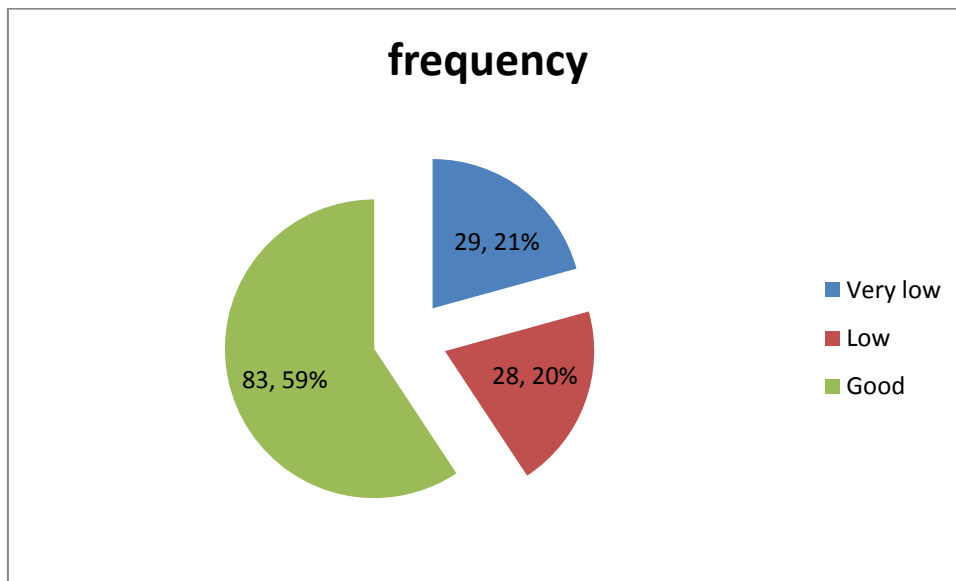


Figure 4. 1: Apgar scores at 5 minutes for full term infants

Figure 4.2 and table 4.1 shows 54 (38.6 %) had normal grades from the Grade Neonatal neurological examination, 44 (31.4%), 19 (13.6 %) had mild, while 23 (16.4 %) had severe.

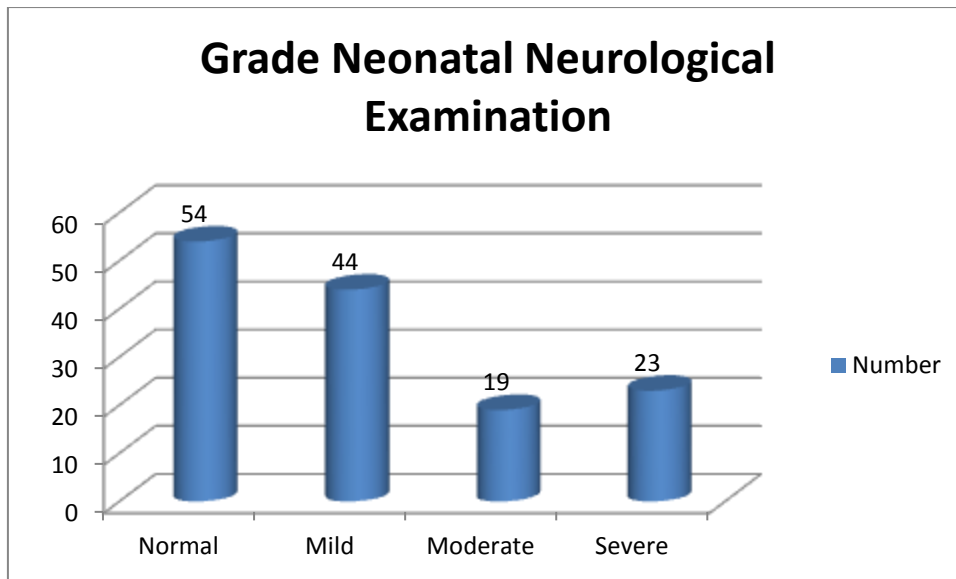


Figure 4.2: Grades for Neonatal Neurological Examination

Figure 4.3 and Table 4.1 shows the results for the Bayley scale of infant development II for the 53 infants who were assessed for mental development. The other 87 were however not assessed. Only 6 had the development not appropriate to their age with 2 (1.4%) having less than 1 month while 4 (2.9%) had one month. Forty seven had mental development appropriate to their age with 45 (32.1%) having 2 months and 2(1.4%) three months.

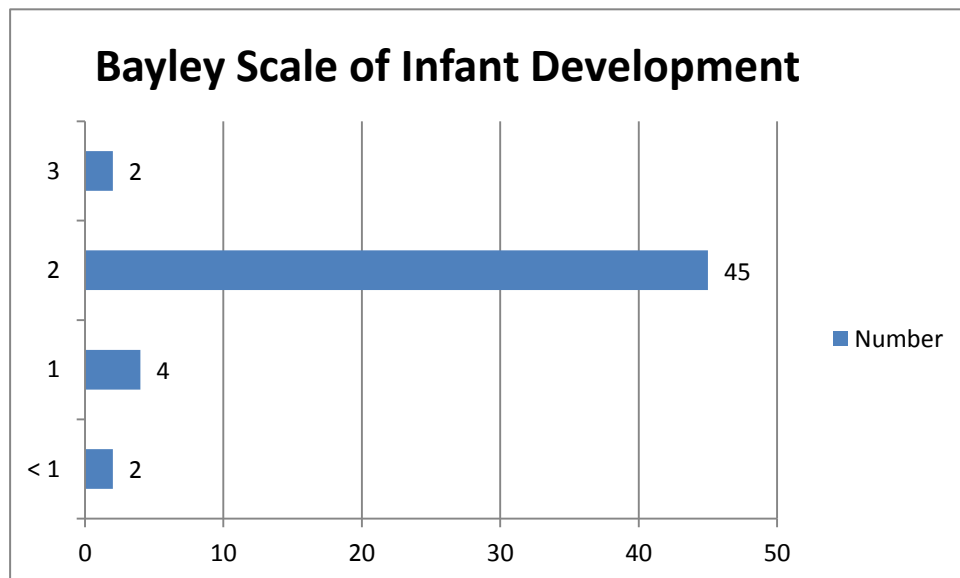


Figure 4.3: Bayley scale of infant development II

Table 4. 1. Infant attributes of the sampling distribution

Variable	Category	n (%)
Sex of infants	Male	87 (62.1)
	Female	53 (37.9)
Weight of infants at birth	Mean \pm SD	3.0 \pm 0.3
Weight of infants at 8 weeks	Mean \pm SD	5.0 \pm 0.4
Head circumference of infants at birth	Mean \pm SD	35.0 \pm 1.2
Head circumference of infants at 8 weeks	Mean \pm SD	39.8 \pm 2.1
Deaths of infants	Dead	31 (22.1)
	Alive	109 (77.9)
Grades for NNE	Normal	54 (38.6)
	Mild	44 (31.4)
	Moderate	19 (13.6)
	Severe	23 (16.4)
Motor BSID II	Not assessed	86 (61.4)
	< 1	3 (2.1)
	1	4 (2.9)
	2	42 (30.0)
	3	5 (3.6)
Mental BSID II	Not assessed	87 (62.1)
	< 1	2 (1.4)
	1	4 (2.9)
	2	45 (32.1)
	3	2 (1.4)

Table 4.1 shows that 87 (62.1%) of the infants were male while 53 (37.9%) were female. The infants had a mean weight of 3.0 ± 0.3 at birth and 5.0 ± 4.4 at eight weeks. The mean head circumferences were 35.0 ± 1.2 at birth and 39.8 ± 2.1 at eight weeks. The mortality rate was 22% with 31 (22%) of the infants having died while 109 (78%) remained alive.

Table 4.2. Maternal attributes of the sampling distribution

Variable	Category	n (%)
Age of mother of infant	< 20 years	32 (22.9)
	20 – 29 years	80 (57.1)
	≥ 30 years	28 (20.1)
Parity	≤ 1	61 (43.6)
	2 – 5	71 (50.7)
	> 5	8 (5.7)
Infants	Lost to follow up	85 (60.7)
Lost to follow up	Followed up	55 (39.3)

Table 4.2 shows that most (57%) of the infants mothers were in the age range 20 – 29 years while 20% had 30 or more years. Interestingly about 23% of the mothers had less than 20 years. The parity of most of them (71%) was 2 – 5 while 61% had a parity of 1 or 0. A few (about 6%) had parity of greater than 5. About two thirds (60.7%) of the infants were lost to follow up and deaths.

Table 4.3. Infants health and development

Variable	Category	n (%)
Apgar scores	Very low (0-3)	30 (21.4)
	Low (4-6)	29 (20.7)
	Normal (7-10)	81 (57.9)
Encephalopathy	Yes	43 (30.7)
	No	97 (69.3)
Delayed neurodevelopment (motor)	Yes	7 (13.0)
	No	47 (87.0)
Delayed neurodevelopment (mental)	Yes	6 (11.3)
	No	47 (88.7)

The proportion or prevalence of encephalopathy was about 30.7% (Table 4.3). About 7 (13.0%) out of 55 assessed had delayed neurodevelopment both in terms of motor development while 6 (11.3%) had delayed mental neurodevelopment (Table 4.3).

Table 4. 4. Infant related factors associated with Apgar scores

Variable	5 minute Apgar scores			P-value
	Very low, n(%) (0-3)	Low, n(%) (4-6)	Normal (7-10)	
Sex				
Male	25 (83.3)	21 (72.4)	41 (50.6)	0.003
Female	5 (16.7)	8 (27.6)	40 (49.4)	
Infant died				
Yes	22 (73.3)	8 (27.6)	1 (1.2)	<0.0001
No	8 (26.7)	21 (72.4)	80 (98.8)	
Grades for Neonatal Neurological				
Normal	2 (6.7)	2 (6.9)	50 (61.7)	<0.0001
Mild	3 (10.0)	12 (41.4)	28 (34.6)	
Moderate	6 (20.0)	11 (37.9)	3 (3.7)	
Severe	19 (63.3)	4 (13.3)	0 (0.0)	
Infant had encephalopathy				
Yes	25 (83.3)	15 (51.7)	3 (3.7)	<0.0001
No	5 (16.7)	14 (48.3)	78 (96.3)	
Delayed neurodevelopment (motor)				
Yes	1 (50.0)	4 (28.6)	2 (5.3)	0.032
No	1 (50.0)	10 (71.4)	36 (94.7)	
Delayed neurodevelopment (mental)				
Yes	1 (50.0)	4 (28.6)	1 (2.7)	0.013
No	1 (50.0)	10 (71.4)	36 (97.3)	
Weight at birth	3.0±0.3	3.0±0.3	3.0±0.3	0.956
Weight at 8 weeks	4.2±0.3	3.0±0.3	3.0±0.4	0.345
Head circumference at birth	35.6±1.2	35.2±1.1	34.7±1.1	0.020
Head circumference at 8 weeks	40.2±1.4	39.6±2.3	39.8±2.2	0.964

Table 4.4. The male infants were significantly more likely to have very low Apgar scores than their female counter parts (83.3% Vs 16.7%, P=0.003). The infants with very low Apgar scores were significantly more likely to die compared to those with low or normal Apgar scores (73.3% Vs 27.6% Vs 1.2%, P < 0.0001). The mortality rate for infants with very low Apgar scores was 73.3%. Those with very low Apgar scores compared to those with low or

normal scores were significantly more likely to have severe NNE scores (63.3% Vs 13.8% Vs 0%, $P < 0.0001$). The prevalence of encephalopathy in those with very low Apgar scores was 83.3%. Those with very low Apgar scores were significantly more likely to develop encephalopathy compared to those with low or normal scores (83.3% Vs 51.7% Vs 3.7%, $P < 0.0001$). Furthermore infants with very low Apgar scores were significantly more likely to have delayed motor neurodevelopment (50.0% Vs 28.6% Vs 5.3%, $P=0.032$). The infants with lower Apgar scores also were significantly more likely to have delayed mental neurodevelopment (50.0% Vs 28.6% Vs 2.7%). The prevalence of delayed neurodevelopment was 50% in those with very low Apgar scores for both motor and mental development. The mean head circumference at birth of those with very low Apgar scores was significantly larger than those with low or normal scores (35.6 ± 1.2 Vs 35.2 ± 1.1 Vs 34.7 ± 1.1 , $P=0.02$). There were however no significant differences between those with very low Apgar scores with those with low or normal in terms of weight at birth, weight at 8 weeks and head circumference at 8 weeks, ($P>0.05$).

Table 4. 5. Maternal related factors associated with Apgar scores

Variable	5 minute Apgar scores			P-value
	Very low, n(%) (0-3)	Low, n(%) (4-6)	Normal (7-10)	
Mothers age				
< 20 years	11 (36.7)	7 (24.1)	14 (17.3)	0.286
20 – 29 years	13 (43.3)	17 (58.6)	50 (61.7)	
≥ 30 years	6 (20.0)	5 (17.2)	17 (21.0)	
Parity				
≤ 1	16 (53.3)	13 (44.8)	32 (39.5)	0.411
2 – 5	11 (36.7)	15 (51.7)	45 (55.6)	
> 5	3 (10.0)	1 (3.4)	4 (4.9)	
Lost to follow up				
Yes	28 (93.3)	15 (51.7)	42 (51.9)	<0.0001
No	2 (6.7)	14 (48.3)	39 (48.1)	

Table 4.5. The mothers of infants with very low Apgar scores were more likely to be in the age group of less than 20 - 29 years. This finding was however not significant (43.3% Vs 36.7% Vs 20.0%, $P>0.05$). The infants with very low Apgar scores compare to those with

low or normal scores were significantly more likely to be lost to follow up (93.3% Vs 51.7% Vs 51.9%, P=0.001).

Table 4. 6. Measure of association between Mortality and 5 minute Apgar scores

Variable	5 minute Apgar scores		OR (95% CI of OR)
	Very low, n(%) (0-3)	Low/normal, n(%) (4-6, 7-10)	
Mortality			
Yes	22 (73.3)	9 (8.2)	30.9 (10.7 – 88.9)
No	8 (26.7)	101 (91.8)	

The Odds ratio in table 4.6 shows that those with very low Apgar scores were about 31 times more likely to die than those with low or normal Apgar scores. This association was significant (OR = 30.9, CI =10.7 – 88.9) because the 95% confidence interval of the odds ratio does not contain 1. This shows that very low Apgar score at 5 minutes is a risk factor for mortality.

Table 4. 7. Measure of association between Encephalopathy and 5 minute Apgar scores

Variable	5 minute Apgar scores		OR (95% CI of OR)
	Very low, n(%) (0-3)	Low/normal, n(%) (4-6, 7-10)	
Encephalopathy			
Yes	25 (83.3)	18 (16.4)	25.6 (8.6 – 75.6)
No	5 (16.7)	92 (83.6)	

The odds ratio for table 4.7 shows that those with very low Apgar scores were 25 times more likely to have encephalopathy than those with low/normal scores. This association was significant (OR = 25.6, CI = 8.6 – 75.6) because the 95% confidence interval of the odds ratio does not contain 1.

Table 4. 8. Measure of association between delayed neurodevelopment (motor) and 5 minute Apgar scores

Variable	5 minute Apgar scores		OR (95% CI of OR)
	Very low, n(%) (0-3)	Low/normal, n(%) (4-6, 7-10)	
Delayed neurodevelopment (motor)			
Yes	1 (50.0)	6 (11.5)	7.7 (0.4 – 139.3)
No	1 (50.0)	46 (88.5)	

According to table 4.8, the Odds ratio show that those with very low Apgar scores are about 8 times more likely to have delayed motor neurodevelopment. This association is however not significant (OR = 7.7, CI = 0.4 – 139.3) because the 95% confidence interval of the odds ratio contains 1.

Table 4. 9. Measure of association between delayed neurodevelopment (mental) and 5 minute Apgar scores

Variable	5 minute Apgar scores		OR (95% CI of OR)
	Very low, n(%) (0-3)	Low/normal, n(%) (4-6, 7-10)	
Delayed neurodevelopment (mental)			
Yes	1 (50.0)	5 (9.8)	9.2 (0.5 – 170.8)
No	1 (50.0)	46 (90.2)	

Table 4.9 shows that the infants with very low Apgar scores are 9.2 times more likely to have delayed mental neurodevelopment. This association was not significant (OR=9.2, CI= 0.5 - 170.8) because the 95% confidence interval of the odds ratio contains 1.

Chapter Five

5.0 Discussion

It has been said that every baby born in a modern hospital anywhere in the world is looked at first through the eyes of Dr. Virginia Apgar. Her simple, rapid method for assessing newborn viability, the "Apgar score," has long been standard practice. Developed in the early 1950s and quickly adopted by obstetric teams, the method reduced infant mortality and laid the foundations of neonatology (The Virginia Apgar Papers, bulk 1925-75).

But critics of the Apgar score question the reliability of the Apgar scores as a "tool" (to measure newborn adaptation to extra-uterine life) and that it is lacking in sensitivity and specificity. *Sensitivity* measures how well the tool captures the infant's condition at birth (stable vs. depressed) and *specificity* refers to how well the tool measures the differences between the values of the scores (0–2 for each of the five categories) (Jepson et al, 1991). Variability exists in how individual health care providers score the assessment. Clark and Hakanson compared the consistency (inner-rater reliability) of Apgar scoring among various health care disciplines. In their study, groups of health care providers were visually shown case presentations and then asked to assign Apgar scores to the infants who were presented. Pediatricians and pediatric house staff had a consistency rating of 68%, obstetricians and obstetric house staff had a consistency rating of 46%, intensive care nursery staff had a consistency score of 42%, obstetric nurses 36%, and community hospital nurses a consistency rating of 24% (Clark and Hakanson, 1988; Livingston, 1990).

Another concern is determining who assigns the Apgar score once the infant is born. According to both Apgar and the Regan Report (1987), the person assisting with the delivery of the infant should not assign the Apgar score as bias may be introduced into the score value, because the individual who attends to the delivery may have a vested interest in the outcome (Montgomery, 2000; Apgar, 1966).

The scenario obtaining in this country's health centres and UTH in particular is that Apgar scores are scored by attendants (midwives) at time of delivery and is usually done in retrospect. Staff shortages may prevent the birth attendants to pause and score the Apgar at required times, as they are preoccupied with the safety of the mother and the baby (each

uncomplicated birth is usually given to one midwife). Most labour rooms do not have appropriate timing devices to aid correct scoring of Apgar.

In this study, attempts were made to minimize these inherent flaws, by retraining the Apgar scorers, providing them with alarm stop watches, and not allowing them to participate in the deliveries of the study subjects.

The proportion/prevalence of newborns who presented with very low/ low Apgar scores at UTH in this study was, 29 (21%) had very low Apgar scores (0-3), 28 (20%) had low Apgar scores (4-6) while 83 (58%) had normal scores (7-10) (Figure 4.1 and Table 4.3).

The newborn with low Apgar scores tended to be very sick who, even after vigorous resuscitation, ended up dying, a situation frustrating to staff working in NICU and the 5 minute Apgar scores appear to correctly predict this. Of the 31 mortalities in the study, 22 (73.3%) scored 0-3 5 minute Apgar scores, compare with 109 (98.8%) who scored 4-10 and survived the neonatal period (Tables 4.4 and 4.6). The Apgar score appears to be the earliest postpartum predictor of death in the newborn.

Newborn brains are still developing and some may completely recover from such events, but it would be impossible to distinguish between those who recover from those who don't, hence the need for long term follow up of all such babies in Paediatric neurology clinics for early diagnosis and management of these adverse outcomes. The Apgar scores have an inherent advantage over the NNE in that they are carried out earlier than any other postpartum investigations and are already currently widely used by all trained birth attendants in the country. They could, cost effectively, be used by frontline health workers as a basis for referral of affected babies to NICU or Paediatric neurology clinics. The NNE protocols on the other hand are specialized tools which can only be conducted by highly skilled personnel who are not always available in out laying areas.

The male infants were significantly more likely to have very low Apgar scores than the females, 83.3% Vs 16.7%, $p=0.003$ (Table 4.4). This could be consistent with the old adage, that male neonates are weaker than their female counterparts, the male disadvantage hypothesis? (Naeye et al, 1971; Kirchengast et al, 2009). If this indeed is true, the need for gender related medical research is warranted, as sex-specific needs and problems can only be addressed through effective interventions when they have been determined by way of clinical

research settings (Unger et al, 2011).

The prevalence of encephalopathy in term newborns (graded as moderate to severe by NNE) at UTH was 30.7% (43/140), (Table 4.3, Figure 4.2). The study subjects with very low (0-3) 5 minute Apgar scores, 63.3% (19/30) had severe encephalopathy in the 6 to 12 hour postpartum period compared to the controls (7-10), none had encephalopathy and only 4/30 (13.3%) low Apgar scorers (4-6) had severe encephalopathy (Table 4.4). This again, shows the Apgar score as being the earliest postpartum predictor of adverse neurodevelopmental outcome. No other studies have shown encephalopathy at this age to compare with. This however should be viewed with caution because at this stage, resuscitation can modify the eventual outcomes.

The study has shown that very low Apgar scores (0-3) at 5 minutes is associated with high mortality (Table 4.4) a finding consistent with other similar studies (Casey, 2001; Dijxhoorn et al, 1986; Nelson & Ellenberg, 1981; Ellis, 1999; Collins & Paneth, 2001; Nalubamba, 2003) that low Apgar scores (< 7) is associated with significant encephalopathy (NNE score moderate or severe) at age 6-12 hours (compare Tables 4.4 and 4.7). The encephalopathy appears to be an ominous indicator of adverse outcome with 81% mortality.

Diagnosing developmental delay is complex and there is no universally agreed definition. One definition requires the child to exhibit a 20% delay in functioning when compared to his or her age peers, while another uses a score 2 or more standard deviations below the mean of a reference group. Regardless of the criteria used, the BSIDII provides adequate developmental age level information to aid the diagnosis of delay. It should be noted however, that to base a diagnostic decision only on results of a single evaluation would not be sound practice. Relevant background social and medical history should be taken into account for such a decision to be made.

The 79.5% of study subjects who scored 7-10 5- minute Apgar scores (controls) had (2 month) appropriate for age motor grade at eight weeks postnatal age by the BSID II motor (Table 4.8), the Odds ratio show that those with very low Apgar scores are about 8 times more likely to have delayed motor neurodevelopment. This association is however not significant OR = 7.7, CI = 0.4 – 139.3 (Tables 4.4, 4.8, and Figure 4.3).

And 87.2% of the study subjects who had 7-10 5 minute Apgar scores were graded (2 months) appropriate for mental age at 8 weeks postnatal age by the BSID II mental. The study however showed that the infants with very low Apgar scores are 9.2 times more likely to have delayed mental neurodevelopment. This association was not significant OR=9.2, CI= 0.5 -170.8 (Tables 4.4, 4.9 and Figure 4.3).

The not statistically significant results in the BSID II tests in both mental and motor was attributed to a high mortality in the neonatal period of the study subjects who scored 0-3 5 minute Apgar scores, this left very few study subjects in this Apgar group (Tables 4.8, 4.9). Compare with similar results by Dag Moster et al. in his Population based cohort study in Norwegian children (Moster D et al, 2001).

In the Paediatric neurology clinic at UTH, it is quite common to hear mothers of the neurologically challenged children saying either they had a difficult delivery or that the baby did not 'cry immediately after birth' or both in respect to these children. This 'did not cry immediately after birth' is usually translated as that the baby had depressed Apgar scores. In Zambia, Apgar scores are not indicated on the under five cards for child immunization follow ups or on birth records. This may pose a challenge for neurologists to effectively follow up children with low Apgar scores for assessments and early management.

It would be of benefit for this country's Paediatricians and other Child Health Specialists to lobby authorities to introduce a more robust and detailed childhood development follow up programme for children as the current under five immunizations and growth monitoring, good as it has been so far, lack in details and depth. This should include, among other things, information about occurrences in the intrapartum and immediate postpartum periods. Happenings during this period may have a profound influence on the future wellbeing of the individual.

At the end of this study, efforts were made to find out the cause of this poor follow up, 140 were recruited and participated in the first part of the study, 31 died in the neonatal period and 54 were lost to follow up (Table 4.5). Most study subjects lost to follow up were healthy babies with Apgar scores (4-10) whose parents felt no need to take them to the hospital for just study follow up (93.3% Vs 51.7% Vs 51.9%, P=0.001). A few had relocated and expressed inability to come for follow up for financial reasons. Three mothers reported to have lost their babies through death. It was not possible to 'kitty bag' the study to antenatal

clinic visits because the mothers attended different clinics near their localities.

The study did not however, attempt to suggest that low Apgar scores are causalities of the adverse neurological outcomes but that factors affecting the Apgar scores are.

Chapter Six

6.0 Conclusion

Apgar scores are not given due attention. This simple tool can accurately predict mortality and encephalopathy in the newborn and neonatal periods.

The study found that very low Apgar scores 0-3 at 5 minutes was associated with high mortality (73.3%) in the neonatal period. Infants with a 5 minute Apgar score <7 (81%) had significant encephalopathy at 6-12 hours of age and that this encephalopathy was an ominous sign of later adverse outcome.

An association between very low 5 minute Apgar scores and developmental delay in full term infants at eight weeks postnatal age was established, and Apgar scores can therefore, be used to screen for infants requiring further neurodevelopmental follow ups in neurology clinics.

It can therefore be said that Apgar scores, when correctly scored, can be simple, effective indicators of the newborn at higher risk of mortality and encephalopathy, hence in need of more vigorous resuscitation in labour rooms and may need immediate referral to NICU at UTH.

6.1 Study limitations

- The study has not helped to categorize the causes of neonatal encephalopathy i.e. sepsis etc.
- Follow up time was limited as subtle neurological deficits may not be obvious at 8 weeks postnatal age.
- The high mortality of study subjects (22.1%) with very low 5 minute Apgar scores and the high follow up loss (38.6%), (Table 4.8 and 4.9) made the neurodevelopmental assessment with more controls than the affected study subjects.

6.2 Recommendations

Midwives and other staff conducting deliveries, should be encouraged to obtain quality Apgar scores and to this end, supplied with stop watches to do this accurately.

Apgar scores should be included on the child development monitoring cards (under 5 cards) because this can provide vital information about the child with developmental deficits.

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APPENDIX

A. Apgar Scoring chart

Name: Sex: F/M Date:...../...../..... Birth weight:

OFC: pp.: Gravid: Para:

Age of mother: Time of Birth:

Score	0	1	2
Heart Rate	Absent	Less than 100 beats per minute	More than 100 beats per minute
Tick			
Respiration	Absent	Slow, irregular; weak cry	Good; strong cry
Tick			
Muscle Tone	Limp	Some flexing of arms and legs	Active motion
Tick			
Reflex*	Absent	Grimace	Grimace and cough or sneeze
Tick			
Color	Blue or pale	Body pink; hands and feet blue	Completely pink
Tick			
Total Score			

Comments (e g resuscitation etc):

.....

Scored by:

.....

B. Consent form

Title of Research: The use of Apgar scores as predictor of neurodevelopmental delay in term infants at eight weeks postnatal age.

Investigator

Dr Ronald Chola. A Post Graduate student at the University of Zambia /UTH

Information Sheet

Apgar score is a tool most Labour wards throughout the world use to assess the condition of a newborn baby.

Five parameters are assessed at 1 minute, 5 minutes and at times 10 minutes after birth.

These are:

1. Cry (breathing) immediately after birth. A good strong cry gets 2 and absence of a cry gets 0.
2. Colour of the baby, blue to pink (the whole body from head to toes).
3. Heart beat; more than 100 beats/min is assigned 2, absence 0.
4. Muscle tone, Active and strong gets 2, completely floppy gets 0.
5. Reflexes, a grimace and a cough when the back of the tongue or nostril is lightly stroked gets 2 and no response gets 0.

A total of 7-10/10 is considered good while 0-3/10 is considered not.

It has been observed that those babies with poor Apgar scores tend to have difficulties later on in life. These difficulties include an early death to delays in acquiring certain life skills like unable to sit/walk at a certain age most babies do or behavioral or learning difficulties later on in life.

This study attempts to identify such babies at risk, so that measures can be put in place to assist them.

Apgar scores will be taken at birth,

At about 6 hours from birth an assessment of the state of the muscles, ability to suckle etc. will be done. No painful procedure will be undertaken on the baby.

At 8 weeks after birth, another similar test will be done to determine whether the calendar age corresponds to the neurodevelopmental age of the baby, again no painful procedures will be done to the baby.

Information collected will be analyzed and the parents may be told the outcome upon request.

Unless in very obvious cases the results will only indicate the child's development at that particular age and will in no way indicate the future wellbeing of the child.

Those with more unfavourable outcomes will be followed up further in the neurology clinic (with permission from the care giver) to see if they have any special needs.

Procedures

I agree to participate, the following things will happen:

1. I will answer a few questions about the way the baby was delivered.
2. I will allow my baby's information on his/her neonatal form to be used for the purpose.
3. I will allow my baby to be clinically assessed by the investigator at least three times.

Benefits

Babies found to be at increased risk of developing Developmental delay will be enrolled and followed up in neurology clinic for a much longer period to see if they will have any special needs (with consent from the parents).

Risks

No appreciable risks to the baby are expected. Babies will only be examined, no painful procedures will be applied.

Confidentiality

Results of the study will be communicated to me if so wish and my baby's identity will be kept confidential as far as the law allows.

Right to refuse or withdraw

My participation in the study is entirely voluntary and I reserve the right to refuse or withdraw at any stage in this study without jeopardizing the future medical care of my baby.

Query contacts

Any queries will be answered by the Principal investigator at Cell 097846648. E- mail ronaldchola @yahoo.co.uk or

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Consent

I agree for my baby to participate in the study. I have been given a copy of this form and had a chance to read it.

Name:

.....

Signature/thumb print:

.....

Signature of clinician:

.....

Witness:

.....

Date:

.....

C. Neonatal Neurological Examination Form

Name: Age: Sex F/M OFC:

Time of Examination:

The bold items must be present for the baby to receive the grade. Tick where appropriate.

	NORMAL	GRADE ONE (MILD)	GRADE TWO(MODERATE)	GRADE THREE(SEVERE)
1. Consciousness level	0.Normal	1. Irritable/hyper alert	2.Lethalgie	3. Comatose
2. Tone	0.Normal	1.Mildly Abnormal(hyper /hypo)	2 Moderate abnormal (hypotonic or dissociated)	3. Severely abnormal (hypotonia)
3.Suck	0.Normal	1Abnormal	2.Poor	3, Absent
4.Primitive reflex (moro ,grasp)	0.Normal	1. Exaggerated	2.Depressed	3.Absent
5.Brain stem reflex (corneal, gag)	0.Normal	0. Normal	0.Normal	3.Impaired
6.Seizures	0.Normal	0.Absent	2. Present	2.Present
7.Respiration	0.Normal	1.Tachypnea	2. Occasional apnea	3.Severe apnea

Abnormality of tone OR suck should accompany altered conscious level to assign grade.(Adapted from Prectl and Baintema).

Grade:

Comments (e.g. fit, /death, ventilation etc.):

.....

Graded By:

