APPRIOPRIATE INTERVENTIONS TO REDUCE PERINATAL MORTALITY AND MORBIDITY IN LOW-RESOURCED SETTINGS

FETAL HEART RATE ASSESSMENTS

AND

BASIC ACTIONS AT BIRTH

Thesis for the degree philosophiae doctor (PhD)
Cand Med Hege Langli Ersdal

Department of Anaesthesiology and Intensive Care
Stavanger University Hospital

Faculty of Medicine
University of Oslo
2012
~ To the unborn child ~
AKNOWLEDGEMENTS

I would like to give my sincere appreciation to many people who have played important roles in this PhD project.

Eldar Søreide – my dear mentor and supervisor – this PhD started because of you. You believed in me and made me realize that I could pick up research again. You showed me the way and you found new paths when I got stuck.

Johanne Sundby – my main-supervisor – you welcomed me to the University of Oslo. You gave me the chance to study what I always wanted to, even if it was not in your field of expertise. You encouraged and had confidence in my ideas when I was in doubt, and I knew that you would stay loyal to the decisions taken.

Jeffrey Perlman – the supervisor who has followed me closely through this PhD – your overview, experience, knowledge, and true passion have been essential for my work. Patiently, you have answered all my questions related to neonatology, given me valuable advices along the road, and led me through the project with great insight and care. Through you, I have received a deeper understanding of research.

Tore Lærdal – tireless working to help save millions of maternal and newborn lives – you gave me the opportunity to engage with the Helping Babies Breathe program. Your visions, enthusiasm, and never-ending efforts have been extremely motivating and inspiring.

Estomih Mduma – my dear co-investigator and research manager at Haydom Lutheran Hospital (HLH) – the studies at HLH would not have been possible without you. You have taught me a lot about implementing research and how to make it sustainable. Your sacrifices and hard work to improve health care in your country are extraordinary.

The research assistants at HLH – observing and recording data day and night – your unique contribution is fundamental for this ongoing project.

Maternity staff at HLH – providing required information in spite of all your routine tasks – your collaboration is essential.

The management at HLH – approving this unusual project – your support is crucial.

Erling Svensen – my co-investigator at HLH – your help in managing this project has been very important and educative for me. Your calm analytic approach to every obstacle we faced was especially useful.
Bjørn Auestad – statistician at University of Stavanger – you have unpacked the “world of statistics” for me. Your critical questions and assistance have increased my understanding of science.

Siri Tau Ursin – head of Department of Anaesthesiology and Intensive Care, Stavanger University Hospital – from the beginning you have supported my research activities and demonstrated great flexibility.

Elsa Søyland – head of Stavanger Acute Medicine Foundation for Education and Research (SAFER) – you included me as a member of the team at SAFER and let me benefit from the infrastructure and expertise at SAFER.

Tove and Lars Langli – my dear mother and father – you have raised me with love, trust, and freedom to explore.

Margot and Anton Ersdal – my dear parents in-law – your readiness to assist in everyday life is highly appreciated.

Tor Albert – my beloved husband – you are not a typical man. You can think of many things simultaneously and manage everything in my absence. Nothing is a problem for you. Thank you for understanding me better than I do, and taking care of me.

Mia Elida, Oda Aurora, and Trym Aleksander – our beautiful children – you have been willing to share your mother for the improvement of other children’s health.

FINANCIAL SUPPORT

The candidate received research grants, and HLH received project funds from The Laerdal Foundation for Acute Medicine.

The financial source had no role in study design, data collection, data analysis, data interpretation, writing of the articles, or in the decision to submit for publication.

All authors had no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years or no other relationships or activities that could appear to have influenced the submitted work.
ABBREVIATIONS

COSTR = Consensus on Science and Treatment Recommendations

DOC = Data Oversight Committee

FHR = Fetal heart rate

FMV = Face mask ventilation

FSB = Fresh Stillbirth (intrapartum stillbirth)

GA = Gestational age

HBB = Helping Babies Breathe

HLH = Haydom Lutheran Hospital

ILCOR = International Liaison Committee on Resuscitation

MDG = Millennium Developmental Goals

MHSW = Ministry of Health and Social Welfare
DEFINITIONS

**Perinatal Mortality** = intrapartum stillbirths and early neonatal deaths per 1000 live births

**Neonatal Mortality** = newborn deaths in the first 28 days of life per 1000 live births

**Early Neonatal Mortality** = newborn deaths within the first 7 days of life per 1000 live births

**Birth asphyxia** = failure to initiate spontaneous respirations and/or 5 minute Apgar score < 7

**Primary apnea** = heart rate considered to be > 60 beats/minute with compensated blood pressure

**Secondary apnea** = progressive bradycardia < 60 beats/minutes and hypotension with final gasping

**Gestational age** = based on self-report of the last menstrual period and distance from symphysis pubis to the fundus

**Normal outcome** = survival > 24 hours without any detected difficulties

**Fresh/intrapartum stillbirth** = an Apgar score = 0 at both 1 and 5 minutes with intact skin and suspected death during labor/delivery

**Macerated/antepartum stillbirth** = an Apgar score = 0 at both 1 and 5 minutes with macerated skin and suspected death before start of labor
ABSTRACT

To meet the Millennium Developmental Goal (MDG) 4, a significant reduction in early neonatal mortality is required. It is necessary to define appropriate and effective low-tech interventions that can be implemented with high coverage and low costs worldwide.

“Helping Babies Breathe” (HBB) is a simulation-based educational program in basic neonatal care and resuscitation for use in resource limited areas developed by the Global Implementation Task Force of the American Academy of Pediatrics.

Tanzania was selected as the first country to pilot national implementation of HBB and the process was initiated in 2009. Closely linked to this project several observational open cohort studies, in the delivery room, were initiated in a rural referral hospital in Northern Tanzania. Research assistants/observers were trained to observe birth attendants performance related to delivery and newborns, using a stop watch, and record the findings on a data collection form following every delivery.

The data collected in this PhD project document 1) that fetal heart rate abnormalities, intermittently detected using a fetal stethoscope, identify the compromised fetus with increased risk for requiring face mask ventilations at birth, early neonatal death, or intrapartum death (fresh stillbirth), 2) the normal respiratory adaption of infants at birth, 3) that the majority of babies with birth asphyxia (i.e. failure to initiate spontaneous respirations) are in primary apnea and will respond to early stimulation and/or face mask ventilations, and 4) that the proportion of newborns in need of lifesaving help, and the proportion of birth asphyxia related deaths in this rural population, is much higher than the suggested global estimates. Supplemental material (Appendix 1) documents that implementation of the simulation-based HBB education enhanced the basic skills of birth attendants, and thereby reduced the incidence of early neonatal mortality.

These findings are proof of concept that the majority of perinatal deaths in low-income countries are largely preventable with the simple actions of intermittent assessment of fetal heart rate to guide the process of labour, coupled with immediate stimulation and/or face mask ventilation of non-breathing neonates at birth.
ORIGINAL PAPERS

This thesis is based on the following papers which will be referred to in the text by their Roman numerals:

Paper I


Paper II

Ersdal HL, Mduma E, Svensen E, Perlman JM. Early initiation of basic resuscitation interventions including face mask ventilation may reduce birth asphyxia related mortality in low-income countries. Resuscitation 2012;83:869-873

Paper III


SUPPLEMENTAL MATERIAL

Appendix 1

Haydom Lutheran Hospital is one of eight sites in the national HBB implementation study. The supplemental material presents site specific data before/after full HBB implementation at this site.

The manuscript summarising the final effects of the HBB program in Tanzania is still under consideration for publication and is not yet official.
# CONTENTS

**BACKGROUND** .......................................................................................................................... 11
Millennium Developmental Goals .................................................................................................... 11
Global burden of perinatal mortality and morbidity ........................................................................ 11
Fetal Heart Rate assessment and Intrapartum-related hypoxia ......................................................... 14
Basic Neonatal Resuscitation .......................................................................................................... 15
Statement of the problem in Tanzania ............................................................................................... 26
Summary ............................................................................................................................................ 27

**OBJECTIVES AND HYPOTHESIS** ............................................................................................... 28
Specific Objectives ............................................................................................................................. 28
Specific Research questions ................................................................................................................. 29
Hypothesis ........................................................................................................................................... 29

**METHODS** .................................................................................................................................... 30
Setting and study population .............................................................................................................. 30
Study design ....................................................................................................................................... 33
Data collection .................................................................................................................................... 38
Data analysis and statistics ................................................................................................................ 40
Ethical considerations ........................................................................................................................ 40

**MAIN FINDINGS** .......................................................................................................................... 41
The value of intermittent FHR assessment to predict intrapartum-related hypoxia ............................ 41
The normal neonatal respiratory adaption at birth ............................................................................. 41
Newborns in need of basic resuscitation ............................................................................................. 42
The importance of the “Golden Minute” after birth .......................................................................... 42
The presumed causes of neonatal death within the first 24 hours ................................................... 42
Effects of the HBB program – supplemental material ...................................................................... 44

**DISCUSSION** ................................................................................................................................ 44
Study design, Biases, and Validity ....................................................................................................... 44
Main findings ...................................................................................................................................... 49

**FUTURE PERSPECTIVES** ............................................................................................................ 55

**REFERENCES** ............................................................................................................................... 56

**PAPERS I-III** .................................................................................................................................. 62
Paper I ................................................................................................................................................ 62
Paper II ............................................................................................................................................... 79
Paper III ............................................................................................................................................. 84

**APPENDICES** ............................................................................................................................... 91
Appendix 1 .......................................................................................................................................... 91
Appendix 2 .......................................................................................................................................... 92
Appendix 3 .......................................................................................................................................... 94
Appendix 4 .......................................................................................................................................... 95
BACKGROUND

MILLENNIUM DEVELOPMENTAL GOALS

In 1994 the International Conference on Population and Development set a number of goals and objects to be attained by 2015 including universal access to comprehensive reproductive health services with reduction in maternal and perinatal mortality and morbidity (1). The United Nations Millennium Declaration from 2000 emphasizes many agenda items from the above programme in the eight Millennium Developmental Goals (MDG) (2). The MDG 4 (Child Health) and 5 (Maternal Health) have a series of time-bound targets with deadline of 2015, that are behind schedule (3,4). The MDG 4 of reducing the mortality of children under 5 years by two thirds from 1990 (13, 2 mill) to 2015 (target; 5 mill) requires a substantial reduction in neonatal mortality, accounting for 41% of the total under 5 mortality, in the remaining years (3,4). Progress in maternal health, and the closely linked stillbirth rate and newborn health, is too slow in many developing countries and requires urgent attention and guidelines for action.

GLOBAL BURDEN OF PERINATAL MORTALITY AND MORBIDITY

Perinatal Mortality is defined as intrapartum stillbirths and early (one week) neonatal deaths per 1000 live births. Perinatal health globally has received increasing international attention over the past 15-20 years. However, almost 99% of all deaths still occur in resource-poor settings (4-8) and stillborn babies are not even included in MDG 4 goals. Each year, intrapartum-related hypoxia (often equated with birth asphyxia) is estimated to account for about two million perinatal deaths worldwide including intrapartum stillbirths and early neonatal deaths (4,5,9-11). The intrapartum stillbirth rate is estimated to around 10 per 1000 births (9). The vast majority of intrapartum-related neonatal deaths occur within the first week of life and the risk for intrapartum-related death on the first day of life is estimated to about 11 per 1000 births (9). An additional one million of the surviving infants develop neurocognitive problems such as cerebral palsy and learning difficulties (6). Official figures probably underestimate perinatal mortality and morbidity rates because of considerable under-reporting (12,13). The psychological and sociological burdens are impossible to measure.
There are several causes contributing to perinatal mortality and morbidity. Adverse perinatal outcome secondary to intrapartum fetal organ damage due to poor oxygenation may be difficult to distinguish from other conditions including infections and trauma. However, these conditions often co-occur, and intrapartum fetal hypoxia and ischemia is probably the final common pathway for many intrapartum-related fresh stillbirths (FSB) and early neonatal deaths, whether the event is obstructed labour, hemorrhage, cord prolapse, pre/eclampsia, or maternal infection/sepsis. Depending on the severity and duration of intrapartum hypoxia the baby may die during labour and present as a FSB, or be delivered with variable degree of hypoxic-ischemic injury. Strategies for prevention of intrapartum-related adverse outcome can be divided into three phases:

1) Primary prevention of the insult by adequate fetal monitoring and correct use of the partogram coupled with timely obstetric interventions. That should have an important impact on reducing both maternal and perinatal mortality and morbidity.

2) Secondary prevention after the insult by immediate resuscitation of the non-breathing baby.

3) Tertiary prevention of complications in the baby by adequate postnatal treatment.

A consequence of improved obstetric care may be an increase in neonatal mortality because babies that previously would have died during labour (FSB) might be born alive with hypoxic-ischemic insults. Similarly, improved resuscitation may hinder or delay neonatal deaths, but increase neonatal morbidity.

Neonatal mortality is defined as death before one month of age and recent global estimates range from 2.9 to 3.6 million deaths per year (4,10,14,15). Of these, 50-70 percent occur within the first day of life (4,16-20). The presumed causes of neonatal deaths have remained unchanged over the past decade and include infections (~ 30%), preterm birth (~ 30%), and birth asphyxia (~ 25%) (5,10,21,22). However, uncertainty surrounds these estimates due to an almost complete lack of reliable vital registration systems from settings where mortality is highest (15). Thus analyses are based on retrospective household surveys, and most cause specific data rely on verbal autopsy without consistent definitions and algorithms. Intrapartum-related deaths within the first 24 hours are likely under-reported or misclassified as stillbirths (9,15,23). Nevertheless, early neonatal mortality, especially within the first day
of life, is thought to contribute substantially to the overall neonatal mortality rates (15,18-20,23,24).

“BIRTH ASPHYXIA” AND INTRAPARTUM-RELATED DEATHS

Intrapartum hypoxia and the consequences of intrapartum fetal organ damage due to poor oxygenation is often equated with “birth asphyxia”. “Asphyxia” is based on the Greek word meaning “pulseless” and applies to a syndrome that combines hypoxia and metabolic acidosis. In 1997 the World Health Organisation broadly defined “birth asphyxia” as the clinical status of a newborn who “fails to initiate or maintain regular breathing at birth”. This definition does not imply a particular cause (e.g. intrapartum hypoxia); the baby may not breathe because of prematurity, meconium aspiration, intracranial, thoracic or neuromuscular diseases. Therefore, additional makers (e.g. Apgar score and fetal distress) have been used to indicate possible intrapartum hypoxia and acidosis. The most commonly used indicator to identify birth asphyxia in resourcelimited settings is 5 minute Apgar score < 7. The scoring is often done by the same person who has delivered the baby, and the total score includes several subjectively assessed variables (Table 1). Thus, Apgar scores may be an inaccurate and unreliable indicator of birth asphyxia. Furthermore, many babies with intrapartum hypoxic-ischemic injury are likely not reported or misclassified as FSB (15,23). Therefore, considerable uncertainty surrounds the “true” proportion of birth asphyxia related mortality.

Table 1 The Apgar Score

<table>
<thead>
<tr>
<th>SIGN</th>
<th>SCORE 0</th>
<th>SCORE 1</th>
<th>SCORE 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>Absent</td>
<td>&lt; 100/min</td>
<td>&gt; 100/min</td>
</tr>
<tr>
<td>Respiration</td>
<td>Absent</td>
<td>Weak</td>
<td>Good</td>
</tr>
<tr>
<td>Muscle Tone</td>
<td>Flaccid</td>
<td>Some</td>
<td>Good</td>
</tr>
<tr>
<td>Reflexes</td>
<td>No response</td>
<td>Grimace</td>
<td>Good</td>
</tr>
<tr>
<td>Colour</td>
<td>Pale/blue</td>
<td>Blue extremities</td>
<td>Pink</td>
</tr>
</tbody>
</table>

Finally, most cause-specific neonatal mortality data has been generated from studies in Asia (25-28), whereas there is a paucity of data from sub-Saharan Africa, the region with the highest neonatal mortality rates and least reduction per year (4,5,10,24).
Understanding the correct distribution and presumed causes of death, in settings with the highest burden, is critical before effective preventative strategies can be implemented. Many of the intrapartum-related deaths and the huge burden of ill-health are thought preventable with appropriate low-tech interventions, and simple learning programs. High-tech, hospital-based, specialist-driven neonatal care should not be required to meet much of the present challenge. Contrary, it is necessary to define appropriate low-tech interventions, and learning programs that can be implemented with high coverage and quality in urban and community settings where most of the deliveries take place.

**Fetal Heart Rate Assessment and Intrapartum-related Hypoxia**

Clearly efforts to meet MDG 4 by 2015 have to focus on reducing perinatal deaths, in particular deaths related to the day of birth. Of the three possible approaches outlined above, primary prevention of the insult is likely to have the greatest impact on intrapartum-related adverse outcome. The ability to detect the fetus at risk of hypoxia during labour is a key and critical catalyst for subsequent interventions to reduce deaths and improve child health. Simultaneously, the obstetrical actions taken are likely to improve the outcome of the mother as well.

Data from high-income countries suggest that fetal monitoring in conjunction with emergency obstetric care and targeted interventions has reduced perinatal mortality significantly (29-31). Continuous electronic FHR monitoring is the “gold standard” for identifying fetuses at high risk in the developed world (32-34), but this device is neither available nor feasible in resource limited settings where the burden is highest (35). Intermittent FHR monitoring with a fetal acoustic stethoscope (fetoscope) is the alternative and most frequent method in these areas (Photo 1), but evidence concerning reliability and efficacy is almost non-existent (36,37). Indeed, there is only one randomised trial comparing the effectiveness of different methods of FHR monitoring in a low-resourced country, indicating worse perinatal outcome when using the Pinard stethoscope (fetoscope) as compared to continuous cardiotocography (CTG) or intermittent hand-held Doppler ultrasound monitoring (38).
In a recent series on stillbirths the presence of skilled care at birth linked with emergency obstetric care was identified as two major components to reduce the number of stillbirths. Interestingly, the necessity or importance of FHR monitoring to detect the babies at highest risk for either intrapartum stillbirths or intrapartum-related neonatal death was not addressed (39,40). Additionally, there are several studies indicating that only a small proportion of birth attendants use the partogram effectively, and even fewer monitor the FHR adequately (41-43).

**Basic Neonatal Resuscitation**

Each year approximately 136 million babies are born globally. It is estimated that about 90 percent make the transition from intrauterine to extra-uterine life without any intervention (23,44,45). This successful transition is depending on several factors (e.g. the health of the mother, the pregnancy, and the labour process), and healthy fetuses are likely to tolerate some intrapartum hypoxia remarkably well. However, with severe or sustained lack of oxygen during labour progression to hypoxic-ischemic injury will occur and a non-breathing baby is born. Approximately, ten percent or 13.6 million newborns are delivered with absent or poor respiratory effort and need some degree of support to achieve cardiopulmonary stability. It is estimated that between three to six percent need assisted positive pressure ventilation, and less than one percent require advanced resuscitation including intubation, chest compressions, and medications (44). However, these estimates are based on five reports (44-48), none of which reflect Sub-Sahara Africa where the burden of perinatal deaths and morbidity is considered to be highest (4,5,23). Therefore, recently published global estimates on immediate postpartum neonatal needs and interventions are uncertain due to a paucity of data from low-and middle-income countries and almost a complete lack of reliable data from rural community-based settings.
CONSENSUS ON NEONATAL RESUSCITATION SCIENCE

The International Liaison Committee on Resuscitation (ILCOR) is committed to develop and publish consensus on resuscitation science every five years. The most recent Consensus on Science and Treatment Recommendations (CoSTR) statement was published in 2010 (49,50). The CoSTR document is used as a basis for developing specific resuscitation guidelines appropriate for implementation in respective countries.

Current CoSTR Neonatal Resuscitation Guideline suggests about 30–60 seconds of time following delivery should be allocated to assess spontaneous respiratory and heart activity before initiating intermittent positive-pressure ventilation if indicated (49,50) (Figure 1). Failure to initiate spontaneous respirations at birth in most cases is believed to be secondary to intrapartum hypoxia and the state of primary apnea (heart rate > 60 beats/minute with compensated blood pressure) (51). These infants invariably respond fairly promptly to early interventions like drying, stimulation, clearing the airways as indicated, as well as face mask ventilation (FMV) applied within the first minute (Figure 2). Delaying basic resuscitation in apneic infants is thought to result in a progressive decrease in heart rate and blood pressure (secondary apnea) and eventual death and/or brain injury in those who start gasping and/or breathing. If a baby is born in the state of secondary apnea or if it evolves after birth, it is more difficult to resuscitate and restore cardio-respiratory status (severe birth asphyxia). These assumptions are based on the experimental cardio-respiratory responses described in asphyxiated newborn monkeys (51). Scientific evidence from human beings is almost non-existing.

The guidelines for resuscitation of newborns is based on limited research with few cases and encloses several knowledge gaps (52,53). Therefore, defining the transitional changes at birth in the newborn is critical towards a better understanding of the problem of intrapartum-related hypoxia and the importance of basic interventions in the first minutes after birth.
Figure 1 Newborn Resuscitation Algorithm

1. Term gestation? Breathing or crying? Good tone?
   - No: Warm, open airway, dry, stimulate
   - Yes: Stay with mother

2. HR below 100, gasping, or apnea?
   - Yes: PPV, consider SPO$_2$ monitoring
   - No: Labored breathing or persistent cyanosis?
     - Yes: Consider SPO$_2$ monitoring, Consider CPAP
     - No:继续流程

3. HR below 100?
   - Yes: Ensure adequate ventilation
     Consider ET Intubation!
   - No: HR below 60?
     - Yes: Chest compressions
       Coordinate with PPV
     - No: HR below 60?
       - Yes: IV Epinephrine

4. Routine Care
   - Provide warmth
   - Assure open airway
   - Dry
   - Ongoing evaluation

5. Post-resuscitation care
**Figure 2** Cardio-respiratory changes in the asphyxiated monkey over time
Adapted from reference (51)

<table>
<thead>
<tr>
<th>$\text{PCO}_2$</th>
<th>45</th>
<th>100</th>
<th>150</th>
<th>200</th>
<th>40</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.3</td>
<td>7.0</td>
<td>6.8</td>
<td>6.75</td>
<td>7.1</td>
</tr>
</tbody>
</table>

**Graph:**
- **Gasps/min**
  - **Primary Apnea**
  - **Last Gasp**
  - **Secondary or Terminal Apnea**
  - **Onset of Gasping**

- **Beats/min**
  - **Heart Rate**

- **Blood Pressure**

- **Time from Onset of Asphyxia (min)**
THE “HELPING BABIES BREATHE” EDUCATIONAL PROGRAM

Helping Babies Breathe (HBB) is an evidence-based curriculum in basic neonatal care and resuscitation for use in resource limited areas (54). It is developed by the Global Implementation Task Force of the American Academy of Pediatrics in response to the need for an evidence-based, appropriate, and feasible training program in neonatal resuscitation to meet the challenges of MDG 4 (54,55). The scientific basis is the neonatal evidence evaluation of ILCOR.

The simulation-based educational program was developed to train large numbers of birth attendants in low-income countries using a cascade model. The objective of the project is “to ensure that all babies are born with a skilled birth attendant present” – a person who has the knowledge, skills, and competency to care for a newborn baby. The global curriculum is designed to be used by birth attendants who are responsible for the care of both the woman and the newborn infant at delivery, and who may not have assistance from a second trained helper. HBB is an intervention tool to ensure immediate assessment of the baby, temperature support, stimulation to breathe, and assisted ventilation as needed, all within "The Golden Minute®" after birth. These basic tenets of neonatal resuscitation coupled with appropriate available equipment should reduce FSB rates, neonatal mortality, and improve intact survival.

The educational kit includes an action plan, a culturally adopted flip-over facilitator guide, and a student workbook (Figure 3). The course material is largely pictorial with simple text. Though aimed at midwives, the curriculum can also be adapted for community health workers and even traditional birth attendants with limited literacy. The Action Plan is a pictorial guide with very few words to the evaluations, decisions, and actions that should be taken to help every baby. The colors signify the level of care – green for Routine Care needed by all babies. Yellow signifies the key concept of "The Golden Minute®" – the first minute after birth, when prompt action to stimulate breathing or begin ventilation is thought vital to prevent deaths and disability. Finally, the red zone indicates the need for more prolonged or advanced resuscitation. Supplemental oxygen, intubation, chest compressions, and medications do not enter the algorithm – these interventions or actions are not relevant in most resource-limited settings.
Figure 3 The HBB Course Material

Action Plan wall poster
Clinical Reminder wall poster
26 Flipcharts
Learner Workbook
To augment this program Laerdal Medical has developed a low-tech, low-cost neonatal simulator (NeoNatalie, Figure 4) for low resource areas and an affordable manual resuscitator and a bulb suction (that can be easily cleaned for reuse) to meet the training and clinical equipment needs (Figure 5). NeoNatalie enables the instructor to simulate the presence or absence of crying, breathing, and pulse by squeezing bulbs. No electricity or computers are needed. The mannequin is shipped collapsed, but filled with 2.5 liters of warm water it provide realistic weight, temperature, and tone that mimics a lifeless baby.

**Figure 4** NeoNatalie
Skills training and simulations using the simulator form the foundation of the course (Photos 2-6). All the way through participants work in pairs or teams using the simulator - together to help one another learn the skills – recognizing that they learn best when they are teaching. "The Golden Minute®" highlights the importance of immediate action and every participant has to practice and simulate until he/she masters every scenario in the course.

The HBB material and equipment should be left behind after a course. The majority of birth attendants do not manage non-breathing babies frequently. Therefore, it is believed that they need to re-train regularly using the simulator and the student workbook to retain knowledge, skills, and competency, although, studies on transfer of performance from a simulated setting to a similar clinical situation are almost non-existing.
Photo 2 Facilitator running with a non-breathing baby

Photo 3 The baby is not crying – the students dry and stimulate – still no breathing. The facilitator is squeezing the red balloon behind her back making a slow umbilical pulse

Photo 4 They take away the wet clothing and wrap the baby in dry clothing. The facilitator presents no breathing and a slow pulse….
Photo 5 The student recognizes no breathing and start ventilating the baby within the first minute. The helper feels for the pulse and taps the rate on the leg to show the provider. She struggles to ventilate correctly and the pulse decreases - she asks for help…..

Photo 6 … the helper manages to ventilate correctly and after some ventilations the heart rate increases. Finally the baby starts breathing and crying. The operator now squeezes the green balloons.
STATEMENT OF THE PROBLEM IN TANZANIA

In Tanzania, specific attempts have been made to address maternal, newborn and child health challenges through national health policies (Health Sector Reforms, Health Sector Strategic Plan 2003-2007, National Strategy for Growth and Reduction of Poverty, and Primary Health Services Development Program). Furthermore, the Reproductive and Child Health Strategy (2005-2010) and the National Road Map Strategic Plan to Accelerate the Reduction of Maternal, Newborn and Child Mortality 2008 - 2015 were also developed to respond to these challenges. “The Road Map” formulates adequate policies and plan interventions due to the perceived discrepancy between what exists and what is the planned situation, and aims to ensure improved coordination of interventions and delivery of services across the continuum of care (56). Existing neonatal initiatives are; Integrated Management of Childhood Illnesses, Essential Newborn Care, Care of the Low birth weight babies (Kangaroo Mother Care), and Life Saving Skills training for health workers providing care to antenatal, perinatal and postnatal women. The decline of under-five mortality has in part been attributed to these strategies, which is being rolled out countrywide by the Ministry and District Councils. Major support for these initiatives is derived from the Government and Council budgets. The Ministry of Health and Social Welfare (MHSW) clearly considers prevention of birth asphyxia related mortality and morbidity a major priority. Nevertheless, while there are several programs aimed at newborn resuscitation and care, it is also clear from a “Situation Analysis of Newborn Health in Tanzania” report published in 2009 (57), that the incidence of birth asphyxia related mortality has remained unchanged over the past 15 years, the number of “skilled providers” (formally approved) present at delivery has remained < 50%, and there is a global lack of essential basic resuscitation equipment. The “Situation Analysis of Newborn Health in Tanzania” (57) describes the magnitude and distribution of needs as well as available health resources. The neonatal mortality rate approximates 32/1000 live birth. A comparable number of fresh stillborn (FSB) (29/1000 live births) babies are also delivered annually, many of which may be wrongly classified stillbirths, i.e. non-breathing newborns with a heart activity at delivery.
THE MHSW RESPONSE TO THE BIRTH ASPHYXIA CRISES

The MHSW was optimistic that the HBB program would address the many needs described in the “Situation Analysis of Newborn Health in Tanzania”. They recognized the need to integrate HBB with the other existing newborn programs mentioned above to fill the critical void of birth asphyxia related mortality in the Tanzanian Health Care Program. Following a Request for Application processes in early 2009, the national implementation of HBB was initiated in September of 2009. Eight sites were selected by the MHSW to study the implementation process and the effects of the program through a before-after intervention design. One of the sites was Haydom Lutheran Hospital (HLH) in Northern Tanzania. To further investigate underlying research questions and knowledge gaps related to newborn resuscitation, several non-intervention epidemiologic observation studies (prospective descriptive and analytic open cohort studies) were initiated in August and November of 2009 at this site.

SUMMARY

The incidence of intrapartum-related stillbirths and neonatal deaths has remained essentially unchanged over the past 15 years despite efforts to intervene and meet MDG 4. Especially, the lack of impact on perinatal mortality rates the first day of life is a major concern. MDG 4 cannot be met without a substantial reduction in mortality within the first 24 hours after birth, and interventions and implementation strategies to target this gap is required.

Therefore, several observational studies in the delivery room linked to the national implementation and evaluation of the HBB program was initiated in Tanzania in 2009. The relevance, feasibility, political acceptance, applicability, and urgency of the present studies are classified as very good. There is no risk of duplication and good ethical acceptability.
OBJECTIVES AND HYPOTHESIS

The overall aim of this thesis was to document the value of intermittent FHR assessment (using a fetoscope) to predict intrapartum-related hypoxia, to define the proportion of newborns in need of basic resuscitation, and to assess the importance of the “Golden Minute®” after birth to determine the possible effects of the HBB program.

SPECIFIC OBJECTIVES

- To determine whether the routine detection of FHR abnormalities (using a fetoscope) would be associated with labour complications, an increased frequency of caesarean section, the need for basic resuscitation (stimulation, suction and/or FMV), a 5 minute Apgar score < 7, early neonatal morbidity or death, and stillbirth (antepartum or intrapartum) (Paper I)

- To describe the normal neonatal respiratory adaption at birth (Paper II)

- To document interventions by birth attendants in the delivery room, the proportion of newborns in need of basic life support, and the importance of basic interventions in the first minutes after birth in the prevention of cardiac collapse (Paper II)

- To evaluate the reliability of 5 Minute Apgar Score as an indicator of birth asphyxia (Paper III)

- To determine the presumed causes of neonatal death within the first 24 hours (Paper III)

Supplemental material: to determine whether implementation of the HBB educational and training program will enhance the basic skills of birth attendants, and thereby reduce the incidence of early neonatal mortality and the number of FSB (Appendix I)
SPECIFIC RESEARCH QUESTIONS

- If routinely detected FHR abnormalities (using a fetoscope) will identify compromised fetuses with increased risk for FMV, morbidity, early neonatal death, or intrapartum death (FSB) (Paper I)

- If the majority of babies with birth asphyxia are in primary apnea and will respond to early basic resuscitation (Paper II)

- If the estimated proportion of neonates in need of basic resuscitation and the estimated ratio of birth asphyxia related deaths are underestimated (Paper II and III)

HYPOTHESIS

Implementation of the HBB educational and training program in Tanzania will reduce the incidence of early neonatal mortality by 50% and the incidence of FSB by 25% (Paper II and III and Appendix I).
METHODS

The field of this research includes global environment, perinatal health, and clinical medicine. This specific PhD project is based on a scientific tradition of clinical and epidemiological research, and includes several non-intervention studies that are closely linked to the national HBB intervention study. The PhD candidate is the Principal Investigator of all ongoing non-intervention HBB related studies at HLH. The MHSW in Tanzania is responsible for the ongoing national HBB intervention study with Dr. Georgina Msemo (Newborn & Child Health Program Manager, MHSW) as Principal Investigator. The PhD candidate is responsible for HLH as one of eight sites in this multicenter study. The candidate has represented HLH in the national HBB Data Oversight Committee (DOC), contributed to the design of the national intervention study and the national data collection form. She has been responsible for data collection and processing at HLH, visited several of the other sites for quality control, and contributed in the writing of the manuscript still under consideration for publication. This manuscript is not yet official; therefore, to partly demonstrate the effects of the HBB intervention, a site specific presentation of HLH is attached as supplemental material (Appendix 1).

SETTING AND STUDY POPULATION

THE UNITED REPUBLIC OF TANZANIA

Tanganyika became independent form British colonial rule in 1961. In 1964 Tanganyika and Zanzibar joined to form the United Republic of Tanzania. It is a large country in East Africa, twice as large as France. The country is one of the 20 poorest countries in the world with a population of about 44 million and 36% living below one US dollar a day (58). The pressure on the social service is high with one of the lowest doctor to population ratio. Selected health indicators from WHO Global Health Observatory Data Repository are summarized in table 2(59).
Table 2 Selected health indicators for Tanzania

<table>
<thead>
<tr>
<th>Health Indicators</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of deliveries per year</td>
<td>1.5 millions</td>
</tr>
<tr>
<td>Population growth (%)</td>
<td>2.8</td>
</tr>
<tr>
<td>Population living in urban areas (%)</td>
<td>26</td>
</tr>
<tr>
<td>Total expenditure on health per capita (Intl $, 2009)</td>
<td>68</td>
</tr>
<tr>
<td>Life expectancy at birth male/female (years)</td>
<td>53/58</td>
</tr>
<tr>
<td>Births attended by a certified provider (%)</td>
<td>48</td>
</tr>
<tr>
<td>Maternal mortality (2010)</td>
<td>790/100 000</td>
</tr>
<tr>
<td>Under five mortality (2010)</td>
<td>76/1000</td>
</tr>
<tr>
<td>Infant mortality (2010)</td>
<td>50/1000</td>
</tr>
<tr>
<td>Neonatal mortality (2009)</td>
<td>32/1000</td>
</tr>
<tr>
<td>Fresh stillborn rate (2009)</td>
<td>29/1000</td>
</tr>
</tbody>
</table>

Description of the health system in Tanzania

The Government operates a decentralized health system, which broadly falls into three functional levels: District (Level I), Regional (Level II) and Referral hospitals (Level III). The District level I provides primary health care services through Dispensaries located at the ward level catering for 3-5 villages with an average population of 10,000. The Health Center is the referral level for the Dispensary and it provides a slightly broader range of services, including in-patient care and it is used to cover an average population of 50,000. Some Health Centers have been upgraded to provide comprehensive emergency obstetric care. District Hospitals provide services to an average of 250,000 people. Tanzania comprises of 126 districts. The Regional level II hospitals serve as a referral point for level I facilities and offer more specialized services and cater to a population of about 1,000,000 people. At the level III are the Referral and Specialized hospitals.

Levels of skilled birth attendants according to the functional level:
Level I: Nurse Midwife, Medical Officer, Clinical Officer, Maternal and Child Health Aid
Level II: Nursing Officer, Nurse Midwife, Medical Officer, Assistant Medical Officer
Level III: Specialists, Nursing Officer, Nurse Midwife, Medical Officer
Haydom Lutheran Hospital (Paper I-III and Appendix 1)

HLH is located in Northern Tanzania, 1700 meters above sea level on a highland plateau, at the Southern border of Mbulu district in Manyara region, 300 km west of Arusha, which is the nearest urban center. The infrastructure in Manyara is typically rural with gravel roads and a public transport system, but much of the population cannot afford this transport. It is large seasonal variations between dry and rainy seasons, which make the poor agricultural population vulnerable.

HLH is a Referral hospital (level II). The immediate catchment area, including about 500,000 people, consists of a smaller Lutheran Hospital, two governmental Health Centers (level I), 19 governmental Dispensaries (level I), and four dispensaries run by other religious voluntary agencies. Childbirths are conducted at all levels. The greater reference area covers about 2 million people, which is ethnically and geographically diverse, with all four main language groups of Sub-Saharan Africa represented (60). The area consists of four administrative divisions (Dongobesh, Haydom, Basotu, and Nduguti) in two different regions (Manyara and Singida). Both regions have governmental owned Regional hospital (level II) and one District hospital (level I) per district. All the health facilities in the reference area collaborate through the District Health Management Teams (in the respective districts) which in turn collaborate with the MHSW. HLH is part of this governmental network. The districts assist each other through ambulance, radio and telephone contact.

HLH is a 400-bed hospital owned by the Mbulu Diocese of the Evangelical Lutheran Church in Tanzania, and is fully incorporated in the national health plan under the MHSW (60). HLH is financed by donation from the Royal Norwegian Embassy in Tanzania, gifts, patient fees, and government funding through staff and bed grants. The hospital provides surgical, medical, gynecological, comprehensive emergency obstetric, and basic emergency newborn care. Since 2009, HLH has offered free transport service for delivering women with an increase in annual number of deliveries from 3000 in 2008 to 5000 in 2011.

No Specialists in Gynecology/Obstetrics or Pediatrics have been employed at the hospital during the study period. Maternity Ward has been covered by a Medical officer/doctor during day-time and one officer/doctor (Medical officer, Assistant Medical Officer, or Clinical Officer) on call evenings and nights, covering the entire hospital. Therefore, midwives largely conduct deliveries and newborn resuscitation if indicated, alone. Currently, there are
25 midwives employed at the maternity ward, but this number is constantly changing due to a high turnover of staff. The labour ward has eight delivery beds, and during day shifts, there might be three midwives present, but on evening and night shifts, there are only two midwives. In case of a caesarean section, one of them will leave for the theatre. After birth, infants requiring more than routine care are triaged to an adjacent neonatal area. This is a 10-m² room with one long bench, with the capability of providing intravenous fluids and antibiotics. The neonates are intermittently cared for by family members and the labor staff.

A retrospective analysis of perinatal outcome at HLH 1996 – 2002 reveals a macerated stillbirth (MSB) rate of 13.3, a FSB rate of 17.8, and early (one week) neonatal mortality of 22/1000 live births in 1996 (17). Standardized protocols of obstetric and neonatal care were introduced in 1998. In 2002, the MSB rate was 18.1, the FSB rate 9.9, and the early (one week) neonatal mortality was 15/1000 live births (17).

STUDY DESIGN

NON-INTERVENTION STUDIES AT HLH (PAPERS I - III)

STUDY UNIT AND SUBJECTS
Maternity Ward at HLH; all women in labor and their offspring admitted to HLH, as well as the health care staff.

EPIDEMIOLOGICAL OBSERVATION STUDIES
A comprehensive research infrastructure is established under the research protocol “Towards MDG 4&5 studies at HLH” which is an ongoing open (or dynamic) Cohort study. The prospective observational descriptive and analytic open cohort studies included in this PhD thesis (Figure 6) were initiated in August (Papers II) and November (Paper I and III) of 2009 (Figure 7). The inclusion of a baby is with the first FHR assessment during labor, and the end point is 24 hours after birth (Figure 6). Rough sample size calculations were performed for several variables to demonstrate significant differences between groups. We concluded that one year of data collection (approximately 5000 cases) should be sufficient.
Schematic presentation of the prospective observational descriptive and analytic open Cohort studies:

Observations by the research assistants:
Registration of FHR measurements and labor interventions

Observations by the research assistants:
Registration of newborn characteristics and Time interval to initiation of spontaneous respirations

If resuscitation is attempted:
Stimulation, suction, heart activity, FMV, and the time periods from birth to start of breathing or start of FMV, and the time period of applied FMV are noted

Figure 6 Timeline and data collection from inclusion of a baby to the endpoint 24 hours after birth. FHR = fetal heart rate, FMV = face mask ventilation
**Figure 7** Presentation of Helping Babies Breathe (HBB) implementation and the different time periods of data collection at Haydom Lutheran Hospital

### Timeline

- **2009**
  - July: Training of Research Assistants and start of observation in the delivery room, mid July
  - August: Start of Data collection for Paper II

- **November 2010**
  - Start of Data collection for Paper I and III

- **April**
  - Start of Baseline data collection for the national HBB study and Supplemental material

- **First HBB course; 50% of the staff was trained and no local HBB implementation factors were introduced**
  - Start of After intervention data collection for the national HBB study

- **November 2011**
  - End of Data collection for Paper II and III

- **First HBB re-training: including the entire staff**
  - Introduction of the “HBB program” including several local implementation factors
  - Start of After intervention data collection presented in Supplemental material

- **2012**
  - January: End of Data collection for Paper I
  - February: End of Data collection for Supplemental material
  - April: End of Data collection for the National HBB study
HBB INTERVENTION STUDY (REPRESENTED AS APPENDIX 1)

STUDY UNITS

The MHSW selected eight research sites to monitor and evaluate the implementation and impact of the HBB program (Figure 8); three Referral University Affiliated Hospitals (Muhimbili, Kilimanjaro Christian Medical Centre, and Bugando) serving a predominantly urban population, four Regional Hospitals linked to the three Referral Hospitals (Amana, Buguruni, Mawenzi, and Sekotoure) serving people from the suburbs, and finally HLH serving a predominantly inborn rural population.

Figure 8 Map of Tanzania with the eight research sites

All the designated research sites had a corresponding institution with a teaching history as well as research activities including involvement with multicenter studies. Hence computerized data processing and analysis could be done successfully by trained staff.

IMPLEMENTATION OF HBB

The implementation of the simulation-based HBB educational program is based on a “train the trainees” cascade model. HBB was launched in September of 2009 with two days training of 40 master instructors selected from four referral and several regional hospitals. The overall aim is to train the national workforce; 1332 regional/zonal instructors and over 10,000 health providers within 2013. Instructors and trained providers should continue to provide on job and refresher training to other health providers in the facilities where they are working. Since midwives attend most deliveries great emphasis has been put on their training. While
the initial training of the master instructors was conducted in English, the training for other levels were/will be bilingual; i.e. in both English and Swahili. The global lack of basic resuscitation equipment represents a major barrier to reducing birth asphyxia related mortality. Therefore, appropriate equipment such as manual resuscitators and suction devices, have been and will be made available in every health care facility in concurrence with the HBB program. A Steering Committee was established to monitor the National HBB implementation process.

**QUASIEXPERIMENTAL EVALUATION OF HBB**

This quasiexperimental study (without randomization) involved a structured, simulation-based improvement intervention (HBB), designed to be scaled up at country level. A prospective before/after HBB intervention design has been used to evaluate potential impact of HBB. The baseline period (to serve as the control group) was decided to be two months prior to HBB at each site in the national HBB study. The baseline collection was initiated at different dates at each site according to when it was suitable to conduct HBB trainings. The baseline period at HLH started February 15th of 2010, and the first HBB course was held by trained Tanzanian master instructors 15th-16th of April 2010 (Figure 7). Less than half of the staff at maternity ward was able to attain this training and no local HBB implementation factors was initiated. The lack of impact was recognised at the bi-annual DOC meeting with following organisation of a period of HBB (re-)trainings, conducted by a Tanzanian master instructor, almost one year later – in February/March of 2011 (Figure 7). At this time the entire staff was trained, including the management at Maternity Ward, four strategic midwives at HL were selected as “HBB nurses” and trained as HBB regional instructors, HBB educational materials (Figure 3-5) was left behind, and several HBB implementation factors were introduced; i.e. regular “low-dose high-frequency” simulation training with NeoNatalie in the labor ward, HBB action-posters on the walls where resuscitations are taking place, and steady equipment supply. All these implementation strategies will be referred to as the “HBB program” in contrast to a single HBB course.

Specific sample size and statistical power calculations for HLH (using descriptive observational baseline data from HLH with a neonatal mortality of 11/1000 live births and 16/1000 FSB) revealed less than 5000 cases needed in each group (before and after intervention) to detect a 50% reduction in neonatal deaths (significance level = 0.05 and
power = 80 percent). Almost 10000 deliveries were required in each group to detect a 25% reduction in FSB. Therefore, to show a significant change at HLH, separated from the other sites, one year of baseline collection was required for neonatal mortality and two years for FSB.

**DATA COLLECTION**

**DATA COLLECTION AND MANAGEMENT AT HLH (PAPER I-III)**

The research period included in this thesis is from August of 2009 through December of 2011 (Figure 7). In this period the research assistants/observers (n=16) have been continuously present in the labour ward and observed every delivery and newborn and the routine practice given by health care staff in the delivery room as well as in the neonatal area. The observers have worked in three shifts over 24 hours. Three observers have covered each shift to support and help each other; two have been located in the labour ward or in the theatre; the third, in the adjacent neonatal area. Observations were timed using a standardized stop watch, and the quantitative findings were recorded on the “HBB Data Collection Form” (Appendix 2) during and immediately following the delivery. This form includes all the core variables in the “National Data Collection Form” (Appendix 3) with additional observational variables like FHR assessments and time intervals. The research assistants also reviewed the partograms that were filled out by the birth attendants and/or the responsible midwives. The indicators of the variables are described in a Standard Operating Procedure (Appendix 4). All variables are clearly defined. Data collection for the observation studies started six months prior to the onset of the national HBB baseline collection at HLH (Figure 7).

The local research manager, Estomih Mduma (EM), reviewed the data collection forms on a daily basis for quality control issues. If missing information or inconsistency the responsible research assistant was asked to clarify. This was an opportunity to re-train the assistant and sort out potentially misunderstandings. The pre-categorized data was double entered in EpiData 3.1 (EpiData Association, Odense, Denmark) by two different trained data clerks. Random crosschecks of the entered data were undertaken intermittently, with double data extraction and data entry of all cases. If there was any discrepancy between the two entered databases, the data entering individuals rechecked the original data (the source document) together and correct where necessary. The raw data is securely stored in cabinets at HLH.
Copy of the raw data was regularly sent to the PhD candidate (HLE) for further cleaning, analysis, and interpretation.

All the research assistants have been selected by the research manager (EM) at HLH. They are female Tanzanian, have accomplished secondary school, and live in the area around Haydom. The research assistants were carefully trained over two weeks by EM in the background of the research, the indicators and definition of the variables in the “HBB Data Collection Form”, the observation technique, how to use the stop watch, and how to behave and not interfere in the delivery room. Pre-test of the research procedure and instruments was undertaken in the delivery room for another two weeks (Figure 7). The data from this period is not included in the studies. The health care staff at Maternity Ward was also thoroughly informed about the study. Through the research period the assistants were continuously supervised and re-trained by EM and HLE.

HBB INTERVENTION STUDY (REPRESENTED AS APPENDIX 1)

The “National Data Collection Form” (Appendix 3) was developed by the DOC and includes only necessary core variables to make the form very user friendly. At HLH research assistants have observed and registered the data (Figure 6 and Appendix 2). After quality control and data entering (see above) copies were sent to the PhD candidate (HLE) for further cleaning. HLE prepared the preformed National HBB Excel sheet (including the national HBB core variables) and transferred the data on a monthly basis to a central repository in the MHSW in Dar es Salaam.

At the other seven sites in the National HBB study midwives have reported all deliveries on the “National Data Collection Form” (Appendix 3). One or two “HBB nurses” at each site was/were trained in data entry into the preformed National HBB Excel sheet and responsible to enter the (mostly) pre-categorized data on a weekly basis. For this purpose a computer was placed in or close to every labor ward; dedicated for data entry and subsequent transmission of data to the central repository in the MHSW. The Principal Investigator Dr Georgina Msemo performed quality control checks regarding completeness and internal consistency and communicated with the “HBB nurse/s” on site if data were missing or inconsistent. Preliminary analysis for data presentation at the DOC meeting and random crosschecks of entered data at the primary sites have been undertaken every six months.
DATA ANALYSIS AND STATISTICS

Analysis has been performed using Statistical Package for Social Sciences (SPSS) 17, and includes descriptive statistics, chi-square calculations, fisher's exact test, independent-samples t-tests, and multiple logistic modelling. All data are presented as mean ± standard deviation unless as otherwise stated.

ETHICAL CONSIDERATIONS

The national implementation and evaluation of HBB is approved by the National Institute for Medical Research in Tanzania. The more detailed data collection at HLH is covered by a NIMR approval of the “Towards MDG 4&5 studies at Haydom Lutheran Hospital”.

The Regional Committee for Medical and Health Research Ethics, Western Norway considers the project “The Helping Babies Breath Program - evaluation of the educational material, the dissemination cascade model, and the effects of simulation training on management strategies and skill retention among health care workers in Tanzania” - reference number 2009/302 - to be an educational program among certified health care workers and a evaluation of the program. Formal approval from Norwegian ethical committee is thus not required. The study is approved by the representative (Privacy Ombudsman) of the Norwegian Social Science Data Service at Stavanger University Hospital (internal id: ID250).

Oral consent was not required and not obtained.

The observation is directed towards health care workers and not patients. There are no individual level interventions and no expected harm from the observation for the patients or the health care workers. Anyway, data related to health staff performance was recorded anonymous to not inflict any harm. Data is collected without possible identification of the patient and without interfering with the treatment or patient outcome. De-identified raw data is securely stored at HLH, separated from the identification key. Copies of the data have been sent to Norway for quality control, analysis and interpretation. Overall, the study seems to be well accepted among birth attendance and mothers.

There are several potential benefits of this research. First, there is an increased survival of neonates born at the study sites. Second, there has been a local capacity building due to advanced research projects and increased local competence in the area of natal and antenatal
care. Finally, knowledge gaps on neonatal resuscitation are filled with potential impact on international guidelines, educational strategies, clinical practice, and neonatal outcome globally.

MAIN FINDINGS

THE VALUE OF INTERMITTENT FHR ASSESSMENT TO PREDICT INTRAPARTUM-RELATED HYPOXIA

Paper I includes 10271 infants born at HLH November 2009 through December 2011, and documents that an intermittently detected abnormal FHR is strongly associated with labour complications, risk of intrapartum stillbirth (FSB), newborn need for FMV, longer duration of FMV, morbidity, and early neonatal death (Figure 9). A non detected FHR was a powerful predictor of a subsequent stillbirth with the probability of a true stillbirth found to be 0.95.

FHR was abnormal (i.e. <120 or >160 beats/minute) in 2.7 percent and absent in 1.9 percent of the fetuses. One third of the intrapartum-related stillbirths were found to have either an abnormal or normal FHR, and many of the intrapartum-related deaths were associated with labour complications, thus potentially preventable with appropriate obstetric care (Figure 9). Conversely, almost 75% of the babies that either died or were admitted to the neonatal area had a normal FHR record.

THE NORMAL NEONATAL RESPIRATORY ADAPTION AT BIRTH

Of the liveborn babies at HLH almost 84 percent initiated spontaneous respirations and did not require any intervention (Paper II). The majority (93%) started breathing within 30 seconds, and 99.3 percent were breathing spontaneously within one minute after birth. The mean time to spontaneous respirations was 10.2 second (median 5.0 second).
**NEWBORNS IN NEED OF BASIC RESUSCITATION**

At HLH, observed basic resuscitation, i.e. specific stimulation of the back, suction and/or face mask ventilation (FMV) was attempted in 942/5845 (16%) infants from August 2009 through October of 2010 (Paper II). Approximately 50 percent of these infants initiated breathing after stimulation and/or suctioning only, and the remaining infants (8%) received FMV. Thus, the majority of babies with birth asphyxia, i.e. failure to initiate spontaneous respirations and/or 5 minutes Apgar score < 7, were in primary apnea and did respond to early basic resuscitation within 3-4 minutes. More than 90 percent of the babies accomplished the transition from intrauterine to extra-uterine environment spontaneously or with the basic steps of stabilization including drying and stimulation to initiate breathing (Figure 9).

**THE IMPORTANCE OF THE “GOLDEN MINUTE®” AFTER BIRTH**

The data in Paper II documents a significant relationship between a delay in the initiation of FMV and early neonatal death and morbidity (Figure 9). Specifically the risk for early death and morbidity increases 16 per cent for every 30 seconds delay in initiation of FMV up to six minutes when adjusted for BW, GA, pregnancy, and labor complications. The mean time from birth to application of FMV in infants who died or who were admitted to the neonatal area was 100 ± 92 seconds as opposed to infants with normal outcome 79 ± 55 second (p = 0.035).

**THE PRESUMED CAUSES OF NEONATAL DEATH WITHIN THE FIRST 24 HOURS**

Paper III reveals that over 60 percent of early (24 hours) neonatal deaths at HLH are related to birth asphyxia and failure to initiate spontaneous respirations. Other causes of deaths are prematurity (18%), low birth weight (8%), congenital abnormalities (8%), and infection (2%). The remaining 2 percent is unclear. Of the asphyxiated infants who died at HLH 47 percent had a 5-minute Apgar score < 7.
Figure 9 Pathway of Intrapartum-related hypoxia and appropriate interventions to avoid fetal injury and prevent perinatal morbidity and mortality

Onset of labor

- Intermittent FHR monitoring
- Abnormal FHR - take actions to accelerate delivery

Absent FHR

Be prepared at BIRTH

Absent Breathing

- Primary Apnea
  - Immediate Drying + Stimulation ± Suction

- Secondary Apnea
  - Delayed Intervention
  - Immediate Drying + Stimulation ± Suction + FMV within the “Golden Minute®”

Spontaneous Breathing

Severe Birth Asphyxia

- Early Death

Hypoxic-Ischemic Encephalopathy

Antepartum death

True FSB

Early death - Missclassified FSB

FHR = Fetal Heart Rate, FSB = Fresh Stillbirth, FMV = Face Mask Ventilation
Effects of the HBB Program – Supplementary Material

Appendix 1 presents data on 4876 births prior and 4734 births following full HBB implementation at HLH (Figure 7). Providers trained in HBB who performed newborn resuscitation increased from 68 to 91 percent following full implementation and utilization of the “train the trainers” cascade. The percentage of newborns who were stimulated increased from 14 to 16 percent with a concurrent decrease in the use of FMV from 7.2 to 5.7 percent. The data demonstrates an almost 40 percent reduction in early neonatal deaths within the first 24 hours from 11.1/1000 to 7.2/1000 live births and a non-significant decline in FSB from 16.0/1000 to 14.4/1000 live births.

Discussion

This PhD project builds on Philosophy of biology and the tradition of scientific realism, claiming that science aims at truth and that one ought to regard scientific theories as approximately true or likely true. The scientific reasoning (context of justification) relies on the notion of “induction”, allowing one to formulate a general truth from specific observations in a population. A major weakness is that all observations are subjective and not fully representing the truth. There is an ongoing debate to justify the theory of induction.

Study Design, Biases, and Validity

Two broad types of error afflicts epidemiologic studies; random and systematic errors. Random errors can be corrected for by appropriate (large) sample size and statistical methods. Systematic error is referred to as bias and cannot be corrected for by sample size or statistical methods – these threats to validity should be eliminated as far as possible through appropriate study design and selection of study units/subjects.

Study Design

The non-intervention observational open Cohort studies at HLH (Papers I – III) involved a systematic collection and presentation of data to give clear quantitative descriptive pictures of the situation, combined with analytic attempts to establish causes and risk factors for certain problems. In these open (or dynamic) Cohort studies new babies (cases/study subjects) were
included as time passed and followed over a period of time to compare the occurrence of problems and determine whether a greater proportion of those with risk factors were affected. The study subjects (the babies) were included at a specified event (the first HFR assessment) and followed with the same intensity (Figure 6). A prospective descriptive/analytic open cohort study was preferred over a retrospective case control study to be able to establish causal relationships. Causality is the relationship between a cause, or a set of causes, and an effect, where the effect is a consequence of the cause/s. In papers I – III causality is assessed through multiple logistic regression modelling.

Due to clinical experiences over the years, animal experiments, and some human research international guidelines for FHR monitoring and newborn resuscitation are well-established. Therefore, we found it unethical to set up a randomised controlled trial to answer the pre-identified knowledge gaps and study questions. A 24 hours observational descriptive/analytic study in a setting with limited resources, a study population at high risk, and sub-optimal care had the potential to describe many of the knowledge gaps.

The quasiexperimental HBB intervention study in Tanzania (Represented as Appendix 1) used a before-after design to test the effect/s of HBB implementation (the experiment) on perinatal outcome (dependent variable). A quasiexperimental study always includes manipulation but misses at least one of the two other characteristics in a “true” experimental study; a control group or randomization which eliminates the effect of confounding variables. Due to existing knowledge and international guidelines on newborn resuscitation the MHSW found it unethically to set up a true experimental study – a randomised controlled trial. Since the HBB study is not randomized it cannot actually prove causation.

**Selection bias**

Selection bias is a systematic error that stems from the selection of study units/subjects and factors that may influence these units/subjects which do not influence non-participants (61). Bias in sampling leads to distortions in the results and reduces the generalization.

Every baby born at HLH in the study period has been included in the prospective open Cohort studies (Papers I – III). There are no missing cases, drop out, or seasonal bias, and the sample sizes are large. The problem related to these studies is that the women who tend to deliver at HLH may differ systematically from women who deliver at home or in other facilities. A
survey of facilities providing obstetric services (n=129) in six districts in Northern Tanzania reveals a low number of basic emergency obstetric care units, a relatively high number of comprehensive emergency obstetric care units (4.6/500,000), and several voluntary agencies and private for-profit facilities in the region (62). Therefore, 57% of the expected deliveries in the Mbulu district take place in a facility. This is higher compared to other rural areas in Tanzania (63). Women in this region tend to deliver at comprehensive emergency obstetric care facilities and voluntary agencies like HLH, indicating that they are willing to travel long distances for adequate care (62). Additional, the free ambulance service at HLH has enabled all categories of women to reach the hospital. On the other hand, women tend to arrive late because of the free transport. They try to deliver at home, relying on the ambulance service if complications occur. If the population of women who deliver at HLH represents a selection bias, is difficult to say. There might be a predominance of primigravida and potentially complicated deliveries. Nonetheless, it is unlikely that risk factors during labor associated with perinatal outcomes should be different among these women compared to non-participants. Therefore, we consider the external validity of the studies as high.

The MHSW selected eight research sites to monitor and evaluate implementation and impact of the HBB program for a national scale. The sites were selected to ensure that most levels in their health system were represented, but their main focus was to demonstrate potential impact at Level III and II hospitals as a model to follow. Another selection criterion was the ability to process good quality data to minimize information bias, i.e. all the designated research sites had a corresponding institution with a teaching history as well as research activities including involvement with multicenter studies. As a consequence, the gathered data do not fully represent health care workers at Level I including health centers and dispensaries. On the other hand, migration of health care staff in Tanzania is very high, allocating between the different health levels. Further, perinatal mortality was high and had remained unchanged for many years at the Level III hospitals before HBB implementation. These two factors suggest that the positive impact of HBB may extend nationally, particularly since a basic intervention such as stimulation appears to be the important factor in reducing newborn mortality. HLH is considered to be representative of regional/referral Level II-III voluntary faith-based hospitals in rural areas with a poor population. The baseline figures at
HLH were low compared to the other study sites and the national estimates (60), therefore a significant reduction in neonatal mortality at this site is especially promising (Appendix 1).

**INFORMATION BIAS**

Bias in information collection (improper data collection techniques or tools) is a distortion in the gathered data making it not representative of the true situation (61).

At HLH, it is possible that the presence of the research assistants may have influenced performance of the providers (Hawthorne effect). Data presented in Paper II are collected from the onset of observations in August 2009 and describes a high average proportion of babies being stimulated (16%) and ventilated (8%) in the period up to November of 2010 (Figure 7). The use of stimulation and FMV is especially high during the first three months of observations – then declining. Thus, the average percentage of babies being stimulated and ventilated from November 2009 up to November 2010 is 13 and 6.5 percent respectively (Paper III). This observed change in behavior among the group under study (the health providers) may be due to the fact that they were observed.

The observers were in general very unobtrusive and not allowed to influence provider management. Nevertheless, to reduce a possible Hawthorne effect, we included an adaptation time of six months for the provider to get used to being observed, before onset of baseline registration related to the national HBB intervention study. We do not consider any effect of the observation on perinatal characteristics and associations between risk factors and perinatal outcome (Papers I – III).

It was a great concern to make the data collection forms (Appendix 2 and 3) as short and user friendly as possible to reduce information errors. A simple everyday language was applied with predefined (mostly) categorical options. Anyway, misclassifications could occur by the midwives reporting the births attended by themselves (participatory research), but also by the nonparticipant observers at HLH who did not have a medical background. To minimize this kind of systematic error at HLH; comprehensive training and pre-testing were undertaken prior to implementation, all data went through strict quality control for missing cases and obvious inconsistency, with consistent and frequent feedback, supervision, re-training of the data collectors, and repeated information about the objectives of the study. Importantly, the
trend of reported performance in the delivery room with related outcomes pre/post HBB is similar at HLH and the other sites.

We consider particularly two of the variables included in these studies to be somewhat unreliable. The Apgar scores were subjectively assessed by the midwives, making the overall definition of birth asphyxia (5 minute Apgar score < 7) less precise. The assessment of GA varied greatly, thus making the overall definition of prematurity (GA < 37 weeks) imprecise.

CONFOUNDING

A central problem in all non-experimental research is little control over possible confounding factors that can create bias and mask cause and effect relationships, or suggest correlations where there are none. In epidemiological studies and quasiexperimental studies without randomisation it is impossible to fully control for confounding variables. In the analytic cohort studies at HLH possible unknown confounding factors were tested and adjusted for through logistic regression modeling (Paper I – III). Nevertheless, one confounding factor could be an uncertain accessibility of equipment; bulb suction and neonatal resuscitator. If these devices were missing or not functioning newborn resuscitation (and thereby neonatal outcome) would be affected. The MHSW was responsible for adequate equipment supply to all sites.

RANDOM ERRORS, CHANCE, SAMPLE SIZE, AND STATISTICS

Random errors are variability in the data that we cannot readily explain. Statistics plays two main roles in the analysis of epidemiologic data; 1) to assess variability in the data to distinguish chance from findings that might be replicated if the study is repeated, and 2) to estimate effects after correcting for biases such as confounding (61).

Testing of the null hypothesis in the supplemental material from HLH was done by use of simple chi-square calculations. The commonly used statistical significance level $p < 0.05$, tells nothing more than whether the $p$ value is less than the numerical value, but typically, if an analysis gives a result that is statistically significant, the null hypothesis is rejected as false. Conversely, if a result is not statistically significant it means that the null hypothesis is correct. Decisively, no data analysis can determine definitely whether the null hypothesis is true or false even with appropriate sample size (to prevent type I and II errors; to falsely refusing or accepting the null-hypothesis respectively). All the studies included in this thesis
have large sample sizes, and several statistically significant findings when comparing different subgroups within the data set. It is important to remember that the given quantitative p values confounds two main aspects of the data; 1) the strength of relation between exposure and disease, and 2) the precision with which that relation is measured (61). Actually, estimation of confidence intervals will express both strength of relation (effect/s) and precision in epidemiologic data more correctly, and interpretation should consider the general width and location of an interval. In causal research, such as paper I, multivariate regression models are commonly used to evaluate associations of one or more factors, and simultaneously control for possible confounding effects of other factors.

All the studies at HLH involved a complete sample with no missing cases, enabling extensive use of descriptive statistics (Papers I – III).

To show any effect of HBB implementation at HLH separated from the other sites, one year of baseline data was required to detect a significant reduction in early neonatal deaths (Figure 7). The baseline period for the HBB intervention study at HLH was initiated, after an adaptation time to minimize Hawthorne effect, in February 2010 – two months prior to the first HBB course. Data reported to the DOC meeting revealed a lack of impact after this single HBB course conducted in April of 2010. Therefore, new comprehensive HBB trainings and introduction of the “HBB program” were organized in February/March 2011. We consider the period from February 2010 up to implementation of the “HBB program” one year later, as a proper baseline period to compare changes pre/post HBB implementation at this site (Appendix 1).

**Main Findings**

The included studies are important because it for the first time give accurate observational data on 1) the value of intermittent FHR assessments for the prevention of adverse perinatal outcome and anticipation of required FMV at birth, 2) the normal respiratory adaption of infants at birth, 3) the need for basic resuscitation interventions in a poor African country, 4) the importance of the first minutes after birth to stabilize depressed newborn babies and prevent cardiac collapse, and included as supplemental material 5) the effects of the HBB program on provider performance and perinatal outcome.
THE VALUE OF INTERMITTENT FHR ASSESSMENT TO PREDICT INTRA-PARTUM RELATED HYPOXIA

Paper I demonstrates the value of routinely performed intermittent FHR monitoring during labor using a fetal stethoscope for the detection of the fetus at risk for FMB, birth asphyxia, early neonatal death or morbidity, and FSB in a resource limited setting (Figure 9). This supports the well-established thesis that an abnormal FHR is an important indicator of fetal compromise. Moreover, the findings indicate a significant association between an abnormal FHR and labor complications. The results presented in Paper I clearly show the value of intermittent FHR auscultation, even when using an obsolete fetoscope, as a most important fetal measurement to guide the process of delivery (early transport or advanced local care) in the prevention of FSB and birth asphyxia (Figure 9).

THE NORMAL NEONATAL RESPIRATORY ADAPATION AT BIRTH

Paper II describes the natural transitional respiratory adaption of newborn babies in a rural setting. There are some newborn infants in this dataset that would have been resuscitated in a typically high-tech hospital due to delayed onset of breathing, but the number is limited and does not affect the descriptive statistics very much. Therefore, the findings can provide supportive evidence of the current ILCOR Guidelines on Newborn Resuscitation (Figure 1) which suggests a need for positive-pressure ventilation if spontaneous respirations has not started within 30 seconds after birth (49,50).

THE AMOUNT OF NEONATALS IN NEED OF BASIC RESUSCITATION

According to our data (Papers II and III) the proportion of neonates in need of basic stabilisation (stimulation and/or suction) is much higher than estimated global numbers (23,44,45), but comparable to recent findings obtained from a district setting in Zambia (64). The findings (Papers II and III) also suggest that the proportion of birth asphyxia related deaths in this most vulnerable setting, is much higher than hitherto described. Birth asphyxia has for a long time been estimated to account for approximately 25 percent of neonatal mortality worldwide (5,10,21,22). In paper III we propose that this huge discrepancy is due to the imprecise definition of Apgar score, often used as an indicator to identify birth asphyxia. Approximately 50 percent of the “asphyxiated infants” were assigned a 5-minute Apgar score < 7 at HLH (Paper III), which supports a long held notion that the Apgar score is an inaccurate and unreliable indicator of birth asphyxia.
THE IMPORTANCE OF THE “GOLDEN MINUTE®” AFTER BIRTH

Paper II reveals that 84 percent of neonates initiated spontaneous respirations within the “Golden Minute®” without any interventions. Among non-breathing neonates there was a significant relationship between a delay in the initiation of FMV and admission to the neonatal area (morbidity) and/or death (Figure 9). Specifically the risk for death and morbidity increased 16 percent for every 30 seconds delay in initiation of FMV up to six minutes, and more than two thirds of the deaths occurred when ventilation was administered beyond four minutes. Over 90 percent of babies accomplished the transition from intrauterine to extra-uterine environment spontaneously or with the immediate basic steps of stabilization (drying, stimulation and/or suction) (Papers II and III). Figure 9 shows the potential outcomes in a non-breathing infant at birth. Infants in primary apnea would in general respond to drying and stimulation only. If intervention is delayed there will be progression to secondary apnea, and with no intervention there will be progression to death or an “apparent FSB”. We found that infants born in secondary apnea responded, in most cases, to drying, stimulation, and early application of FMV with the onset of spontaneous breathing. Only a few neonates required supplemental oxygen, endotracheal intubation or chest compressions. A small minority responded more slowly (longer duration of FMV) and initiated spontaneous respirations, but most likely with a progression to a state of hypoxic-ischemic encephalopathy. Another group did show initial signs of life but died within 24 hours. These findings are consistent with the cardio-respiratory responses to asphyxia characterized in the newborn monkey with induced hypoxia presented in Figure 2 (51); during the initial minute/s with apnea heart rate was greater than 60 beats per minute and blood pressure was still compensated – a state referred to as primary apnea. With intervention at this stage, and relief of the asphyxial process, there was an immediate increase in heart rate and blood pressure with initiation of spontaneous respirations. However, if there were no interventions and the asphyxial process was allowed to continue there was progressive bradycardia and hypotension with final gasping (after approximately four to five minutes) before secondary apnea developed. Once this state evolved it became more difficult to resuscitate and restore cardio-respiratory status (similar to severe birth asphyxia). Our findings from a poor setting (Papers II and III) indicate that most non breathing babies at birth are in primary apnea and will respond to the basic steps of stimulation and/or suction within the first minute after birth (Figure 9). Delaying resuscitation, even for brief periods, drives the process towards
secondary apnea which makes it more difficult to effectively restore cardio-respiratory function. A smaller proportion of newborns are in secondary apnea at birth and depending on the severity of intrapartum-related hypoxia, these babies will respond variably to the above described immediate actions and FMV (Figure 9). If no/delayed interventions are provided the baby will most likely die or develop hypoxic-ischemic encephalopathy.

THE EFFECTS OF THE HBB PROGRAM

The analysis following one year of full HBB implementation at HLH (Supplemental material – Appendix 1) demonstrate increased use of stimulation with a concomitant decrease in the use of FMV, and an almost 40 percent reduction in early neonatal deaths within the first 24 hours. The significant reduction in neonatal mortality likely reflects the increase in immediate stimulation of babies with the induction of spontaneous breathing among newborns in primary apnea, reversing the asphyxial process and preventing the need for FMV (Figure 9).

At HLH half of the health care staff at Maternity were trained in HBB April of 2010, and 67 percent of resuscitated babies were resuscitated by a provider who had attended the course. However, in April 2010 no local implementation factors described as the “HBB program” were introduced, and “after intervention data” reported to the DOC did not demonstrate changes in provider performance or perinatal outcome after this first HBB course.

Conversely, after the first period of re-trainings (February/March 2011), including all health care providers at Maternity ward and introduction of local implementation factors to facilitate sustainability, significant changes were detected (Appendix 1). The following year almost 91 percent of babies were resuscitated by providers trained in HBB with regularly short refresher trainings in the delivery room. The decline from 100 to an average of 90 percent trained HBB providers reflects the rapid turnover of staff in Tanzania and thus the need for regularly refresher trainings to ensure sustainability.

The reported decrease in FSB at HLH is not statistically significant; consistent with the power calculation this might be a type II error (see above). The observed decline in “apparent FSB” is most likely due to previous misclassification of liveborn infants without obvious signs of life (secondary apnea), not timely and correctly stimulated (Figure 9). This phenomenon has been suggested in other reports as well (65).
The findings at HLH – representative of the national findings – are compelling when viewed in the context of the prior long history of an unchanged neonatal mortality rate in Tanzania despite newborn resuscitation training (57). We believe much of the success can be explained by the “Utstein Formula of Survival” which states that patient outcome is a product of medical science, educational efficiency, and implementation (Figure 10). It is predicted that all factors in the formula contribute equally to patient outcome. Hypothetically, if all the factors are optimal, patient survival would be 100 percent; 1 x 1 x 1 = 1 (66). There can be good medical evidence, but often it is difficult to implement in our daily clinical practice. The data in this PhD supports the current ILCOR guidelines for neonatal resuscitation (the medical science). We consider the educational efficiency of the HBB course as very good. The simple and practical hands-on simulation based HBB training with main focus on the importance of the “Golden Minute®” is one critical factor for the success.

![Figure 10 The Utstein Formula of Survival](image)

However, site specific data from HLH (Appendix 1) suggests that several additional strategies for implementation are equally important:
1) MHSW commitment to the prevention of birth asphyxia and reducing early neonatal mortality nationally, thus a commitment to follow-up
2) Appointment of a Pediatrician within the Ministry as the leader to oversee the implementation and follow-up when required (as happened at HLH)
3) Bi-annual DOC meetings with involvement of personnel including physicians and midwives from all sites were conducted in Dar es Salaam where the implementation process was examined in detail and specific needs were revealed
4) HBB training was targeted at the midwife, most likely the single provider to stabilize and/or resuscitate a newly born infant
5) Use of the cascade model to continually train all providers
6) Selection of dedicated HBB midwives given the responsibility of short regular refresher trainings
7) Placement of the simulator in the labor room where every provider had to document practice of basic skills including FMV regularly
8) Steady supply of basic equipment

All these strategies have been important for establishment of local ownership and accountability, transfer of new competency into clinical practice, and sustainability. The stepwise approach of national implementation has been critical to demonstrate that the HBB program worked in the major institutions, and to delineate gaps and pitfalls before moving to a full national rollout.

CONCLUSION
The findings in this PhD thesis demonstrate how appropriate low-tech interventions can reduce perinatal mortality and morbidity. Additional, the data is essentially supportive of existing international guidelines for neonatal resuscitation and the HBB educational program, currently promoted in an increasing number of low-income countries lagging behind MDG 4. Furthermore, the findings express the potential effects of careful FHR monitoring on preventing intrapartum hypoxic injury, demonstrating the need to focus on the partogram and timely obstetric actions to reduce perinatal mortality further.

Our data define contributors to adverse perinatal outcome that can be summarized in a concept of vital delays in receiving appropriate care. “The three delays model” described for maternal ill-health (67) is applicable to perinatal adverse outcome: 1) delay in recognizing fetal hypoxia, 2) delay in actions to accelerate delivery, and 3) delay in basic stabilization at birth.

Importantly, all the interventions evaluated in this thesis are possible to implement in community settings, where 50% of all births are taking place, assisted by non-certified health providers such as traditional birth attendants and lay community people at home.
FUTURE PERSPECTIVES

This report is a proof of concept that the majority of early neonatal deaths in low-income countries are largely preventable if basic resuscitative actions like those described in the HBB educational program can be implemented in clinical practice and extended down to the community level. Tanzania has demonstrated a sustained reduction in perinatal mortality following two years of HBB implementation. The Tanzanian model, guided by the MHSW with great focus on implementation, should serve as a template for other resource limited countries.

The need for prolonged ventilatory support in a subset of babies that die, calls for further investigation to decide on optimal ventilation parameters (pressure, volume, positive end expiratory pressure, and frequency) to quickly restore cardio-respiratory stability and equipment design that facilitate high-quality performance.

Understanding the factors contributing to the observed delays in recognizing the fetus at risk, progression of labor when recognized, and initiation of FMV at birth are important to potentially reduce perinatal mortality further. Excellent HBB management can never reverse a true FSB and hardly help a severely asphyxiated newborn. Thus, a global priority should be to develop and study non-invasive Doppler ultrasound devices that are robust and affordable, do not require electricity, permit more reliable measures, and are easy to use during labour by providers extending down to the community level. A downstream consequence may be a reduction of asphyxiated newborns, early neonatal deaths, and FSB by accelerating delivery as well as anticipating the need for neonatal resuscitation. This approach coupled with the “Golden Minute®” should help low-income countries accelerate towards meeting MDG 4 goals by 2015.
REFERENCES


33. Fetal health surveillance: antepartum and intrapartum consensus guideline. JOGC 2007;9 suppl 4:3-56.


57. Situation Analysis of Newborn Health in Tanzania. March 2009. http://events.maildirect.se/30/Show.aspx?AccountId=984400ac-d9e4-4f7a-b54d-4f87249280e6&IssueId=03704252-4538-45d3-8bd3-4a268bcdd0c6&ContactId=29761fac-3d50-4ff0-b07f-50d9886445f8


59. http://apps.who.int/ghodata/?vid=20700&theme=country


61. Rothman KJ. Epidemiology.


PAPERS I-III

PAPER I

In press, Neonatology

Intermittent Detection of Fetal Heart Rate Abnormalities Identify Infants at Greatest Risk for Fresh Stillbirths, Birth Asphyxia, Neonatal Resuscitation, and Early Neonatal Deaths in a Resource Limited Setting

A prospective descriptive observational study at Haydom Lutheran Hospital

Hege Langli Ersdal¹², Estomih Mduma³, Erling Svensen³⁴, Johanne Sundby², Jeffrey Perlman⁵

1 Department of Anaesthesiology and Intensive Care, Stavanger University Hospital, Norway
2 Department of International Health, University of Oslo, Norway
3 Haydom Lutheran Hospital, Tanzania
4 Centre for International Health, University of Bergen, Norway
5 Department of Pediatrics, Weill Cornell NY, USA

Short title
Fetal heart rate abnormalities identify fetal compromise

Key words
Intermittent fetal heart rate monitoring
Perinatal morbidity and mortality
Millennium Developmental Goal 4
Abstract

**Background** Intermittent fetal heart rate (FHR) monitoring during labour using an acoustic stethoscope is the most frequent method for fetal assessment of well-being in low/middle-income countries. Evidence concerning reliability and efficacy of this technique is almost non-existent.

**Objectives** To determine the value of routine intermittent FHR monitoring during labour in the detection of FHR abnormalities, and the relationship of abnormalities to the subsequent fresh stillbirths (FSB), birth asphyxia (BA), need for neonatal face mask ventilation (FMV), and neonatal deaths within 24 hours.

**Methods** This is a descriptive observational study in the delivery room from November 2009 through December 2011. Research assistants/observers (n=14) have prospectively observed every delivery and recorded; labour information including FHR and interventions, neonatal information including responses in the delivery room, and fetal/neonatal outcomes (FSB, death within 24 hours, admission neonatal area, or normal).

**Results** 10271 infants were born. FHR was abnormal (i.e. <120 or >160 beats/minute) in 279 (2.7%) and absent in 200 (1.9%) fetuses. Postnatal outcomes included FSB n=159 (1.5%), need for FMV n=695 (6.8%), BA (i.e. 5 min Apgar score <7) n=69 (0.7%), and deaths n=89 (0.9%). Abnormal FHR was associated with labour complications (OR=31.4;95%CI:23.1-42.8), increased need for FMV (OR=7.8;95%CI:5.9-10.1), BA (OR=21.7;95%CI:12.7-37.0), deaths (OR=9.9;95%CI:5.6-17.5), and FSB (OR=35;95%CI:20.3-60.4). An undetected FHR predicted FSB (OR=1983;95%CI:922-4264).

**Conclusions** Intermittent detection of an absent or abnormal FHR using a fetal stethoscope is associated with FSB, increased need for neonatal resuscitation, BA, and neonatal death in a resource limited setting. The likelihood of an abnormal FHR is magnified with labour complications.
Introduction

Each year, intrapartum hypoxia is estimated to account for about two million perinatal deaths worldwide including intrapartum stillbirths and early neonatal deaths, with 98-99% of the burden in low-and middle income countries [1-3]. An additional one million of the surviving infants develop neurocognitive problems such as cerebral palsy and learning difficulties [4]. The incidence of intrapartum-related stillbirths and neonatal deaths has remained essentially unchanged over the past 15 years despite efforts to intervene and meet Millennium Development Goal (MDG) 4 [2,3,5].

The goal of fetal heart rate (FHR) monitoring is the early detection of a hypoxic fetus which should trigger appropriate and timely response/s to reverse the processes resulting in organ injury and death. Cardiotocography is the “gold standard” for identifying fetuses at high risk in high-resourced settings [6], but this device is neither available nor feasible in resource limited settings where the burden is highest [7]. Intermittent FHR monitoring with a fetal acoustic stethoscope is the most frequent method in these areas, but evidence concerning reliability and efficacy is almost non-existent [8,9]. Indeed, there is only one randomised trial comparing the effectiveness of different methods of FHR monitoring in a low-resourced country [10].

In a recent series on stillbirths the presence of skilled care at birth coupled with emergency obstetric care were identified as two major components to reduce the number of stillbirths globally. Interestingly, the necessity or importance of FHR monitoring to detect the babies at highest risk for either intrapartum stillbirths or neonatal death was not addressed [11,12].

We hypothesized that an abnormal FHR, routinely detected using a fetal stethoscope, would identify the fetus at highest risk for intrapartum death/fresh stillbirth (FSB), birth asphyxia (BA), the need for face mask ventilation (FMV) and/or special care, and neonatal death within 24 hours postpartum. The study objectives were to determine whether the detection of FHR abnormalities is associated with BA, an increased likelihood for neonatal resuscitation, early neonatal morbidity or death, and stillbirths.
Methods

This is an ongoing descriptive observational study initiated in November of 2009 at Haydom Lutheran Hospital (HLH); a rural referral hospital in Northern Tanzania. HLH provides comprehensive emergency obstetric care and basic emergency newborn care to a population of approximately 500,000 people, while the greater reference area covers about two million people [13]. Midwives largely conduct deliveries with doctors on call 24 hours. FHR during labour is routinely monitored by an attending midwife using a fetal stethoscope.

Research assistants/observers are continuously present in the labour ward. The observers work in three shifts over 24 hours. Three observers cover each shift; two are always located in the delivery room or in the theatre; one in the adjacent neonatal area. Altogether 14 local women have been trained to observe the health care workers performance related to the deliveries and the newborns. Observations are timed using a stop watch. The findings are recorded on a data collection form and include: labour information and FHR categorized as normal, abnormal, absent, or not measured; neonatal characteristics and interventions in the delivery room; and perinatal outcome (normal, admitted neonatal area, death within 24 hours, or stillbirths) (Appendix 1). The research assistants also review the partograms that are filled out by the birth attendants. The frequency of FHR monitoring is not recorded; therefore, the categorization of FHR is based on multiple measurements throughout labour. Abnormal is classified as one or more FHR measurement/s <120 or >160 beats/minute.

GA was based on self-report of the last menstrual period and distance from symphysis pubis to fundus (on admission). Normal term GA at HLH is routinely defined as 36 weeks. Thus prematurity was defined as a GA <36 weeks. BA was defined as 5 minute Apgar score <7. Normal outcome was defined as survival >24 hours without any detected difficulties. Intrapartum death/FSB was defined as an Apgar score = 0 at both 1 and 5 minutes with intact skin and suspected death during labour/delivery. Antepartum death/macerated stillbirth (MSB) was defined as an Apgar score = 0 at both 1 and 5 minutes with macerated skin and suspected death before start of labour.
Data Management at HLH

The research assistants are supervised and re-trained by the local research manager (EM) who reviews the data collection forms on a daily basis for quality control issues including missing information or potential errors. The data are double entered in EpiData3.1 by two different people. For this report the data collection was from November 2009 through December 2011.

Statistical Analysis

Analysis has been performed using Statistical Package for Social Sciences 17. Descriptive statistics were used to present data as mean ± standard deviation unless as otherwise stated. Chi-square calculations and independent-sample T-tests were utilised to compare different sub-populations. The significant associated dependent categorical variables were identified after multiple logistic modelling (logistic regression with forward and backward selection). Notably each dependent variable was subjected to multiple logistic modelling. Odds ratios (OR), 95% confidence intervals (CI), and p-values were also determined. The categorical covariates were entered as follows; pregnancy complications (yes or no), maternal infections (yes or no), GA (<36 or ≥36 weeks), BW (≤2500 or >2500 grams), fetal presentation (abnormal or normal), labour complications (yes or no), and FHR (abnormal or normal). Estimates of specificity and predictive values were calculated using “Vassar Stats” Clinical Calculator 1.

Ethical considerations

The National Institute for Medical Research in Tanzania has approved this ongoing study.

The Regional Committee for Medical and Health Research Ethics, Western Norway considers the project (reference number 2009/302) to be an evaluation program among certified health care workers. Formal approval from Norwegian ethical committee is thus not required. Informed consent was not obtained.
Results

The patient population included all infants (n=10271) born during the time period. Of these, 9888 were singletons, 190 were of a twin set and 3 of a triplet set. Perinatal outcome by 24 hours postpartum with associated population description is presented in Table 1. Specifically, the death rate was 9 per 1000 births and the FSB rate was 15 per 1000 births. Sixty-nine (0.7%) infants had an Apgar score <7 at 5 minutes. Stimulation and/or suction was attempted in 1603 (15.6%) cases and resuscitation including FMV in 695 (6.8%) infants because of failure to initiate spontaneous respirations with stimulation and/or suction. Duration of FMV was significantly longer in babies with FHR abnormalities versus normal FHR i.e.13min±21min versus 6min±13min (p=0.006).

The frequencies of the different perinatal outcomes, related labour complications, and mode of delivery are shown in Table 2. Abnormal fetal presentation, labour complications, assisted breech delivery, vacuum extraction, and CS were significantly more frequent in infants with adverse outcome (i.e. death, admission to the neonatal area, and FSB) compared to normal infants. The MSB were not included in the analysis due to suspected death before onset of labour.

Fetal heart rate and associated outcomes

The FHR was recorded as normal in 9649 (94%) cases, abnormal in 279 (2.7%), not detected in 200 (1.9%), and not measured in 143 (1.4%) cases (Figure1). Approximately 38% (59/154) of the FSB (with FHR recordings) had a normal or abnormal FHR record; the remainder had no detectable FHR (Figure 1). An undetected FHR predicted a FSB with an odds ratio (OR) of 1983 (95% confidence interval (CI) 922–4264*), a specificity of 0.99 (95%CI: 0.998–0.999), and a probability of 0.92 (95%CI: 0.85–0.96). Conversely, the probability of an alive baby with an undetected FHR was 0.08 (95%CI: 0.04–0.15).

A CS was performed in 1271 women (12.4%) including 1019/9649 (10.6%) cases with a normal FHR and 212/279 (76.0%) cases with an abnormal FHR (p≤0.0005) (Figure 2). An abnormal outcome (i.e. admitted or death at 24 hours, and FSB) was more likely when CS was performed because of an abnormal versus normal FHR i.e. 30/212 (14%) versus 36/1019 (3.5%) (OR=4.5;95%CI:2.7–7.5*). In 67 of the 279 (24.0%) cases with an abnormal FHR, the infants were delivered vaginally (Figure 2). An abnormal outcome was 56 times more
likely (OR=56.7;95%CI:32.9–97.9*) in those infants with abnormal FHR i.e. 24/67 (35.8%) as compared to 88/8630 (1.0%) infants with a normal FHR delivered vaginally. Finally, a FHR was not detected in the remaining 40/1271 infants who underwent a CS (Figure 2). The stillbirth rate in this group was 95% (38/40) cases.

Table 3 summarises the significant associated relationships between the dependent variables and associated factors. (The non-significant associated factors that were included in the modelling are not presented in the table). An abnormal FHR during labour was associated with labour complications (OR=31.4;95%CI:23.1–42.8*). An abnormal FHR in turn was associated with the need for FMV (OR=7.8;95%CI:5.9–10.1*), a 5 minute Apgar score <7 (OR=21.7;95%CI:12.7–37.0*), neonatal death (OR=9.9;95%CI:5.6–17.5*), continued admission (OR=3.0;95%CI:1.2–7.8*), and FSB (OR=35.0;95%CI:20.3–61.4*).

*(p≤0.0005)

Discussion

This prospective observational report demonstrates for the first time the value of routinely performed intermittent FHR monitoring during labor using a fetal stethoscope for the detection of the fetus at risk for FMV, BA, early neonatal death or morbidity, and FSB in a resource limited setting. This supports the well-established thesis that an abnormal FHR is an important indicator of fetal compromise. Moreover the findings indicate a significant association between an abnormal FHR and labour complications.

Many of the intrapartum-related deaths in this report were associated with labour complications and potentially preventable with targeted obstetric interventions. There were several babies with abnormal FHR and abnormal outcome delivered vaginally, who might have benefited from a more expedited delivery. Clearly the impact of FHR monitoring is dependent upon several factors including correct interpretation of an abnormal finding, decision-making coupled with appropriate communication, and timely effective interventions [6,9]. On the other hand, almost 75% of the babies that either died or were admitted to the neonatal area had a normal FHR record. Several factors may have influenced this observation.
including the inability to perform measurements correctly and as often as recommended [14], as well as different causes of deaths [15].

An undetected FHR was noted in nearly two per cent of the records and was a powerful predictor of a subsequent stillbirth. Importantly, five infants with an undetected FHR had a normal outcome, which indicate the potential of false positives for fetal death when using the fetal stethoscope, and maybe an explanation for why several CS were performed with an absent FHR. Conversely, over one third of the FSB had either an abnormal or normal FHR. This indicates an unnecessarily high FSB rate, and we can only speculate that infrequent auscultations, uncertainty around the findings, and/or delay in interventions are potential reasons. No specific reasons were noted for not monitoring the FHR in 143 cases. One factor can be that a single midwife takes care of many delivering women simultaneously, due to limited human resources. Finally, the FHR was recorded as normal or abnormal in 14 MSB, maybe due to difficulty in distinguishing FHR from maternal heart rate when using the fetal stethoscope.

There are several limitations to this study. First, an observational study limits interpretation of whether an alternative obstetrical management strategy would have altered neonatal outcomes. Second, an abnormal FHR was broadly defined. Third, the duration of an abnormal FHR, the frequency of FHR monitoring and the provider response to an abnormal tracing was not part of the data retrieval. Fourth, the presence of observers might have affected the staff.

The Pinard stethoscope is reported to be difficult to use, time-consuming, and often painful for the mother [7,16], and several shortcomings are demonstrated in this study. An alternative technique is the hand-held Doppler ultrasound that is considered to cause less pain, be easier to handle and more reliable [7,10,16]. The superiority of the Doppler technique over the Pinard stethoscope for the detection of abnormal FHR and improved neonatal outcomes has been shown in one study [10]. The authors concluded almost two decades ago that “Doppler ultrasound monitoring should be promoted in developing countries where electronic monitoring is not feasible”. Despite this recommendation there has been no advancement in FHR monitoring technology in low-resource countries. The current Doppler technology is rarely available because of cost and the need for batteries or electricity [8,16], and the lack of
attention towards promoting intermittent FHR monitoring in recent publications remains puzzling [11,12,17].

This report demonstrates the predictive value of intermittently detected FHR abnormalities, and thus shows how early identification of the fetus at increased risk can be a critical catalyst to reduce perinatal mortality and morbidity in low-resourced settings. A global priority should be to develop and study non-invasive Doppler ultrasound devices that are robust and affordable, do not require electricity, permit more reliable measures, and are easy to use during labour by providers extending down to the community level. The early detection of FHR abnormalities should alert the (single) provider to seek obstetrical assistance locally or refer the mother to more advanced obstetrical care (if possible) in time. Furthermore, the (single) provider should identify a helper prior to delivery, prepare for newborn resuscitation, and draw attention towards stabilizing the compromised baby upon delivery before managing the mother.

This approach coupled with the “Golden Minute®” concept adopted by the “Helping Babies Breathe” program [18,19] should help low-income countries accelerate towards meeting MDG 4 goals by 2015.

Conclusions

An abnormal FHR, routinely detected using a fetal stethoscope, is associated with FSB, increased need for neonatal FMV, BA, and early neonatal death in a resource-limited setting. An absent FHR is strongly associated with FSB. Thus a global priority should be to develop and study the potential role of novel Doppler devices. A downstream consequence may be a reduction of perinatal morbidity and mortality by accelerating delivery as well as anticipating the need for neonatal resuscitation.

Acknowledgements

This study was made possible because of the research assistants and health providers working in the Maternity Ward at Haydom Lutheran Hospital. Statistical assistance was provided by Bjørn Auestad, PhD, statistician at University of Stavanger. We thank Professor Eldar Søreide, Stavanger University Hospital for his support.
References


Table 1 Perinatal outcomes at 24 hours after birth defined as Normal, Admitted to a Neonatal Area, Dead, Fresh Stillbirths (FSB), and Macerated Stillbirth (MSB) and Associated Population Description

<table>
<thead>
<tr>
<th>Population Descriptors</th>
<th>Normal</th>
<th>Admitted</th>
<th>Death</th>
<th>FSB</th>
<th>MSB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9870 (96.1)</td>
<td>33 (0.3)</td>
<td>89 (0.9)</td>
<td>159 (1.5)</td>
<td>120 (1.2)</td>
</tr>
</tbody>
</table>

**Antenatal information**

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal care visit</td>
<td>9817 (99.5)</td>
<td>32 (97.0)</td>
<td>89 (100)</td>
<td>156 (98.1)</td>
<td>119 (99.2)</td>
</tr>
<tr>
<td>Pregnancy complication</td>
<td>64 (0.6)*</td>
<td>3 (9.1)*</td>
<td>3 (3.4)*</td>
<td>12 (7.9)*</td>
<td>18 (15.0)*</td>
</tr>
</tbody>
</table>

**Neonatal characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Admitted</th>
<th>Death</th>
<th>FSB</th>
<th>MSB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (grams)</td>
<td>3137 ± 482*</td>
<td>2902 ± 608*</td>
<td>2662 ± 812*</td>
<td>2919 ± 740*</td>
<td>-</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>36.5 ± 1.4**</td>
<td>35.5 ± 2.5</td>
<td>35.0 ± 3.0</td>
<td>36.0 ± 2.6</td>
<td>34.9 ± 3.1**</td>
</tr>
<tr>
<td>5 min Apgar score &lt; 7</td>
<td>28 (0.3)**</td>
<td>5 (15.2)**</td>
<td>36 (40.4)**</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Resuscitation**

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Admitted</th>
<th>Death</th>
<th>FSB</th>
<th>MSB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulation</td>
<td>1472 (14.9)*</td>
<td>24 (72.7)*</td>
<td>73 (82.0)*</td>
<td>25 (15.7)</td>
<td>0</td>
</tr>
<tr>
<td>Suction</td>
<td>1319 (13.4)*</td>
<td>23 (69.7)*</td>
<td>73 (82.0)*</td>
<td>27 (17.0)</td>
<td>0</td>
</tr>
<tr>
<td>Face mask ventilation</td>
<td>578 (5.9)*</td>
<td>20 (60.6)*</td>
<td>70 (78.7)*</td>
<td>27 (17.0)</td>
<td>0</td>
</tr>
</tbody>
</table>

Values given are \( n (\%) \) unless otherwise stated

* Self-reported pregnancy complication were more frequent among mothers of babies that died (p=0.002), those who remained admitted (p≤0.0005), FSB (p≤0.0005), and MSB (p≤0.0005) compared to normal infants.

* The birth weight of infants who died, remained admitted, or FSB was significantly less than of normal infants (p≤0.0005).

- Due to cultural tradition MSB are not weighted at the hospital.

** MSB were of lesser GA than normal babies (p≤0.0005).

** Infants who died and those admitted to the neonatal area were more likely to receive Apgar score < 7 at 5 minutes compared to infants with a normal outcome (p≤0.0005).

* Infants who died and those admitted to the neonatal area were more likely to receive stimulation, suction and/or FMV as compared to infants with a normal outcome (p≤0.0005).
Table 2 Perinatal outcomes at 24 hours after birth defined as Normal, Admitted to a Neonatal Area, Dead, FreshStillbirths (FSB), and Macerated Stillbirth (MSB) and Associated Labour Complications and Mode of Delivery

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal (9870/96.1)</th>
<th>Admitted (33/0.3)</th>
<th>Death (89/0.9)</th>
<th>FSB (159/1.5)</th>
<th>MSB (120/1.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal Presentation</td>
<td>571 (5.8)</td>
<td>6 (18.2)*</td>
<td>17 (19.1)*</td>
<td>41 (25.8)*</td>
<td>33 (27.5)</td>
</tr>
<tr>
<td>Labour Complications</td>
<td>1308 (13.3)</td>
<td>19 (57.6)**</td>
<td>39 (43.8)**</td>
<td>57 (35.8)**</td>
<td>23 (19.2)</td>
</tr>
<tr>
<td>Mode of Delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous Vaginal</td>
<td>8474 (86.0)</td>
<td>14 (42.4)</td>
<td>48 (53.9)</td>
<td>97 (61.0)</td>
<td>92 (76.7)</td>
</tr>
<tr>
<td>Assisted Breech</td>
<td>155 (1.6)</td>
<td>3 (9.1) ***</td>
<td>5 (5.6) ***</td>
<td>11 (6.9) ***</td>
<td>13 (10.8)</td>
</tr>
<tr>
<td>Caesarean Section</td>
<td>1164 (11.8)</td>
<td>13 (39.4) ***</td>
<td>35 (39.3) ***</td>
<td>45 (28.3) ***</td>
<td>14 (11.7)</td>
</tr>
<tr>
<td>Vacuum Extraction</td>
<td>77 (0.8)</td>
<td>3 (9.1) ***</td>
<td>1 (1.1) ***</td>
<td>6 (3.8) ***</td>
<td>1 (0.8)</td>
</tr>
</tbody>
</table>

Values given are n (%)

*There was a higher frequency of abnormal fetal presentation (non cephalic) among babies with abnormal outcome (i.e. admitted or dead at 24 hours, or fresh stillbirth) compared to normal outcome (p≤0.0005).

**Labour complications were more frequent in babies with abnormal versus normal outcome (p=0.0005).

***Assisted breech delivery, CS, and vacuum extraction were more common among babies with abnormal versus normal outcome (p≤0.0005).
<table>
<thead>
<tr>
<th>Dependent categorical variable</th>
<th>Associated factors</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal FHR (vs normal)</td>
<td>Labour complications</td>
<td>31.4</td>
<td>23.1 – 42.8</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>GA &lt; 36 weeks</td>
<td>2.3</td>
<td>1.4 – 3.9</td>
<td>= 0.002</td>
</tr>
<tr>
<td>Non detected FHR (vs normal)</td>
<td>Pregnancy complications</td>
<td>10.4</td>
<td>5.9 – 18.2</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>GA &lt; 36 weeks</td>
<td>6.9</td>
<td>4.7 – 1.2</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>Abnormal fetal presentation</td>
<td>4.9</td>
<td>3.5 – 7.0</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td>Caesarean section (vs not)</td>
<td>Abnormal FHR</td>
<td>26.8</td>
<td>20.2 – 35.5</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td>Need for FMV (vs not)</td>
<td>Abnormal FHR</td>
<td>7.8</td>
<td>5.9 – 10.1</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>BW &lt; 2500g</td>
<td>1.6</td>
<td>1.3 – 2.1</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>GA &lt; 36 weeks</td>
<td>2.0</td>
<td>1.4 – 3.0</td>
<td>= 0.001</td>
</tr>
<tr>
<td>Need for stimulation/suction (no FMV) (vs not)</td>
<td>Labour complications</td>
<td>2.4</td>
<td>2.0 – 2.8</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>BW &lt; 2500g</td>
<td>1.3</td>
<td>1.1 – 1.7</td>
<td>= 0.013</td>
</tr>
<tr>
<td>Apgar score 5 minutes &lt; 7 (vs ≥ 7)</td>
<td>Abnormal FHR</td>
<td>21.7</td>
<td>12.7 – 37.0</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>GA &lt; 36 weeks</td>
<td>4.2</td>
<td>1.9 – 9.3</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td>Neonatal death within 24 hours (vs normal)</td>
<td>Abnormal FHR</td>
<td>9.9</td>
<td>5.6 – 17.5</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>BW &lt; 2500g</td>
<td>4.2</td>
<td>2.3 – 7.4</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>GA &lt; 36 weeks</td>
<td>3.9</td>
<td>2.0 – 7.8</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td>Admitted neonatal area at 24 hours (vs normal)</td>
<td>Pregnancy complications</td>
<td>7.5</td>
<td>2.1 – 27.8</td>
<td>= 0.002</td>
</tr>
<tr>
<td></td>
<td>Labour complication</td>
<td>6.0</td>
<td>2.8 – 13.0</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>Abnormal FHR</td>
<td>3.0</td>
<td>1.2 – 7.8</td>
<td>= 0.023</td>
</tr>
<tr>
<td></td>
<td>BW &lt; 2500g</td>
<td>3.0</td>
<td>1.3 – 6.7</td>
<td>= 0.007</td>
</tr>
<tr>
<td>Fresh stillbirths (vs normal)</td>
<td>Abnormal FHR</td>
<td>35.0</td>
<td>20.3 – 60.4</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>Pregnancy complications</td>
<td>6.0</td>
<td>1.7 – 21.0</td>
<td>= 0.005</td>
</tr>
<tr>
<td></td>
<td>Abnormal fetal presentation</td>
<td>2.3</td>
<td>1.1 – 4.5</td>
<td>= 0.021</td>
</tr>
<tr>
<td>Macerated stillbirths (vs normal)</td>
<td>Pregnancy complications</td>
<td>11.7</td>
<td>6.1 – 22.3</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>GA &lt; 36 weeks</td>
<td>12.2</td>
<td>7.8 – 19.1</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td></td>
<td>Maternal infection</td>
<td>3.7</td>
<td>1.9 – 6.9</td>
<td>≤ 0.0005</td>
</tr>
</tbody>
</table>

FHR = Fetal heart rate, FMV = Face mask ventilation, GA = Gestational age, BW = Birth weight,
**Figure 1** Relationship of fetal heart rate (FHR) recordings and perinatal outcomes at 24 hours after birth

FHR = Fetal Heart Rate, FSB = Fresh Stillbirth, MSB = Macerated Stillbirth
Figure 2 Relationship of fetal heart rate (FHR) recordings and mode of delivery

N = 10271 Deliveries

- FHR normal: N = 9649 (93.9%)
  - Vaginal: N = 8406 (87.1%)
  - Breech: N = 154 (1.6%)
  - Vacuum: N = 70 (0.7%)
  - CS: N = 1019 (10.6%)

- FHR not measured: N = 143 (1.4%)
  - Vaginal: N = 136 (95.1%)
  - Breech: N = 7 (4.9%)
  - Vacuum: N = 0
  - CS: N = 0

- FHR non-detected: N = 200 (1.9%)
  - Vaginal: N = 133 (66.5%)
  - Breech: N = 20 (10.0%)
  - Vacuum: N = 7 (3.5%)
  - CS: N = 40 (20.0%)

- FHR abnormal: N = 279 (2.7%)
  - Vaginal: N = 50 (17.9%)
  - Breech: N = 6 (2.2%)
  - Vacuum: N = 11 (3.9%)
  - CS: N = 212 (76.0%)

FHR = Fetal Heart Rate, CS = Cesarean Section
### Appendix 1 Information Recorded on the Data Collection Form

<table>
<thead>
<tr>
<th>Antenatal information</th>
<th>Antenatal care</th>
<th>yes or no</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy complications</td>
<td>yes or no</td>
<td></td>
</tr>
<tr>
<td>Maternal infections</td>
<td>non, uterine, malaria, HIV, sepsis, or other</td>
<td></td>
</tr>
<tr>
<td>Labour information</td>
<td>Fetal presentation</td>
<td>cephalic, breech, shoulder dystocia, transverse, or other</td>
</tr>
<tr>
<td>Fetal heart rate</td>
<td>Normal: 120 to 160 BPM, abnormal: &lt;120 or &gt;160 BPM, non detected, or not measured</td>
<td></td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>spontaneous vaginal delivery, CS, assisted breech delivery, and vacuum extraction</td>
<td></td>
</tr>
<tr>
<td>Labour complication</td>
<td>prolonged labour, obstructed labour, preeclampsia, eclampsia, uterine rupture, haemorrhage, cord prolapse,</td>
<td></td>
</tr>
<tr>
<td>Neonatal information</td>
<td>Transitional newborn adaption</td>
<td>time intervals (seconds) from birth to initiation of spontaneous respirations and cord clamping</td>
</tr>
<tr>
<td>Gender</td>
<td>male or female</td>
<td></td>
</tr>
<tr>
<td>Birth Weight</td>
<td>Grams</td>
<td></td>
</tr>
<tr>
<td>Gestational Age</td>
<td>Weeks</td>
<td></td>
</tr>
<tr>
<td>Apgar scores</td>
<td>one and five minutes</td>
<td></td>
</tr>
<tr>
<td>Interventions in the Delivering Room</td>
<td>stimulation, suction ± FMV with a self-inflating bag, and time interval (sec) to initiation of FMV</td>
<td></td>
</tr>
<tr>
<td>Specific Observations</td>
<td>newborn heart rate present or not, time interval (seconds) from initiation of FMV to the onset of spontaneous breathing or death</td>
<td></td>
</tr>
<tr>
<td>Perinatal outcome at 24 hours postpartum</td>
<td>Normal</td>
<td>Survival &gt; 24 hours without any detected difficulties</td>
</tr>
<tr>
<td></td>
<td>Admitted</td>
<td>Designated Neonatal Area</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stillbirth</td>
<td>Macerated = Antepartum or Fresh = Intrapartum</td>
</tr>
</tbody>
</table>

BPM = Beat per minute, FMV = Face mask ventilation
Clinical paper

Early initiation of basic resuscitation interventions including face mask ventilation may reduce birth asphyxia related mortality in low-income countries: A prospective descriptive observational study

Hege Langli Erstad1,∗, Estomih Mlumaa,∗, Erling Svenssen1,2, Jeffrey M. Perlman1,∗∗

1 Department of Anaesthesiology and Intensive Care, Stavanger University Hospital, Norway
2 Department of International Health, University of Oslo, Norway
3 Hospital Lutheran Hospital, Mbandaka, Tanzania
4 Centre for International Health, University of Bergen, Norway
5 Department of Pediatrics, Weill Cornell, NY, USA

A R T I C L E  I N F O

Article history:
Received 27 July 2011
Received in revised form 2 December 2011
Accepted 8 December 2011

Keywords:
Newborn initiation of spontaneous respirations
Neonatal resuscitation
MDC 4

A B S T R A C T

Aim of the study: Early initiation of basic resuscitation interventions within 60 s in asphyxiated newborn infants is thought to be essential in preventing progression to circulatory collapse based on experimental cardio-respiratory responses to asphyxia.

The objectives were to describe normal transitional respiratory adaption at birth and to assess the importance of initiating basic resuscitation within the first minutes after birth as it relates to neonatal outcome.

Methods: This is an observational study of neonatal respiratory adaptation at birth in a rural hospital in Tanzania. Research assistants (n=14) monitored every newborn infant delivery and the response of birth attendants to a depressed baby. Time to initiation of spontaneous respirations or time to onset of breathing following stimulation/suctioning, or face mask ventilation (FMV) in asphyxiated infants, and duration of FMV were recorded.

Results: 5845 infants were born; 5889 were liveborn, among these 4789(84%) initiated spontaneous respirations; 93% in <30 s and 99% in <60 s. Basic resuscitation (stimulation, suction, and/or FMV) was attempted in 920/5689(16.0%); of these 450(40.9%) received FMV. Outcomes included normal n=561(99.8%), neonatal deaths n=56(1.0%), admitted neonatal area n=20(0.3%), and stillbirths n=156(2.7%). The risk for death or prolonged admission increases 16.5 for every 30 s delay in initiating FMV up to six minutes (p=0.045) and 6% for every minute of applied FMV (p=0.001).

Conclusions: The majority of lifeless babies were in primary asphyxia and responded to stimulation/suctioning and/or FMV. Infants who required FMV were more likely to die particularly when ventilation was delayed or prolonged.

© 2011 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Each year approximately 136 million babies are born globally. It is estimated that about 90% make the transition from in utero to extrauterine life without any intervention.1,2 The remaining ten per cent or 13.6 million newborns are delivered with absent or poor respiratory effort and need some degree of support to achieve cardiorespiratory stability. Between three to six per cent need assisted positive pressure ventilation, and less than one per cent require advanced resuscitation including intubation, chest compressions, and medications.3 However, these estimates are based on five reports,2–5 none of which reflect Sub-Saharan Africa where the burden of perinatal deaths and morbidity is considered to be highest.6

Current International Guidelines on Newborn Resuscitation suggest about 30–60 s of time following delivery should be
allocated to assess spontaneous respiratory and heart activity before initiating intermittent positive-pressure ventilation if indicated. Failure to initiate spontaneous respirations at birth in most cases is thought to be secondary to primary apnea, and the infant should respond fairly promptly to early intervention, i.e. drying, stimulation, clearing the airways as indicated, as well as face mask ventilation (FMV) applied within the first minute. Delaying basic resuscitation in apneic infants is thought to result in a progressive decrease in heart rate and blood pressure and eventual death and/or brain injury in those who may eventually start gasping and/or breathing (frequently called “birth asphyxia”), based on the cardio-respiratory responses described in asphyxiated newborn monkeys (Fig. 1). However, the definition of “birth asphyxia” is imprecise. In low-income countries it has been defined as a failure to initiate spontaneous regular respirations after birth and/or a 5 min Apgar score < 7. This is distinct from the definition in high-income countries which is more comprehensive and includes biochemical evidence of interruption of placental blood flow with a cord arterial pH < 7.00; a distinctive marker of severe acidemia and the need for resuscitation in the delivery room as well as a low 10 min Apgar score. The use of more precise terms to describe “birth asphyxia” is advocated in several recent papers. Irrespective of definition, defining transitional changes at birth is critical towards understanding the problem of intrapartum-related hypoxia and the importance of basic interventions in the first minutes after birth.

Global estimates on immediate postpartum neonatal needs and interventions are uncertain due to a paucity of data from low- and middle-income countries and almost a complete lack of data from rural community-based settings. Haydon Lutheran Hospital (HLH) is located in rural Northern Tanzania, 300 km, from the nearest urban centre, with a poor rural population in the catchment area. It is the referral hospital for approximately 500,000 people, while the greater reference area covers over two million people. HLH provides comprehensive emergency obstetric and basic emergency newborn care. Midwives are the primary providers at most deliveries as well as the initiators of neonatal resuscitation when indicated, with doctors on 24 h backup call. The midwives are trained in basic resuscitative actions (stimulation, mouth suctioning, and providing face mask ventilation when indicated) during nursing school and sporadically re-trained by doctors at HLH. Following birth, infants requiring more than routine care are triaged to a neonatal area: a ten square meter room located within the labour ward, with the capability of administering oxygen, use of wall suction, and providing intravenous fluids and antibiotics. No mechanical ventilation support device is available, thus if required, respiratory support is provided with a self-inflating bag. The infants who are admitted to this area are cared for by family members and labour staff.

The objectives of this study were to define the normal transitional respiratory adaption at birth, to describe interventions performed by birth attendants in the delivery room with ensuing short-term outcomes of the newborns at 24 h, and to assess the importance of the “Golden MinuteSM” after birth as it relates to early neonatal outcome.

2. Methods

This is an ongoing descriptive observational study initiated in August of 2009 at HLH, a rural referral hospital in Northern Tanzania. Research assistants (observers) are continuously present in the labour ward to observe the routine practice of health care providers in the delivery room as well as in the neonatal area through the initial 24 postnatal hours. The observers work in three shifts over 24 h. Three observers cover each shift; two are always located in the labour ward or in the theatre; one in the adjacent neonatal area. Altogether 14 local women have been trained. Observations are timed using a stop watch, and the findings are recorded on a data collection form immediately following the delivery. The research assistants also review the partograms that are filled out by the midwives.

The following information was recorded:

1. Antenatal information: antenatal care, pregnancy complications, and maternal infections (i.e. non, uterine, malaria, HIV, sepsis, or other);
2. Labour information: fetal presentation (i.e., cephalic, breech, shoulder dystocia, transverse, or other), labour complication (i.e., prolonged labour, obstructed labour, preeclampsia, eclampsia, uterine rupture, haemorrhage, cord prolapse, CS, and vacuum extraction), FHR (normal was defined as 120–160 BPM, abnormal as < 120 or >160 BPM, not detected, or not measured), and mode of delivery (i.e., spontaneous vaginal delivery, CS, assisted breech delivery, and vacuum extraction);
3. Neonatal information: transitional newborn adaption including time intervals from birth to initiation of spontaneous respirations and cord clamping; gender, BW, GA, and Apgar scores at one and five minutes;
4. Interventions in the delivery room i.e. stimulation, suction = FMV with a self-inflating bag, time interval to initiation of FMV, as well as the time interval from initiation of FMV to the onset of spontaneous breathing or death, and the presence or absence of any newborn heart activity;
5. Perinatal outcome at 24 h postpartum categorized as either normal, admitted to the designated neonatal area, death within 24 h, or stillbirths (macerated/anepartum or fresh/intrapartum).
GA was based on self-report of the last menstrual period and distance from symphysis pubis to the fundus. Normal term GA at HLH is routinely defined as 36 weeks.

Prematurity was defined as a GA < 36 weeks.

Low birth weight was defined as BW < 3rd centile for GA.

Birth asphyxia was defined as a failure to initiate spontaneous respirations and/or 5 min Apgar score < 7.

Normal was defined as survival > 24 h without any detected difficulties.

Fresh/intrapartum stillbirth was defined as an Apgar score = 0 at both 1 and 5 min with intact skin and suspected death during labour/delivery.

Macerated/intrapartum stillbirth was defined as an Apgar score = 0 at both 1 and 5 min with macerated skin and suspected death before start of labour.

2.1. Data management at HLH

The research assistants are continuously supervised and trained by the local research manager (EM) who reviews the data collection forms on a daily basis for quality control issues including missing information or potential errors. The data are double entered in Epidata 3.1 by two different people. Random crosschecks of the entered data are undertaken intermittently, with data extraction and data entry of all cases. If there is any discrepancy between the two entered databases, the data entering individuals recheck the original data together and correct where necessary. For this report the data collection was from August of 2000 through October of 2010.

2.2. Statistical analysis

Statistical analysis has been performed using statistical packages for social sciences (SPSS) 15 and 17 and includes descriptive statistics, chi-square calculations, independent-samples t-tests, and multiple logistic modelling. All data are presented as mean ± standard deviation unless otherwise stated.

2.3. Ethical considerations

The Regional Committee for Medical and Health Research Ethics, Western Norway (REK West) consider the project – reference number 2009/302 – to be an evaluation program among certified health care workers. Formal approval from Norwegian ethical committee is thus not required. The National Institute for Medical Research in Tanzania has approved the ongoing study.

3. Results

During the 14 months of the observational period, 5845 newborns were born and evaluated. Of these 5689 infants (97.3%) were liveborn; 56 infants (0.9%) (9 per 1000 live births) died within 24 h and 20 infants (0.3%) remained in the neonatal area at 24 h. Infants who died were of lower BW (p = 0.0005) and GA (p = 0.0005) as compared to normal infants (Table 1). There were 156 (2.7%) stillborns of whom 93 (1.6%) were categorized as fresh/intrapartum (16 per 1000 births) and 63 (1.1%) as macerated/intrapartum.

3.1. Normal transitional respiratory adaptation

Of the liveborn babies 4769 (83.8%) initiated spontaneous respirations and did not require any intervention (Fig 2). The majority i.e. 4435 (93%) started breathing within 30 s, and 4735 (99.3%), were breathing spontaneously within one minute after birth. Five babies initiated spontaneous respirations between two and three minutes, one between three and four minutes, and three after four minutes; they were all classified as normal at 24 h. The mean time to spontaneous respirations was 10.2 ± 15.0 s (median 5.0 s) (Table 1). The outcome was as follows: 4755 infants (99.7%) were classified as normal at 24 h, nine (0.2%) died, and five (0.1%) remained in the neonatal area at 24 h (Fig 2). The time to initiate spontaneous respirations was delayed among newborns who died as compared to those with normal outcome (p = 0.003) (Table 1).

3.2. Respiratory responses to basic resuscitation

Overall, basic resuscitation, i.e. stimulation, suction + FMV, was attempted in 942/5845 (16.1%) infants: 22 of the newborns were fresh/intrapartum stillborns in whom stimulation/suction and FMV were initiated due to uncertainty about heart activity (Fig 2). Of the remaining 920 infants, approximately 50% (n = 461) responded by breathing after stimulation and/or suctioning only, and the remaining infants (n = 459) received FMV in addition to stimulation and/or suctioning (Table 1 and Fig 2).

Among the babies that started breathing following stimulation and/or suctioning 436/461 (95%) responded within four minutes of birth, and 25 began breathing after four minutes. Overall in the group who received stimulation/suctioning (Fig 2), two newborn died, one was still admitted, and the rest were classified as normal at 24 h. Among infants who required FMV the majority i.e. 447/459 (97%) were ventilated within four minutes after birth. In 12 babies FMV was initiated after four minutes; the outcome in these infants was normal (n = 7), death (n = 4), and seizures (n = 1).
Fig. 2. Schematic overview of different pathways to outcome at 24 h.

Of the 459 infants who received FMV 45 (9.8%) died (Fig. 2). Fifteen (33%) were never able to establish spontaneous respirations; therefore ventilation was discontinued after a median time of 23 min. The remaining 30 babies (67%) initiated spontaneous respirations in response to FMV before they died. Of the survivors, 400 were normal while 14 remained in the neonatal area at 24 h including live with seizures (Fig. 2). Thus infants who died i.e. 45/56 (80%) and those admitted to the neonatal area, i.e. 14/20 (70%) were more likely to receive FMV as compared to infants with a normal outcome, i.e. 39/5812 (7%) (OR = 42; 95%CI: 25–72, p < 0.0005) (Table 1). The mean time from birth to application of FMV was delayed in infants who died or who were admitted to the neonatal area (100 ± 92 s) as opposed to those infants with normal outcome (79 ± 55 s) (p = 0.003). This risk for death and morbidity increases 16% for every 30 s delay in initiation of FMV up to six minutes (OR=1.005; 95%CI: 1.000–1.010, p = 0.045) when adjusted for BW, GA, pregnancy, and labour complications.

The mean duration of FMV administration was 534 ± 1411 s (median time 248 s or approximately four minutes). Only 6/459 newborns (1.3%) were ventilated for less than one minute. The mean duration of FMV was longer in infants who died or who were admitted to the neonatal area (1694 ± 3601 s) as opposed to those infants with normal outcome (352 ± 511 s) (p = 0.003). More specifically, the likelihood for death increased when the duration of FMV was greater than four minutes, i.e. 34/226 as compared to 10/227 when the duration of FMV was less than four minutes (p = 0.0001). In 6/459 cases (1.3%) the duration of FMV was not specified. By logistic modelling the risk for death and morbidity increases six per cent for every minute of FMV (OR = 1.001; 95%CI: 1.000–1.001, p = 0.001). Pregnancy complications, labour complications, BW, GA, and time to initiation of FMV did not influence this risk when analysed by multiple logistic regression.

4. Discussion

The data in this report for the first time describe the natural transitional respiratory adaption of newborns delivered in a rural setting in a low-income country, and the population of newborns needing basic stabilization/resuscitation in the delivery room. Thus 84% initiated spontaneous respirations within the “Golden Minute” with an additional 13% responding to stimulation/suctioning alone or with FMV by initiating breathing. This proportion of newborns in need of basic resuscitative interventions is much higher than estimated global numbers, but comparable to recent findings obtained from a district setting in Zambia.

An important observation is that death was significantly more likely to occur in infants who were administered FMV with almost ten per cent mortality noted in this group. Moreover, there was a significant relationship between a delay in the initiation of FMV and admission to the neonatal area and/or death. Specifically the risk for death and morbidity increases 16% for every 30 s delay in initiation of FMV up to six minutes, and more than two thirds of the deaths occurred when ventilation was administered beyond four minutes. The association between delayed FMV and adverse neonatal outcome was found after multiple logistic modelling and adjusted for BW, GA, pregnancy, and labour complications. Nevertheless, other potential confounding factors, i.e. severe fetal acidemia, might have influenced this association. The reasons for the delay in initiating FMV in some infants is unclear, but may reflect a gradual learning curve of some of the single providers to first manage a depressed baby rather than the mother.

The cardio-respiratory responses to asphyxia has been characterized in the newborn monkey (Fig. 1). Thus during the initial minutes’ with apnoea heart rate is greater than 60 beats per minute and blood pressure is still compensated – a state referred to as primary apnoea. With intervention at this stage, and relief of the asphyxial process, there is an immediate increase in heart rate and blood pressure with initiation of spontaneous respirations. However, if there are no interventions and the asphyxial process is allowed to continue there is progressive bradycardia and hypotension with final asystole (after approximately four to five minutes) before secondary apnoea develops. Once this stage evolves it becomes more difficult to resuscitate and restore cardiorespiratory status and in those who do recover the likelihood for hypoxic–ischemic brain injury is markedly increased. The findings in this report are consistent with these observations. Thus almost 50% of the apnoic infants responded to stimulation and suctioning only, and the outcome in this group was favourable (only two deaths). On the other hand, although half of the infants administered FMV initiated spontaneous respirations within four to five minutes of delivery, death was significantly more likely in this
group particularly with more prolonged ventilation as well as when there was a delay in onset of FMV.

These observations are initial critical steps towards the understanding of “birth asphyxia” and by default interventions to reduce its occurrence in the developed world. Thus, this data indicate that the overwhelming majority of lifeless babies at birth are in primary apnea and will respond to basic interventions with or without FMV particularly when initiated within the “Golden Minute”. Moreover, if spontaneous breathing is initiated within four minutes in response to interventions the mortality rate is approximately 1.2 per 1000 live births i.e. comparable to that observed in the developed world. However, if there is a delay beyond four minutes in the onset of breathing, mortality rates increases and approximates 7.0 per 1000 live births. In this regard the predominant cause of death was secondary to “birth asphyxia”, with prematurity, low birth weight, and congenital abnormalities additional causes.

The association of duration of FMV and mortality may be related to several factors. First, some babies may have been in secondary apnea and depending on the extent of their apnea collapse likely to respond to stimulation, suction, and ventilation only. We have reported separately that many of the infants in need of resuscitation presented with obstructed complications and fetal heart rate abnormalities. Moreover, no infant received chest compressions, medications, or mechanical ventilation. It is unclear whether these interventions would have reduced mortality. Second, application and administration of FMV may have been suboptimal. Thus in a non-breathing infant establishment of functional residual capacity, which is critical to effective ventilation, can be extremely difficult without the application of continuous positive airway pressure or prolonging the inspiratory time which are both difficult to achieve with a self-inflating bag.

An interesting observation is of a substantial delay in onset of spontaneous respirations and normal outcome at 24 h in a limited number of infants. Thus three babies initiated spontaneous respirations and 25 newborns begun breathing when stimulated/suctioned after four minutes and 27/28 were classified as normal at 24 h. Even in the group of 12 babies who received FMV at birth, 12/13 infants were classified as normal. This suggests that the infants were most likely in primary apnea and/or they had shallow breathing not detected by the provider or the observers. In this regard, data from the collaborative study in the United States noted in babies with a 20 minute Apgar score <3 that 62% died and of the survivors 40% were abnormal. These combined observations speak to the adaptive resilience of the fetus in response to a hypoxic environment.

5. Conclusion

The majority of newborn infants, delivered in a rural institution in sub-Saharan Africa, spontaneously initiate respirations within one minute and a substantial number of apneic babies begin breathing in response to basic actions (stimulation/suction) and/or FMV with a favourable short term outcome in the majority of infants. Infants who required FMV were more likely to die particularly when the intervention was delayed or prolonged. Understanding the factors contributing to the delay in initiation of FMV and the need for prolonged ventilatory support is likely to be extremely important in potentially reducing mortality in this subset of infants. Documentation of strategies to improve the skills of basic neonatal resuscitative actions is needed.

Conflicts of interest

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that: (1) HLE has received research grants from The Endo Foundation for Acute Medicine for the submitted work; (2) Haydon Lutheran Hospital has received project funds from The Endo Foundation for Acute Medicine for the submitted work; and (3) JMP has no conflict of interest. The financial source had no role in study design, data collection, data analysis, data interpretation, writing of the report, or in the decision to submit the paper for publication.

Acknowledgements

This study was made possible because of the research assistants and health workers providing in the Maternity Ward at Haydon Lutheran Hospital. Statistical assistance was provided by Bjorn Auestad, PhD, statistician at University of Stavanger. We thank Professors Johannes Sundby, University of Oslo and Ekdar Sereide, Stavanger University Hospital for their support.

References

Birth Asphyxia: A Major Cause of Early Neonatal Mortality in a Tanzanian Rural Hospital
Hege Langli Erstad, Estomih Mduma, Erling Svensen and Jeffrey Perlman

*Pediatrics*; originally published online April 16, 2012;
DOI: 10.1542/peds.2011-3134

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/early/2012/04/11/peds.2011-3134
Birth Asphyxia: A Major Cause of Early Neonatal Mortality in a Tanzanian Rural Hospital

WHAT'S KNOWN ON THIS SUBJECT: The presumed causes of neonatal deaths globally have remained unchanged over the past decade and include infections (~30%), prematurity (~30%), and asphyxia (~25%). Great uncertainty surrounds these estimates and, in addition, cases are likely misclassified as stillbirths.

WHAT THIS STUDY ADDS: These observational findings indicate that asphyxia accounts for a much higher percentage (60%) of early deaths. Prematurity (18%), low birth weight (8%), and overt infection are much less common. The 5-minute Apgar score is an unreliable indicator of birth asphyxia.

abstract

OBJECTIVE: Early neonatal mortality within the first 24 hours contributes substantially to overall neonatal mortality rates. The definition of birth asphyxia (BA) is imprecise, and reliable cause-specific mortality data are limited; thus the estimated proportion of BA-related deaths globally remains questionable. The objective was to determine the presumed causes of neonatal death within the first 24 hours in a rural hospital in Northern Tanzania.

METHODS: This is a prospective descriptive observational study conducted in the delivery room and adjacent neonatal area. Research assistants were trained to observe and record events related to labor, neonatal resuscitation, and 24-hour postnatal course. BA was defined as failure to initiate spontaneous respirations and/or 5-minute Apgar score <7, prematurity as gestational age <36 weeks, and low birth weight (LBW) as birth weight <3rd centile for gestational age. Data were analyzed with $\chi^2$ and Student's t tests.

RESULTS: Over 1 year, 4720 infants were born and evaluated. Of these, 256 were admitted to the neonatal area. Forty-nine infants died secondary to BA (61%), prematurity (18%), LBW (8%), infection (2%), congenital abnormalities (8%), and unclear reason (2%). The 5-minute Apgar score was $\geq 7$ in 50% of the infants who died secondary to BA.

CONCLUSIONS: Most cases of early neonatal mortality were related to BA, and prematurity and LBW are additional important considerations. Reducing perinatal mortality requires a multifaceted approach with attention to issues related to BA, potential complications of prematurity, and LBW. The 5-minute Apgar score is a poor surrogate of BA.

Authors: Hegge Langli Ersdal, MD,1* Estomih Mduma, DLSHTM1 Erling Swensen, PhD,1* and Jeffrey Perlman, MD, ChB

1Department of Anaesthesiology and Intensive Care, Stavanger University Hospital, Stavanger, Norway; 2Department of International Health, University of Oslo, Oslo, Norway; 3Fredrik Lutheran Hospital, Haydon, Tanzania; 4Centre for International Health, University of Bergen, Bergen, Norway and 5Department of Pediatrics, Weill Cornell, New York, New York

KEY WORDS: millennium developmental goal 4, neonatal mortality, low-resource settings, causes of neonatal deaths

ABBREVIATIONS
BA—birth asphyxia
BMV—bag mask ventilation
BW—birth weight
FHR—fetal heart rate
GA—gestational age
LBW—low birth weight

Dr Ersdal had the idea for the study and is the guarantor (the contributor who accepts full responsibility for the finished article, had access to any data, and controlled the decision to publish); Drs Ersdal and Perlman performed the literature search and managed the research process, including study design, data collection, data analysis and interpretation, writing of the report, revision, and final approval of the version to be published; and Drs Mduma and Swensen participated in study design, data collection and analysis, revision of the report, and final approval of the version to be published. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

www.pediatrics.org/cgi/doi/10.1542/peds.2011-3134
doi: 10.1542/peds.2011-3134

Accepted for publication January 5, 2012

Address correspondence to Hegge Langli Ersdal, MD, Specialist in Anaesthesiology and Intensive Care Medicine, Department of Anaesthesiology and Intensive Care, Stavanger University Hospital, POB 1010, 4068 Stavanger, Norway. E-mail: hele@hus.no

PEDiATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4279.
Copyright © 2012 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by The Laerdal Foundation for Acute Medicine. Dr Ersdal has received research grants and Haydon Lutheran Hospital project funds. The financial source had no role in study design, data collection, data analysis, data interpretation, writing of the report, or in the decision to submit the article for publication.
Neonatal mortality is defined as death before 1 month of age, and recent global estimates range from 2.9 to 3.6 million deaths per year.1,2 Of these, ~50% occur within the first 24 hours. The presumed causes of neonatal deaths have remained unchanged over the past decade and include infections (~30%), preterm birth (~30%), and birth asphyxia (BA; ~25%).2,3,6 However, uncertainty surrounds these estimates due to an almost complete lack of reliable vital registration systems from settings where mortality is highest.6 Thus analyses are based on retrospective household surveys, and most cause specific data rely on verbal autopsy without consistent definitions and algorithms. Deaths within the first 24 hours are likely underreported or misclassified as stillbirths.3,7 Nevertheless, early neonatal mortality, especially within the first day after birth, is thought to contribute substantially to the overall neonatal mortality rates.5,7,8 Currently, neonatal deaths account for ~40% of the under 5 years child mortality. This proportion is steadily increasing due to the annual rate of decline in childhood mortality without a corresponding decrease in neonatal mortality.1,2 Clearly, efforts to meet Millennium developmental goal 4 by 2015 have to focus on reducing neonatal deaths, in particular early deaths within the first 24 hours. Understanding the presumed causes of death, in settings with the highest burden, is critical before effective preventive strategies can be implemented. BA has for a long time been estimated to account for ~25% of neonatal mortality worldwide.2,3,6,9,10 However, the definition is imprecise in part because the Apgar score, often used as an indicator to identify BA, is inaccurate or unreliable. Furthermore, many affected infants are likely not reported or misclassified as fresh stillbirths.3,7 Therefore, considerable uncertainty surrounds the “true” estimated proportion of BA-related mortality. Finally, most cause-specific mortality data have been generated from studies in Asia,9,11,12 whereas there is a paucity of data from sub-Saharan Africa, the region with the highest neonatal mortality rates and least reduction per year.3,8

Haydom Lutheran Hospital is located in rural Northern Tanzania, 500 km from the nearest urban center, with a poor rural population in the area. It has an immediate catchment of ~500 000 people and serves as a referral hospital for ~2 million people.13 The hospital provides comprehensive emergency obstetric and basic emergency newborn care. Midwives largely conduct deliveries with doctors on call 24 hours. After birth, infants requiring more than routine care are triaged to an adjacent neonatal area (a 10-m² room with 1 long bench, with the capability of providing intravenous fluids and antibiotics) and are intermittently cared for by family members and the labor staff. Most infants transition rapidly and are discharged; however, a subset dies for different reasons. Our objective for this study was to determine the presumed causes of death within the first 24 hours of birth in this scarcely resourced rural referral hospital.

METHODS

This is an ongoing descriptive observational study initiated in November of 2009 at Haydom Lutheran Hospital: a rural referral hospital in Northern Tanzania. Research assistants (observers) are continuously present in the labor ward to observe the routine practice of health care providers in the delivery room as well as postnatally in an adjacent neonatal area through the initial 24 postnatal hours. The observers work in 3 shifts over 24-hours. Three observers cover each shift; 2 are always located in the labor ward or in the theater, and 1 in the adjacent neonatal area. Altogether, 14 local women have been trained to observe the performance of the health care workers related to the deliveries and the newborns. Observations are timed by using a stop watch, and the findings are recorded on a data collection form immediately after the delivery (Table 1). The research assistants also review the partograms that are filled out by the birth attendants and the responsible midwives.

The following definitions were used. Gestational age (GA) was based on self-report of the last menstrual period and distance from symphysis pubis to the fundus. Normal term GA at Haydom Lutheran Hospital is routinely defined as 36 weeks. Thus prematurity was defined as a GA <36 weeks and low birth weight (LBW) as birth weight (BW) <3rd centile for GA.14 BA was defined as a failure to initiate spontaneous respirations and/or 5-minute Apgar score <7: the most commonly used indicator to identify BA in resource limited settings. If a premature infant also had a history of suspected intrapartum related hypoxia (abnormal fetal heart rate [FHR], labor complication, no respiratory efforts, and/or 5-minute Apgar score <7), the primary cause of death was categorized as BA. Normal was defined as survival >24 hours without any detected difficulties. Fresh/intrapartum stillbirth was defined as an Apgar score of 0 at both 1 and 5 minutes with intact skin and suspected death during labor/delivery. Macerated/antepartum stillbirth was defined as an Apgar score of 0 at both 1 and 5 minutes with macerated skin and suspected death before start of labor.

Data Management at Haydom Lutheran Hospital

The research assistants are continuously supervised by the local research manager (Dr Mdu and) who reviews the data collection forms on a daily basis for quality control issues including missing information or potential errors.
The data are double entered in EpiData 3.1 (EpiData Association, Odense, Denmark) by 2 different people. Random cross-checks of the entered data are undertaken intermittently, with double data extraction and data entry of all cases. If there is any discrepancy between the 2 entered databases, the data entering individuals recheck the original data (the source document) together and correct where necessary. For this report, the data collection is from November 2009 through October 2010.

**Statistical Analysis**

Analysis has been performed by using SPSS 17 (SPSS, Inc, Chicago, IL) and includes descriptive statistics, \( \chi^2 \) calculations, Fisher’s exact test, and independent-samples \( t \) tests. All data are presented as mean ± SD unless otherwise stated.

**Ethical Considerations**

The Regional Committee for Medical and Health Research Ethics, Western Norway consider the project (reference number 2009/502) to be an evaluation program among certified health care workers. Formal approval from Norwegian ethical committee is thus not required. The National Institute for Research in Tanzania has approved this ongoing study as an evaluation of health care workers’ performance with standardized anonymous collection of related routine data on patient outcomes. Informed consent was not obtained.

**RESULTS**

During the 12 months of observation, 4720 infants were born in the hospital and included in the study. Of these, 4595 (97.3%) were liveborn and 256 (5.6%) were admitted to the neonatal area (Fig 1). Perinatal outcomes at 24 hours’ postpartum included the following: normal infants (\( n = 4595 \); 96.0%), still admitted in the neonatal area (\( n = 17 \); 0.4%), neonatal deaths (\( n = 48 \); 1.0%), fresh/intrapartum stillbirths (\( n = 75 \); 1.6%), and macerated/antepartum stillbirths (\( n = 50 \); 1.0%).

Infant characteristics, obstetric history including FHR recordings, and basic resuscitation provided as related to neonatal outcome are presented in Table 2. Infants who died were of lesser BW and GA as compared with normal infants (\( P \leq .0005 \)). The proportion of premature and LBW infants was higher among infants who died than among normal infants (\( P \leq .0005 \)).

Labor complications, delivery via cesarean delivery, abnormal FHR, and the need for basic resuscitation were more frequently recorded among those who died versus normal infants (\( P \leq .0005 \)). There was a delay in time to initiation of bag mask ventilation (BMV) in infants who died versus those with normal outcome, that is, 100 ± 78 vs 62 ± 58 seconds (\( P = .045 \), respectively. In addition infants who died versus those with a normal outcome required a longer duration of BMV, that is, 16 ± 28 vs 5 ± 8 minutes (\( P = .011 \)). The timing and presumed causes of death in infants admitted to the neonatal area is as follows: 6 died within 15 minutes after birth due to severe BA; 41 died within 24 hours secondary to BA (\( n = 24 \); prematurity (\( n = 8 \); LBW (\( n = 4 \); infection (\( n = 1 \); and congenital abnormalities (\( n = 4 \); Fig 1). Two additional infants not admitted to the neonatal area died within 24 hours; 1 due to prematurity, and the other cause of death was unclear.

The characteristics of infants who died by presumed etiology, the obstetric history including FHR recordings, and resuscitation interventions are presented in Table 3. As anticipated, infants

---

**TABLE 1: Information Recorded on the Data Collection Form**

<table>
<thead>
<tr>
<th>Antenatal information</th>
<th>Yes or no</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal care</td>
<td>Yes or no</td>
</tr>
<tr>
<td>Pregnancy complications</td>
<td>Non, uterine, malnutrition, HIV, sepsis, or other</td>
</tr>
<tr>
<td>Maternal infections</td>
<td>Cephalic, breech, shoulder dystocia, transverse, or other</td>
</tr>
<tr>
<td>Labor information</td>
<td>Normal: 120–160 beats per min; Abnormal: &lt;120 or &gt;160 beats per min; Nondetect, not measured</td>
</tr>
<tr>
<td>FHR</td>
<td>Spontaneous vaginal delivery, cesarean delivery, assisted breech delivery, and vacuum extraction</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>Prolonged labor, obstructed labor, preeclampsia, eclampsia, uterine rupture, hemorrhage, or cord prolapse</td>
</tr>
<tr>
<td>Labor complication</td>
<td>Time intervals (s) from birth to initiation of spontaneous respirations and cord clamping</td>
</tr>
<tr>
<td>Neutritional newborn adoption</td>
<td>Boy or girl</td>
</tr>
<tr>
<td>Gender</td>
<td>Grains</td>
</tr>
<tr>
<td>BW</td>
<td>Wk</td>
</tr>
<tr>
<td>GA</td>
<td>1 and 5 min</td>
</tr>
<tr>
<td>Apgar score</td>
<td>Stimulation, suction = BMV with a self-inflating bag, and time interval (s) to initiation of BMV</td>
</tr>
<tr>
<td>Interventions in the delivering room</td>
<td>Newborn heart rate present or not; time interval (s) from initiation of BMV to the onset of spontaneous breathing or death</td>
</tr>
<tr>
<td>Specific observations</td>
<td>A specific reason for admission is written down on the data collection form</td>
</tr>
<tr>
<td>Indication for admission to the neonatal area</td>
<td>Survival &gt;24 h without any detected difficulties</td>
</tr>
<tr>
<td>Penitential outcome at 24 h postpartum</td>
<td>Designated neonatal area</td>
</tr>
<tr>
<td>Normal</td>
<td>Stillbirth</td>
</tr>
<tr>
<td>Admitted</td>
<td>Inappropriately fresh or fresh = intrapartum</td>
</tr>
</tbody>
</table>

---

87
who died secondary to BA were of greater BW and GA as compared with infants who died of prematurity (P ≤ 0.005). In 1 premature infant, the primary cause of death was considered to be BA (Table 3). Among the premature infants who died, 2 were born of mothers with malaria. The rates of labor complications and cesarean deliveries were similar in the different groups. FHR abnormalities were more frequently detected among the infants who died secondary to BA versus prematurity, that is, 13/37 vs 1/9 (P = .03), respectively. Asphyxiated infants required BMV within the first 2 to 3 minutes after birth due to lack of spontaneous respirations more often than infants who died secondary to prematurity, that is, 29/30 vs 5/9 (P = .008), respectively. There was a strong association between need for BMV and asphyxia-related death, when adjusted for BW and GA (odds ratio = 388, 95% confidence interval: 52–2850, P = .0003). The time to onset of BMV was similar between the 2 groups, but the duration of BMV (until the onset of spontaneous breathing or death) was significantly longer in asphyxiated versus premature infants, that is, 19 ± 31 (median 8.5) vs 6 ± 5 (median 4) minutes (P = .05).

Of the asphyxiated infants, 14/30 (47%) had a 5-minute Apgar score <7 of whom 10 had FHR abnormalities, 5 were delivered via cesarean delivery, and 5 died within 15 minutes after birth. Conversely, the remaining 16 infants who died had a 5-minute Apgar score ≥7.

Of the premature infants who died, 5/9 (56%) received basic resuscitation and 1/9 (11%) remained with an Apgar score <7 at 5 minutes and died shortly after admission. All the LBW infants received basic resuscitative actions, and none were recorded to have a 5-minute Apgar score <7.

**DISCUSSION**

These data for the first time provide prospective descriptive observational information on causes of early neonatal deaths in a rural hospital in a resource limited setting. The findings indicate that BA is the predominant cause accounting for 60% of deaths, with prematurity noted in 18% of cases, and LBW and congenital abnormalities are additional causes. Overt infection was a rare cause of early death. Approximately 50% of the “asphyxiated infants” were assigned a 5-minute Apgar score ≥7, which supports a long held notion that the Apgar score is an unreliable indicator of BA. The assignment of BA as a proximate cause of death in this report was strict. It included a complicated obstetric
Table 3: Infant Characteristics Related to Dead Infants (Within 24 Hours) by Etiology

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>BA (n = 30)</th>
<th>Prematurity (n = 0)</th>
<th>P</th>
<th>LBW (n = 4)</th>
<th>Abnormalities (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW (g)</td>
<td>3013 ± 536</td>
<td>1621 ± 247</td>
<td>.0005</td>
<td>1448 ± 591</td>
<td>2477 ± 1004</td>
</tr>
<tr>
<td>GA (wk)</td>
<td>36.4 ± 12</td>
<td>29.0 ± 2.1</td>
<td>.0005</td>
<td>36.5 ± 6.8</td>
<td>34.5 ± 1.9</td>
</tr>
<tr>
<td>Boy</td>
<td>21 (70)</td>
<td>5 (56)</td>
<td>.42</td>
<td>1 (25)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Premature</td>
<td>1 (3.3)</td>
<td>9 (100)</td>
<td>.0005</td>
<td>0 (0)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>LBW</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>.0005</td>
<td>4 (100)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>Obstetric complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy complication</td>
<td>1 (3.3)</td>
<td>1 (11)</td>
<td>.35</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Maternal infection</td>
<td>0 (0)</td>
<td>2 (22)</td>
<td>.06</td>
<td>0 (0)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>Labor complication</td>
<td>15 (50)</td>
<td>4 (44)</td>
<td>.77</td>
<td>2 (50)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>12 (40)</td>
<td>3 (53)</td>
<td>.72</td>
<td>2 (50)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>FHR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (120–160)</td>
<td>17 (56)</td>
<td>8 (80)</td>
<td>.03</td>
<td>4 (100)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>11 (37)</td>
<td>1 (11)</td>
<td>.03</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nondetected</td>
<td>2 (7)</td>
<td>0 (0)</td>
<td>.00</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Not measured</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Resuscitation</td>
<td>29 (97)</td>
<td>5 (56)</td>
<td>.001</td>
<td>4 (100)</td>
<td>3 (75)</td>
</tr>
<tr>
<td>BMW</td>
<td>29 (97)</td>
<td>4 (44)</td>
<td>.001</td>
<td>5 (0)</td>
<td>3 (0)</td>
</tr>
<tr>
<td>Time to start BMW (s)</td>
<td>80 ± 70</td>
<td>103 ± 125</td>
<td>.71</td>
<td>107 ± 50</td>
<td>198 ± 88</td>
</tr>
<tr>
<td>Duration of BMW (s)</td>
<td>1150 ± 1107</td>
<td>340 ± 300</td>
<td>.05</td>
<td>230 ± 94</td>
<td>952 ± 1102</td>
</tr>
<tr>
<td>Apgar 5 min &lt;7</td>
<td>14 (47)</td>
<td>1 (11)</td>
<td>.05</td>
<td>0 (0)</td>
<td>2 (50)</td>
</tr>
</tbody>
</table>

Values given are n (%). P: BA versus prematurity outcome.

History with abnormal FHR measurement in 50%, a consistent failure of infants to initiate spontaneous respirations coupled with the requirement for basic resuscitative actions including BMV, and the absence of overt signs of infection. The finding of a 60% early mortality rate attributed to BA is consistent with findings from rural Ghana and Bangladesh. However, this observation is not consistent with the global estimates of BA-related neonatal mortality of ~25% within 1 month. We speculate that this striking discrepancy is in part due to underreporting of early neonatal deaths, misclassification of asphyxiated infants as stillbirths (the nonbreathing nonresuscitated infant), and an unreliable "high" 5-minute Apgar score.

A basic tenet of the Helping Babies Breathe program is that initiation of BMV within the Golden first minute after delivery in nonbreathing infants has the great potential to reduce early neonatal deaths and "fresh stillbirths" (the nonbreathing nonresuscitated infant) dramatically. This is a critically important concept because it makes the assumption that most nonbreathing infants are in primary apnea and will respond to the early initiation of BMV. We have previously reported that in the same population ~83% of infants spontaneously initiated breathing within the first minute after delivery, ~8% responded to stimulation and suctioning by initiating breathing, and the majority of the remaining infants responded to BMV by initiating breathing within 4 to 5 minutes. The time to initiation of BMV as well as the duration of BMV were significantly longer among infants who died compared with infants with normal outcome. Specifically, the risk for death increased 16% for every 30 seconds' delay in initiating BMV up to 6 minutes and 6% for every minute of applied BMV. In this report, infants with a diagnosis of BA-related deaths were significantly more likely to receive BMV when corrected for BW and GA. Many of these infants presented with obstetrical complications and FHR abnormalities. Analysis of the same population (and reported separately) reveals that FHR abnormalities intermittently detected with the fetoscope identifies fetal compromise, and the risk for early neonatal deaths and fresh stillbirths. Thus, FHR monitoring and anticipation of the potential need for BMV before delivery should become an important teaching point of the Helping Babies Breathe program.

The data also indicate that a multifaceted approach beyond BMV is necessary to achieve the greatest impact of reducing early neonatal mortality. Thus premature and LBW infants did not require much resuscitation in the delivery room suggesting that other potential factors may have contributed to death including temperature instability, hypoglycemia, and unrecognized or unanticipated infection. In the hospital setting in this record, the initial management of the neonate was by family members and labor staff with no specific education in appropriate care and treatment of newborns. This raises the need for simple neonatal protocols to observe and manage the "seemingly stable" prematurity or LBW infant. The lack of basic monitoring equipment and blood tests in this population might have contributed to an underestimation of early infection as a causative factor of death.

Conclusions

The majority of early neonatal deaths are related to BA and failure to initiate spontaneous respirations. The 5-minute Apgar score is a poor surrogate of BA. In general, the deaths of premature and LBW newborns do not appear to be related to cardio-respiratory depression but presumably to known complications such as temperature instability. Reducing early neonatal mortality requires a multifaceted approach with attention related to FHR monitoring and obstetric care, basic neonatal resuscitation including BMV, and potential complications of prematurity and LBW.
ACKNOWLEDGMENTS
This study was made possible because of the research assistants and health providers working in the Maternity Ward at Haydom Lutheran Hospital. Statistical assistance was provided by Bjørn Auestad, PhD, statistician (University of Stavanger). We thank Professors Johanne Sundby (University of Oslo) and Eldar Sætreide (Stavanger University Hospital) for their support.

REFERENCES
18. Ersdal HL, Mduma E, Svensen E, Sundby J, Perlmann JM. Obstetrical factors that increase the risk for fetal heart rate abnormalities, bag mask ventilation, 5 min Apgar score <7, deaths and fresh stillbirths in a low-resource hospital: In: Abstract Pediatric Academic Societies (PAS) Annual Meeting 2011; May 1–4, 2011; Denver, CO
### APPENDICES

### APPENDIX 1

Supplemental material presenting prospective observational data before/after implementation of the “HBB program” at Haydom Lutheran Hospital

<table>
<thead>
<tr>
<th>Time Period</th>
<th>01.02.10 - 29.01.11</th>
<th>01.02.11 - 31.01.12</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Deliveries</td>
<td>4876</td>
<td>4734</td>
<td></td>
</tr>
<tr>
<td>Babies resuscitated by</td>
<td>67.5 %</td>
<td>90.8 %</td>
<td>≤ 0.0005</td>
</tr>
<tr>
<td>Provider trained in HBB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal Deaths/1000</td>
<td>11.1/1000 (n=54)</td>
<td>7.2/1000 (n=34)</td>
<td>0.047</td>
</tr>
<tr>
<td>FSB/1000</td>
<td>16.0/1000 (n=78)</td>
<td>14.4/1000 (n=68)</td>
<td>0.517</td>
</tr>
<tr>
<td>Number of babies</td>
<td>704 (14.4 %)</td>
<td>758 (16.0%)</td>
<td>0.032</td>
</tr>
<tr>
<td>Stimulated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of babies face</td>
<td>352 (7.2 %)</td>
<td>259 (5.7%)</td>
<td>0.003</td>
</tr>
<tr>
<td>mask ventilated</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Pearson Chi-Square analysis, 2-sided

Absolute Risk Reduction for early neonatal mortality = 0.39
# APPENDIX 2

**ONE FORM FOR EACH DELIVERY TO BE FILLED IN AT HLH**

<table>
<thead>
<tr>
<th>MOTHERS HOSPITAL ID</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>NEWBORN ID</td>
<td></td>
</tr>
<tr>
<td><strong>If Multiples (twins and more)</strong></td>
<td>Newborn number (write 8 if single birth)</td>
</tr>
<tr>
<td>Date of birth</td>
<td>DAY MONTH YEAR</td>
</tr>
<tr>
<td>Time of birth</td>
<td>HOURS MINUTES</td>
</tr>
<tr>
<td>Antenatal care attendance</td>
<td>1 YES 2 NO</td>
</tr>
<tr>
<td>Pregnancy complication</td>
<td>1 YES 2 NO</td>
</tr>
<tr>
<td><strong>Source of admission</strong></td>
<td>Referred from health centre 2 Inpatient</td>
</tr>
</tbody>
</table>

**LABOUR INFORMATION**

| Equipment checked | 1 YES 2 NO |
| Delivery kit present | 1 YES 2 NO |
| Resuscitation kit present | 1 YES 2 NO |
| Maternal Infection | 1 no 2 uterine 3 malaria 4 HIV 5 others |
| Sepsis | 1 YES 2 NO |
| Fetal heart rate | 1 Normal (120-160) 2 Abnormal 3 Not detectable 9 Not measured |
| **Mode of delivery** | 1 SVD 2 C/S 3 ABD 4 Vaccum |
| Presentation | 1 Cephalic 2 Breech 3 Shoulder dystocia 4 Transverse 5 Others |
| HCW attending the delivery | 1 Midwife 2 Ward attendant 3 Student 4 Clinical officer 6 None |

**LABOUR COMPLICATION**

<p>| Prolonged labour | 1 YES 2 NO |
| Obstructed labour | 1 YES 2 NO |
| Vacuum | 1 YES 2 NO |
| Cesarean Section | 1 YES 2 NO 3 Elective |
| Pre-eclampsia | 1 YES 2 NO |
| Eclampsia | 1 YES 2 NO |</p>
<table>
<thead>
<tr>
<th>Condition</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine rupture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cord prolaps</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding (i.e. placenta previa)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NEONATAL INFORMATION**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td></td>
</tr>
<tr>
<td>Gestational age</td>
<td></td>
</tr>
<tr>
<td>Sex of newborn</td>
<td>MALE</td>
</tr>
</tbody>
</table>

**Time intervals**

- Birth – breathing
- Birth - cord clump

**Apgar score (range 0-10)**

1 MIN 5 MIN

**RESUSCITATION ATTEMPTED**

1 YES; Fill in this section 2 NO; go to next section

<table>
<thead>
<tr>
<th>Stimulation</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>suction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bag valve ventilation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Who provided resuscitation**

- Midwife
- Operating Nurse
- Clinical Officer
- Doctor
- Other: ____________________

**Last training in newborn resuscitation**

Was that a HBB course?

<table>
<thead>
<tr>
<th>MONTH</th>
<th>YEAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2 NO</td>
</tr>
</tbody>
</table>

**PERINATAL OUTCOME**

within 30 min

<table>
<thead>
<tr>
<th>NORMAL</th>
<th>Admitted unit (room 20)</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Stillbirth (fresh)

<table>
<thead>
<tr>
<th>Stillbirth (macerated)</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Neonatal outcome**

- at 24 hours postpartum /or
- at discharge ___ hours postpartum

Observer’s initial ____________________________
APPENDIX 3

The “National HBB Data Collection Form”

ONE FORM FOR EACH NEWBORN

| MOTHERS HOSPITAL ID | ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ impres
APPENDIX 4

The Standard Operating Procedure (SOP)

Purpose: The purpose for this SOP is to describe the requirement and procedure to follow in collecting and filling the HBB form in maternity Ward at Haydom Lutheran Hospital (HLH) for standardization and adherence to “Towards MDG4&5” study protocol.

Scope: This SOP applies to all HBB study team involved in collecting the information, filling the forms, doing QC and data entry with the “Towards MDG4&5” study.

Responsibilities: The Investigators (PI and Co-PIs), study supervisor and other staff who will be responsible in the “Towards MDG4&5” are obliged to read, understand and follow this SOP during developing and revision of the SOP to be used in the “Towards MDG4&5” study Protocol.

Procedure:

1. Involved study staff will have to identify all the procedure that will be involved in the “Towards MDG4&5” study. RA will be responsible to fill the form.
2. Whenever possible, the research staff who will be involved in following the SOP should be involved in the SOP development process.
3. The SOP effective date and date of revision should be modified wherever there is change and be started by mentioning the revision date e.g. version 1.0, 1.1, 1.2, 1.3 etc.
4. All those who should be involved in using/following the SOPs for the study procedure conduct should be stated on the scope and sometime including their roles e.g. study.
5. Variables and description of collecting and recording the information:

Abbreviations:
AMO – Assistant Medical Officer
HBB - Helping Babies Breath
HLH - Haydom Lutheran Hospital
MDG – Millennium Development Goal
RA - Research Assistant
SOP - Standard Operating Procedure
QC – Quality Check

<table>
<thead>
<tr>
<th>MOTHERS HOSPITAL ID</th>
<th>Mother ID should be hospital ID and the last 2 digit be last 2 digit of exciting year e.g. 12 (for year 2012). Boxes with no entry filed with 000. e.g. mother ID 2556, year 2012 will be: “000255612”</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEWBORN ID</td>
<td>This is new born unique number, and will be filled during data entry</td>
</tr>
<tr>
<td><strong>If Multiplies (twins and more)</strong></td>
<td>Newborn number(s) if twins write “1” for 1st twin and “2” for 2nd twin etc. If single birth write “8”</td>
</tr>
<tr>
<td>Date of birth</td>
<td>Record 2 digit on date, 2 on month and 2 last digit for</td>
</tr>
<tr>
<td>Time of birth</td>
<td>Record hours on 24 round time, and 2 digits for minutes(s). e.g. “14.08” (for 2pm and 8 minutes)</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Antenatal care attendance</td>
<td>Collect this information from mother of Antenatal card, and record “YES” if attended antenatal care and “NO” if was not enrolled and attending antenatal care</td>
</tr>
<tr>
<td>Pregnancy complication</td>
<td>Information from patient hospital record or caregiver e.g. midwife, doctor etc. Record “1 YES” if there was complication and “2NO” if there was no complication</td>
</tr>
<tr>
<td><strong>Source of admission</strong></td>
<td>If patient was referred from other health facility mark “X” on Referred from health centre box, and if not e.g. from home mark “X” on 2 Inpatient box</td>
</tr>
<tr>
<td><strong>LABOUR INFORMATION</strong></td>
<td></td>
</tr>
<tr>
<td>Equipment checked</td>
<td>Observe If caregiver checked delivery kit equipment before starting conducting delivery mark “X on 1 YES” box, if didn’t check mark “X on 2 NO” box.</td>
</tr>
<tr>
<td>Delivery kit present</td>
<td></td>
</tr>
<tr>
<td>Resuscitation kit present</td>
<td>Observe If care gives checked Resuscitation kit before starting conducting delivery mark “X on 1 YES” box, if didn’t not check mark “X on 2 NO” box.</td>
</tr>
<tr>
<td>Maternal Infection</td>
<td>Collect information from patient file or caregiver if patient have infection and mark “X” on appropriate box YES/NO.</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Collect information from patient or care give if patient have sepsis and mark “X” on appropriate box YES/NO</td>
</tr>
<tr>
<td>Fetal heart rate</td>
<td>Collect information from patient file or caregiver about fetal heart rate and mark “X” on appropriate box. Possible answers are “1 Normal (120-160)”, “2 Abnormal” “3 Not detectable” and “9 Not measured”</td>
</tr>
<tr>
<td><strong>Mode of delivery</strong></td>
<td>Observe or collect from caregiver and mark “X” on appropriate box. Possible answers are “1 SVD”, “2 C/S”, “3 ABD” or “4 Vacuum”</td>
</tr>
<tr>
<td>Presentation</td>
<td>Collect information from patient file or caregiver, and mark “X” on appropriate box possible answers are “1 Cephalic”, “2 Breech”, “3 Shoulder dystocia”, “4 Transverse” or “5 Others”</td>
</tr>
<tr>
<td>HCW attending the delivery</td>
<td>Observe or collect from caregiver and mark “X” on appropriate box. Possible answers are “1”</td>
</tr>
<tr>
<td>LABOUR COMPLICATION</td>
<td>Action</td>
</tr>
<tr>
<td>---------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Midwife”, “2 Ward attendants”, “5 Doctor”, “3 Student”, “4 Clinical officer” or “6 None”</td>
<td>Observe or collect from caregiver and mark “X” on appropriate box. Possible answers are “1 YES” if had complication and proceed to fill in this section, or “2 NO” if there was no complication and skip to next section</td>
</tr>
<tr>
<td><strong>Prolonged labour</strong></td>
<td>Collect from caregiver and mark “X” on appropriate box. Possible answers are “1 YES” if was prolonged and “2 NO”</td>
</tr>
<tr>
<td><strong>Obstructed labour</strong></td>
<td>Collect from caregiver and mark “X” on appropriate box. Possible answers are “1 YES” if was obstructed labour meaning the newborn was not able to pass through the birth canal for any reason e.g. CPD, malposition etc, or “2 NO” if was not obstructed.</td>
</tr>
<tr>
<td><strong>Vacuum</strong></td>
<td>Observe and mark “X” on appropriate box. Possible answers are “1 YES” if vacuum was done.</td>
</tr>
<tr>
<td><strong>Cesarean Section</strong></td>
<td>Observe and mark “X” on appropriate box. Possible answers are “1 YES” if CS was done or “2 NO” if CS was not done, or “3 Elective” if CS was done following pre-plan before starting labour and have to mention the reason on space provided “__________”</td>
</tr>
<tr>
<td><strong>Pre-eclampsia</strong></td>
<td>From caregiver (on few occasion Observe) and mark “X” on appropriate box. Possible answers are “1 YES” if patient was reported to have pre-eclampsia and “2 NO” if not.</td>
</tr>
<tr>
<td><strong>Eclampsia</strong></td>
<td>From caregiver (observation on some occasion) and mark “X” on appropriate box. Possible answers are “1 Yes” if patient has both signs of Pre-eclampsia and Fits, and “2 NO” if not.</td>
</tr>
<tr>
<td><strong>Uterine rupture</strong></td>
<td>Collect from caregiver and mark “X” on appropriate box. Possible answers are “1 YES” if reported to have rupture of uterus, or “2 NO” if uterus was intact</td>
</tr>
<tr>
<td><strong>Cord prolaps</strong></td>
<td>Observe or collect from caregiver and mark “X” on appropriate box. Possible answers are “1 YES” if cord was preceding/ahead of the fetus before deliver or “2 NO” if the cord followed after delivery.</td>
</tr>
<tr>
<td><strong>Bleeding</strong> (i.e. placenta previa)</td>
<td>Observe and collect from caregiver and mark “X” on appropriate box. This involves bleeding that occurred before delivery. Possible answers are “1 YES” if bleeding was estimated to be ≥ 500mls or “2 NO” if bleeding was estimated to be &lt;500mls</td>
</tr>
</tbody>
</table>

| **NEONATAL INFORMATION** | |

| **Birth weight** | Weigh the newborn or collect from caregiver and write the weight in GRAM in the boxes provided and fill all. If Macerated stillbirth, don’t respond |

| **Gestational age** | Observe from ANT card or collect from caregiver and write the WEEKS in the boxes provided. |

| **Sex of newborn** | Observe and mark “X” on appropriate box. Possible answers are “1 MALE” or “2 FEMALE” |

| **Time intervals** | Observe and measure with STOP WATCH time from when the newborn was out of the birth canal to when started breathing/crying. Possible answers write time in SECONDS in 4 boxes provided if resuscitation is needed |

| **birth –breathing** | Observe and measure using STOP WATCH time from when the newborn was out of the birth canal to when the cord was clumped, record time in SECONDS in provided boxes. If clumped before delivery (e.g. In cord prolapsed fill 00) |

| **birth - cord clump** | |

| **Apgar score (range 0-10)** | Collect from Patient file or Caregiver and record score in “1 MIN” and Score at “5 MIN” |

| **RESUSCITATION ATTEMPTED** | Observe if resuscitation was attempted, possible answer is “1 YES” if was attempted or “2 NO” if was not attempted and have to SKIP to next section |

| **stimulation** | If stimulation was done by rubbing the newborn and possible answers are “1 YES” if was done, or “2 NO” if no rubbing was attempted |

| **suction** | If stimulation was done by sucking the newborn and possible answers are “1 YES” if was done, or “2 NO” if no sanction was attempted |

| **bag valve ventilation** | Observe if bag valve was used to ventilate the newborn. Possible answer “1 YES” if was done, and “2 NO” if was not done. |
**heart rate evaluated**

Observe if caregiver evaluated heart rate of the newborn. Possible answers “1 YES” if was evaluated and “2 NO” if was not evaluated. “if 2 NO” SKIP to next question

Collect (ask) caregiver if heart rate was present. Possible answer is “1 YES” if caregiver reported to be present or “2 NO” if heart rate was not detected.

**heart rate present**

**Time intervals**

**birth - breathing or ventilation**

Time from Birth to start breathing in seconds using stop watch and mark “X” on appropriate box. Possible “1 breathing” or “2 ventilation”. If the response is “1” fill seconds on box and skip the following question to who provided. If the answer is “2” record seconds of time from birth to start ventilation.

Record time using stop watch in seconds, possible answer after recording seconds “1 breathing” or “2 Death”.

**ventilation - breathing or death**

**Who provided resuscitation**

Observe or ask and record who provided resuscitation to the new born and mark “X” on appropriate box. Possible answer is “1 Midwife” “2 Operating Nurse”, “3 Clinical Officer”, “4 Doctor” “5 Other” or “6 AMO”, if response is “5” mention designation of who provided resuscitation.

**Last training in newborn resuscitation**

Last time that resuscitation provider attended training on resuscitating newborn, record date in format DDMMYY.

Ask and record if that training in newborn resuscitation was HBB training. Possible answer is “YES” or “2 NO”

**PERINATAL OUTCOME within 30 min**

Observation and confirming from caregiver, The outcome of birth within the first 30 minutes post delivery and mark with “X” on appropriate box. Possible answer is “1 NORMAL, “2 Admitted (room 20)” “3 Death”, “4 Stillbirth (fresh)” or “5 Stillbirth (macerated)” If response is “3”, “4”, or “5” skip neonatal outcome

**Neonatal outcome at 24 hours postpartum /or**

Observe and find more from caregiver, and mark appropriate box with “X”. Possible
<table>
<thead>
<tr>
<th>at discharge ____ hours postpartum</th>
<th>response “1 NORMAL, “2 Seizures”, “3 Death” or “6 Difficulties in breathing”</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>POSTPARTUM MATERNAL COMPLICATION</strong></td>
<td>Find out from caregiver and mark appropriate box with “X”. Possible answer “1 YES or “2 NO”; if response is “1” Fill in separate form (Post partum maternal information), if “2” End of form</td>
</tr>
<tr>
<td>Observer’s initials</td>
<td>Initials of RA/research staff who filled the form</td>
</tr>
</tbody>
</table>