

# University of Malawi



College of Medicine

## **Aetiology of Stillbirths and Adverse Newborn Outcomes at Queen Elizabeth Central Hospital, Blantyre, Malawi**

By

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## **Declaration**

I hereby declare that this thesis is my original work and has not been presented for any other awards at the University of Malawi or any other University.

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## **DEDICATION**

This is for you, Watowa and Wanga. Thanks for always being there and reminding me to eat upon getting home, from work, though it was usually very late.

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## **ABSTRACT**

### **Background**

Death of an infant in utero or at birth is a devastating experience for the mother and of concern in clinical practice. Developing countries struggle to provide comprehensive care to pregnant mothers and the new born. Stillbirths are common in poor countries that their occurrence is perceived inevitable. We aimed to characterize factors associated with stillbirth in our referral hospital population. Intrapartum birth asphyxia is a major contributor of high perinatal mortality in resource limited countries like Malawi. In low and middle income countries, about 59 % of the stillbirths are intrapartum unlike in developed countries where it is significantly lower than 10%. Studies done in Malawi have shown that birth asphyxia is a common cause of stillbirth.

Furthermore, babies born with asphyxia may have increased long-term morbidity such as cerebral palsy, hence the need to identify new-borns at risk.

The analysis of umbilical cord blood gases has been shown to be the gold standard for diagnosis of near-birth metabolic acidosis. Lactate has emerged as the preferred marker of acidosis in clinical practice.

## **Main Objective**

To determine the aetiology of stillbirths and adverse new-born outcomes among women delivering at Queen Elizabeth Central Hospital (QECH), Blantyre, Malawi

## **Methodology**

This was a cross-section study done in two phases. In the first phase, data on all stillbirths that occurred at QECH between 1st August 2016 and 31st September 2016 was collected from the labour ward and Chatinkha operating theatre registries and patients' files. All mothers of stillborn babies during the study period gave informed consent to participate in the study and have their blood samples collected and tested for VDRL, malaria, haemoglobin and fasting blood sugar on the bedside using point of care syphilis testing kit (Determine), malaria rapid diagnostic testing kit, Hemacue and glucometer respectively. The stillbirths were classified using the RECODE system

The second phase was undertaken during April 2017. Data on all 401 births that occurred at QECH were collected from the labour ward and operating theatre registries and patients' files. For all live births, umbilical arterial blood was drawn from a double clamped segment into heparinised plastic syringes. Lactate concentration in Umbilical cord arterial blood was analysed using Nova biomedical point of care devices within 15 minutes. All mothers had their blood samples collected and tested for VDRL, malaria, haemoglobin and fasting blood sugar at the bedside using point of care syphilis testing kit (Determine), malaria rapid diagnostic testing kit, Hemacue and glucometer respectively.

## **Results**

During the first phase of the study, there were 54 stillbirths among 2149 deliveries translating to 25.1/1000births with 61% fresh stillbirths and 35% macerated stillbirth. 34% of the stillbirths were delivered through Caesarean section that was done after more than an hour from decision to undertake the procedure. Common relevant conditions at delivery were anaemia (52%), asphyxia (40%), hypertensive disorders (29%), placenta abruption



(27%), HIV (25%) and syphilis (15%). None of the mothers had malaria or diabetes Mellitus.

In phase two, the perinatal mortality was 44.9/1000births. The leading documented cause of nursery admission was birth asphyxia (41.7%). Shortage of theatre space accounted for all delays to do emergency Caesarean sections. Hyperlactatemia was associated with emergency caesarean sections, meconium stained liquor and vertex vaginal deliveries. There was no association between Hyperlactatemia and antepartum haemorrhage, gestational age, multiple gestation, PPROM, anaemia or malaria. Logistic regression modelling revealed that the odds of a composite adverse outcome (early neonatal death or admission to the neonatal unit) were significantly elevated in the presence of maternal hypertension (OR=2.9, P=0.019(95% C.I. 1.19-7.26)) after adjusting for the degree of hyperlactatemia.

## **Conclusion**

The study highlighted the risk factors for stillbirths at QECH. The risk factors for stillbirths at QECH include; preeclampsia, abruption placenta, anaemia, syphilis, and asphyxia. Poor intrapartum care attributed to lack of theatre capacity was the single most important cause of fresh stillbirths. None of the participating mothers had diabetes mellitus or malaria contrary to findings from other studies where both conditions were associated with increased risk of stillbirth. The ANC coverage was adequate, however, the quality of care provided in the centres needs improvement especially with regard to blood pressure testing and syphilis screening.

Birth asphyxia is the most common cause of admission to the nursery and high perinatal mortality. The Apgar score at one minute is a good predictor of hyperlactatemia, however,

it over-diagnoses acidosis. Hypertensive mothers had 19% higher risk of having poor neonatal outcome for any given level of umbilical cord arterial lactate so additional attention to intrapartum and newborn monitoring for hypertensive mothers is required.

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## **ABBREVIATIONS AND ACRONYMS**

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AAP	American Academy of Pediatrics
ACOG	American Congress of Obstetricians and Gynaecologists
ANC	Antenatal Clinic
APH	Antepartum Haemorrhage
BP	Blood Pressure
CMU	Chatinkha Maternity Unit
CN-ICU	Chatinkha Nursery Intensive Care Unit
COMREC	College of Medicine Research Ethics Committee
CPD	Cephalopelvic Disproportionate
CS	Caesarean Section
CTG	Cardiotocograph
EFM	Electronic Foetal Monitoring
ENND	Early Neonatal Death
ENNM	Early Neonatal Mortality
FBS	Fasting Blood Sugar
FSB	Fresh Still Birth
HIV	Human Immunodeficiency Virus
IUFD	Intra-uterine Foetal Demise
LNMP	Last Normal Menstrual Period



MDHS	Malawi Demographic Health Survey
MRDT	Malaria Rapid Diagnostic Test
MSB	Macerated Stillbirth
OR	Odds Ratio
PPH	PostPartum Haemorrhage
PPROM	Preterm Prelabour Rupture of Membranes
QECH	Queen Elizabeth Central Hospital
RDS	Respiratory Distress Syndrome
RECODE	Relevant Condition at Death
Rh	Rhesus
ROC	Receiver Operating Characteristics
SPR	Specialty Program Registrar
SPSS	Statistical Package for the Social Sciences
SVD	Spontaneous Vaginal Delivery
TTN	Transient Tachypnoea of Newborn
UTI	Urinary Tract Infection
VDRL	Venereal Disease Research Laboratory
WHO	World Health Organisation

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## **Chapter 1: Introduction**

### **1.1 Background Information**

Developing countries are still facing challenges in the care for pregnant women and the new born as evidenced by the perinatal mortality rate which remains unacceptably high. Stillbirths are common in these nations such that their occurrence is perceived inevitable. An estimated 3.2 million babies die every year in-utero in the third trimester with the majority (99%) occurring in poor resource settings [1]. Globally, 2.6 million stillbirths occurred in 2015 alone [2]. About 26% of all stillbirths are related to intrapartum care (fresh stillbirths)[3], and the frequency of Early Neonatal Mortality (ENNM) and macerated stillbirths remains high[4]. About 59% of the stillbirths in low and middle income countries are intrapartum unlike in developed countries where it is less than 10% [2].

Over two-thirds of stillbirths are attributable to causes for which preventive and therapeutic interventions are available like hypertensive disorders in pregnancy, antepartum hemorrhage, underlying maternal illnesses (malaria, syphilis and HIV) and other obstetric complications. Other common causes of stillbirths include post-term pregnancy, fetal growth restriction and congenital abnormalities [2]. Existing maternal chronic conditions such as hypertension, cardiac disease, and diabetes, have also been identified but limited literature is available, especially in developing countries like Malawi, Zimbabwe, Zambia and many more. Fretts and colleagues in Zimbabwe, found obesity, advanced maternal age and socioeconomic status to be associated with stillbirths [5, 6]. However, these conditions are not very common among African women unlike in the western and other developed countries. Different studies have shown that not receiving prenatal care, poor intrapartum

care, breech delivery, instrumental delivery are associated with increased risk of delivering a stillbirth or asphyxiated baby[1-4].

Queen Elizabeth Central Hospital(QECH), Malawi's largest referral and teaching hospital, had a stillbirth rate of 34/1000births in 2005[10]. Most of the stillbirths were attributable to unexplained intrauterine growth restriction, abruption placenta, congenital malformations, infections, intrapartum asphyxia and several others were unexplained[7]. A verbal autopsy done in Mchinji, Malawi's central region rural hospital, found perinatal asphyxia; prematurity; congenital abnormalities and neonatal infections as the leading causes of stillbirths [8, 9]. In these studies, the factors contributing to the high rates of intrapartum asphyxia were not identified and there was no objective measure for the diagnosis of the birth asphyxia. The Apgar scoring, which is a method of assessing clinical status of the new born, is known to have inter-observer variability and can be influenced by maternal sedation and maturity status of the baby rather than hypoxia alone. Furthermore, for the score to be affected, there has to be a significant biochemical disturbance [10]. Different studies have shown that the measurement of lactate at birth is an objective measure for the diagnosis of birth asphyxia occurring immediately before birth [11-15]. However, high rates of intrapartum asphyxia in fetuses weighing more than 2500grams, suggests deficiencies in quality obstetric care. In a meta-analysis by Ruth Fretts, quality intrapartum care was shown to decrease the stillbirth rate by 95% [6]. Health care providers and clients, have expressed dissatisfaction with the quality of services rendered to mothers in perinatal period at QECH, but very limited data is available to support or defy their views[16].

Intrapartum care is influenced by several factors primarily availability of trained personnel, equipment, hospital supplies and drugs. Malawi's health system has been deteriorating over the past decade owing to the ever worsening economic environment which has affected the procurement of drugs, equipment, servicing and maintenance of medical equipment, hospital supplies and deployment and retention of qualified staff [17]. The impact of such hardships is yet to be evaluated across Malawi's health service provision cascade.

## **1.2 Literature review**

### **1.2.1 Lactate and Birth Asphyxia**

Lactate is produced from the reduction of pyruvate by lactate dehydrogenase under anaerobic conditions. The lactate is then released into the blood stream where it accumulates and only to be removed or recycled after restoration of oxygen supply. The blood lactate concentration increases when the rate of production exceeds the rate of removal[18]. High blood lactate levels above 2mmol/L, hyperlactatemia, may occur in hypoxic or ischemic states or as a normal physiologic response to exertion [19]. In patients with hypovolemic and septic shocks, the blood lactate levels are higher than normal as there is tissue hypoxia [15]. Catecholamines produced in shock are also known to increase the lactate production [20].

Birth asphyxia develops due to fetal hypoxia resulting into acidosis and vital function depression. Babies born asphyxiated are known to have increased long-term morbidity such as cerebral palsy, hence the need to diagnose the fetus at risk and appropriately intervene [21]. In different setups, clinical parameters are in use to both diagnose and

predict the prognosis of birth asphyxia, among which are non-reassuring fetal heart rate patterns, meconium stained liquor, low Apgar scores at 5 minutes and mild to moderate acidemia. In January 2003, the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP) formulated criteria that collectively suggest intrapartum timing but are nonspecific to asphyxia insults [22].

In an effort to reduce the occurrence of birth asphyxia, the federation of obstetricians and gynaecologists (FIGO) recommends the use of a partograph where fetal heart rates are checked using battery powered fetal doppler at intervals depending on the stage of labour [23]. Electronic Fetal heart rate Monitoring (EFM) during labour with cardiotocography (CTG) was established to improve intrapartum care. However, the two methods are associated with significantly high false negatives and false positives respectively and thus leading to high rates of caesarean sections for presumed non-reassuring fetal status [21]. Therefore, the measurement of blood gases has become the gold standard for identifying intrapartum fetal hypoxia. These interventions are unavailable in poor resource settings.

In both adults and neonates, plasma lactate concentrations have been used as an indicator of tissue hypoxia and prognostic indicator in critically ill patients [15]. Lactate measurement is a precise tool in assessment of fetal metabolic acidosis [21].

Babies born in Chatinkha Maternity Unit (CMU) are assessed as to whether resuscitation is needed, owing to hypoxia, using Apgar scores. All babies with Apgar scores of  $\leq 7$  at 5 minutes are admitted to Chatinkha nursery with a diagnosis of birth asphyxia. Umbilical blood gases are not measured due to lack of resources and this affects objective diagnosis of asphyxia.

### **1.2.2 Classification of Stillbirths**

The identification of the cause of death for every stillbirth is vital in the development, implementation and monitoring of the preventive interventions of stillbirths. It is challenging to attribute a single condition as a cause of a stillbirth as there is limited knowledge of diseases and normal fetal physiology. This has led to uncertainty about certain conditions being causes of stillbirths. There are over 35 classification systems of stillbirths developed with different backgrounds and purpose [24]. The best classification identifies the pathophysiological entity initiating the chain of events that irreversibly lead to death. Strategies to understand and prevent the occurrence of stillbirths can be derived from these classifications. Stillbirth classification is important as it enhances counselling and education of the parents and health professionals. It also allows the identification of groups of people at risk leading to generation of targeted interventions that would reduce the stillbirths.

All classification have their merits and demerits and their use and application depends on the capacity (well-equipped laboratories) of the health care system in a given country [25]. Another area of contention comes from lack of a single definition of “stillbirth” as it is different between countries, organizations, investigators and classification systems. Some of the classification systems, are designed to include both the stillbirths and neonatal deaths while others do not.

The commonly used classification systems are;

### **Revised Aberdeen**

Designed to identify the factor with the highest probability of initiating the train of events leading to the death of the fetus or neonate for the purpose of prevention of the perinatal deaths. Due to regional differences in its use, the classification was revised and published in 1986 [26]

### **Wigglesworth**

Designed to identify the cause of perinatal death, in order to improve and understanding the causes of stillbirths for the purposes of prevention. It was revised to include autopsy but does not entirely rely on it [26].

### **Tulip**

Developed to identify the underlying cause and mechanism of death for the purpose of counselling and prevention [26]

### **ReCode (Relevant Condition at Death)**

It was developed in 2003 by J. Gardosi and colleagues in West Midlands region, United Kingdom. They classified the stillbirths with the aim of identifying the relevant condition at the time of death in utero. It identifies “what went wrong” and hence good for teaching, counselling, public health policy development [26]. The system is associated with the reduction in proportion of unexplained stillbirths from 66.7% (Wigglesworth classification) to just 15%[26].

The ReCoDe classification system recognizes the difference between the stillbirth and neonatal death hence the separate classification. It also uses the fetal growth status (weight for gestation age) as opposed to the use of the traditional prematurity and birth weight alone. It does not rely on finding the underlying cause thus it can be used in absence of

placental histology and or post-mortem [26]. In this study, the ReCoDe system will be used as the focus is on stillbirths only and does not entirely depend on the histology or post-mortem [26].

**Table 1: Classification of stillbirth by relevant condition at death (ReCoDe) [26].**

<b>Classification system according to Relevant Condition at Death (ReCoDe)</b>		
<b>Group A: Fetus</b>		<b>Group E: Uterus</b>
1. Lethal congenital anomaly		1. Rupture
2. Infection		2. Uterine anomalies
2.1 Chronic		3. Other
2.2 Acute		<b>Group F: Mother</b>
3. Non-immune hydrops		1. Diabetes
4. Isoimmunisation		2. Thyroid diseases
5. Fetomaternal haemorrhage		3. Essential hypertension
6. Twin-twin transfusion		4. Hypertensive diseases in pregnancy
7. Fetal growth restriction*		5. Lupus or antiphospholipid syndrome
<b>Group B: Umbilical cord</b>		6. Cholestasis
1. Prolapse		7. Drug misuse
2. Constricting loop or knot†		8. Other
3. Velamentous insertion		<b>Group G: Intrapartum</b>
4. Other		1. Asphyxia
<b>Group C: Placenta</b>		2. Birth trauma
1. Abruption		<b>Group H: Trauma</b>
2. Praevia		1. External
3. Vasa praevia		2. Iatrogenic
4. Other “placental insufficiency”‡		<b>Group I: Unclassified</b>
5. Other		1. No relevant condition identified
<b>Group D: Amniotic fluid</b>		2. No information available
1. Chorioamnionitis		
2. Oligohydramnios†		
3. Polyhydramnios†		
4. Other		

\* <10th customised weight for gestational age centile.  
† If severe enough to be considered relevant.  
‡ Histological diagnosis



### **1.3 The rationale for the study**

Muula and colleagues found the stillbirth rate to be 34/1000 live births in 2005 [7]. These stillbirths were attributed to unexplained intrauterine growth retardation, abruption placenta, congenital malformations, infections, intrapartum asphyxia and several others were unexplained. They recommended the need to investigate further the factors that may be associated with these diagnoses and consequently leading to stillbirths.

Birth asphyxia has been shown to be the main cause of neonatal admission in Malawi; however, the diagnosis of birth Asphyxia was based on Apgar scores which are known to be subjective and may lead to inaccuracies in the rates of occurrence [27-29].

## **Chapter 2: Study objective**

### **2.1 Main objective**

To determine the aetiology of stillbirths and adverse newborn outcomes delivered at QECH, Blantyre, Malawi.

### **2.2 Specific Objectives**

- To determine the prevalence of birth asphyxia using an objective measure
- To determine the proportion of intrapartum versus antepartum stillbirths
- To classify stillbirths using the RECODE system
- To identify factors associated with the occurrence of intrapartum stillbirths
- To make recommendations for service development for care and support of stillbirth parents

## **Chapter 3: Study methodology**

### **3.1 Study Design**

This was a cross-sectional study. For practicality and due to financial constraints, the study was divided into two phases, each supporting the other in achieving the main objective yet conclusive in its own respective specific objectives.

The first phase focused on the prevalence and factors associated with the occurrence of the fresh and macerated still births. This phase had a sample size of 52 stillbirths that occurred between 1<sup>st</sup> August and 30<sup>th</sup> September 2016. Data on all stillbirths, satisfying the inclusion criteria, was collected from both patients' files and patients themselves

The second phase focused on the intrapartum care and the incidence of birth asphyxia using lactate measurement as an objective biochemical measure. This phase had a sample size of 401 and it ran for 14 days. Data on all births occurring at QECH between 1<sup>st</sup> and 14<sup>th</sup> April 2017 was collected from the labour ward and Chatinkha operating theatre registries and patients' files immediately after birth. For the second phase, all deliveries less than 28 completed weeks were excluded. Gestational age; estimated by the number of days between the first day of the last normal menstrual period (LNMP) and date of birth expressed in completed weeks. Alternatively, first or early second trimester ( $\leq 24$  weeks) ultra sound scan expressed in completed weeks, or Symphysis-fundus height measured at first or early second trimester ( $\leq 24$  weeks) antenatal visit, whichever comes first, expressed in centimetres. Deliveries before arrival at CMU, deliveries in ambulances en-route to, or on arrival at CMU and women arriving at CMU in Second stage of labour were also excluded.

### **3.2 Study setting**

The study was carried out at QECH's CMU which is the largest referral hospital in Malawi. CMU is the largest referral maternity unit in southern Malawi. It is both a secondary and tertiary health care unit for Blantyre residents and the seven surrounding districts respectively. It has a labour ward with 24 delivery beds and has an average of 720 deliveries per month. The labour ward has 22 midwives that work in eight hour day shifts and 16 hour night shifts.

CMU is also a training centre for medical doctors specialising in obstetrics and gynaecology, intern medical doctors, Bachelor of Science students in Obstetrics and Gynaecology, Bachelor of Medicine and Surgery and different nursing courses. Each 24 hour shift has a team comprising of one consultant, two Specialty Program Registrars (SPRs), three intern medical officers and at least 10 medical students studying for Bachelor of Science in Obstetrics and Gynaecology, Bachelor of Medicine and Surgery and different nursing courses. The number of midwives on each shift varies with the availability, and ranges from one (at its worst) to eight midwives. Most midwives work on part time (LOCUM) basis.

High risk patients from surrounding health facilities are referred to the unit without any prior arrangement. All patients are dropped at the admission bay which is manned by a single midwife and admitted into the labour ward upon assessment.

There are two consultant ward rounds that focus on both teaching and patient care. Consultants may visit the ward any number of times in between the ward rounds if there is a problem. In between those ward rounds, SPRs are in constant communication with the on call consultant and intern medical officers. Caesarean sections can be ordered by the

SPRs upon discussion with the on call consultant. Most of the caesarean sections are done by the intern medical officers and SPRs.

### **3.3 Inclusion criteria**

- All stillbirths occurring at CMU between the 1<sup>st</sup> August and 30<sup>th</sup> September 2016, and all deliveries between the 1<sup>st</sup> and 14<sup>th</sup> April 2017
- All stillbirths and poor outcomes delivered at CMU during the study period

### **3.4 Exclusion criteria**

- All preterm births less than 28 completed weeks gestation age.
- Births without information on
  - Apgar Scores
  - Birth-weight; defined as the first measurement of body weight usually in the first hour of life, measured to the nearest gram
  - Gestational age; estimated by
    - The number of days between the first day of the last normal menstrual period (LNMP) and date of birth expressed in completed weeks after LNMP as recorded in the maternity delivery record.
    - First or early second trimester( $\leq 24$ weeks) ultra sound scan expressed in completed weeks
    - Syphyseal fundal height measured at first or early second trimester ( $\leq 24$ weeks) antenatal visit, whichever comes first, expressed in centimetres.
- Deliveries before arrival at CMU
- Deliveries in ambulances en-route to, or on arrival at CMU

- Women arriving at CMU in second stage of labour

### 3.5 Data management

#### 3.5.1 Sample size

All births that satisfied the inclusion criteria were included in the study. CMU has an average of 720 deliveries per month. An informal scrutiny of the February 2016 delivery registry indicated that the asphyxia rate was at 27% and stillbirth rate at 3.4%. 389 deliveries were planned to be analysed for this study. This would give a 95% power at the 5% confidence level. For stillbirths, 51 stillbirth cases will be analysed to give a 95% power at the 5% confidence level.

Population size(for finite population correction factor or fpc)( $N$ ): 720

Hypothesized % frequency of outcome factor in the population ( $p$ ):27%+/-3

Confidence limits as % of 100(absolute +/- %)( $d$ ): 3%

Design effect (for cluster surveys- $DEFF$ ): 1

**Table 2;Sample Size( $n$ ) for Various Confidence Levels**

Confidence	Level(%)	Sample Size
95%		389
80%		241
90%		326
97%		425
99%		482
99.9%		553
99.99%		592

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### **3.5.2 Data collection and analysis**

All unit matrons, midwives and medical doctors were briefed about the research and their expected roles prior to the start of the data collection process. Data on all stillbirths, satisfying the inclusion and exclusion criteria, occurring at CMU between 1<sup>st</sup> August 2016 and 30<sup>th</sup> September 2016 was collected from the patients' files and or labour ward and Chatinkha operating theatre registries. For each birth, the following information was extracted: date of birth; mothers demographic characteristics; referring facility; antenatal clinic attendance; maternal age; core ANC interventions; pregnancy progress and care; current pregnancy complications (anaemia, malaria, antepartum haemorrhage, diabetes, hypertension, trauma, pre-labour preterm rupture of membranes, urinary tract infections); labour and birth; condition of baby; cause of death; avoidable factors/missed opportunity/substandard care. Consent for all investigations and umbilical blood testing was collected on admission into the labour ward for all mothers that fitted the inclusion criteria.

The research assistants were notified upon the occurrence of each stillbirth. Upon getting consent, the enlisted information was extracted from the medical records of the mother. All stillbirths were examined by the Specialty Program Registrar on call within 1 hour of birth to ascertain the type of perinatal death (that is, maceration; freshness or neonatal death) as per department's protocol. However, placental biopsy and swabs for histology and microbiology, culture and sensitivity were not done due to resource constraints.

All babies born between 1<sup>st</sup> and 14 April 2017 had their umbilical artery blood collected by specially trained research Medical Officers. Immediately after delivery, a sample of arterial umbilical cord blood was drawn from a double clamped segment into heparinised plastic syringes. Lactate concentration in the collected blood was checked using Nova biomedical point of care devices within 15 minutes.

All mothers giving birth in the unit during the study period gave consent to participate in the study and have their blood samples collected and tested for VDRL, Malaria, Haemoglobin and Fasting Blood Sugar on the bedside using point of care Syphilis testing kit (Determine), Malaria Rapid Diagnostic Testing kit, Hemacue and Glucometer respectively. Some of the blood was sent to the hospitals main laboratory for full blood count and grouping. On the day of discharge, a postpartum clinic day was arranged for debriefing of all mothers who lost their babies and participated in the research.

Babies that were admitted to Chatinkha neonatal intensive care unit (CN-ICU) were followed up until discharge. There was no follow-up for babies that had good Apgar scores and were discharged with the mother.

Raw data were entered and analysed in SPSS statistics 20. Univariate tables were made to identify factors that are associated with the occurrence of poor outcomes. Logistic regression was used to establish the odds ratio adjusted for different significant variables identified in the univariate tables.

Two outcomes were examined in this study: Birth asphyxia and Stillbirth. A stillbirth was defined as in-utero death of an infant at completing at-least 28 weeks of gestation age or any infant born at  $\geq 28$  weeks of gestation or weighing atleast 1000g and died in utero. Birth



asphyxia is the presence of hypoxia during labour resulting in fetal acidosis, depression of vital functions and an increased risk of long-term morbidity. Poor outcome is defined as births of an infant at  $\geq 28$  weeks of gestation, weighing  $\geq 1000$  g with Apgar score of  $\leq 7$  at 5 minutes.

### **3.6 Ethical Consideration and Approval**

The study proposal was approved by the College of Medicine Research and Ethics Committee (COMREC). Permission to conduct the study was sought from the director of QECH and the head of department for the CMU. All data was handled with strict confidentiality as no maternal direct identifiers like names and contact details were entered in the data sheet and maternal folders were not taken out of the maternity unit. Transfer of participants' information from folders was done by the study investigator or designee (Intern Medical Officer, Speciality Programme Registrar (SPR) or research assistant who abided to strict confidentiality.

## **Chapter 4: Results**

### **4.1 Stillbirths**

During the phase one study period, there were 54 stillbirths out of 2,149 deliveries. Fifty two stillbirths were captured and 2 were lost as the patients left the labour ward before the research assistants could reach them. This happened within the first week of research onset.

#### **4.1.1 Demographic characteristics of the mothers**

With reference to Table 3 below, maternal age ranged from 16 to 39 years with an average of 26 years at delivery. The majority (69.2%) were within the 20years to 35years maternal age group. About 9% of the mothers had never participated in any formal education; 30 (57.7%) attended primary education. Fifteen women (28.8%) had gone through secondary education and 2(3.8) had attended post-secondary school education.

Sixty seven percent of the still births were preterm with 34.6% being late preterm (34 weeks to 36<sup>6/7</sup>). 25percent were primiparous with 9 mothers being grand multiparous. Forty nine (94.2) of the deliveries were singletons.

Table 3: Demographic characteristics of the mothers

<b>Variable</b>		<b>Freq</b>	<b>Percent</b>
<b>Age (years)</b>	<b>Less than 20</b>	<b>8</b>	<b>15.4</b>
	<b>20 to 34</b>	<b>36</b>	<b>69.2</b>
	<b>≥ 35</b>	<b>8</b>	<b>15.4</b>
<b>Parity</b>	<b>1</b>	<b>13</b>	<b>25.0</b>
	<b>2 – 4</b>	<b>30</b>	<b>57.7</b>
	<b>5 above</b>	<b>9</b>	<b>17.3</b>
<b>Gestation (weeks)</b>	<b>28 – 33</b>	<b>17</b>	<b>32.7</b>
	<b>34 – 36</b>	<b>18</b>	<b>34.6</b>
	<b>37 – 38</b>	<b>7</b>	<b>13.5</b>
	<b>39 – 42</b>	<b>7</b>	<b>13.5</b>
	<b>43 above</b>	<b>3</b>	<b>5.8</b>
<b>Body Mass Index</b>	<b>Under weight</b>	<b>4</b>	<b>7.7</b>
	<b>Normal weight</b>	<b>29</b>	<b>55.8</b>
	<b>Overweight</b>	<b>11</b>	<b>21.2</b>
	<b>Obese</b>	<b>8</b>	<b>15.4</b>
<b>Number of ANC visits</b>	<b>1</b>	<b>8</b>	<b>15.4</b>
	<b>2</b>	<b>15</b>	<b>28.8</b>
	<b>3</b>	<b>14</b>	<b>26.9</b>
	<b>4+</b>	<b>15</b>	<b>28.9</b>

#### 4.1.2 Core interventions during the antenatal care

As shown in Table 4 below, all mothers attended antenatal clinic at least once. Sulfadoxine pyrimethamine for prevention of malaria was given once, twice and three times to 48%, 28.8% and 23.1% of the mothers respectively. None of the mothers got albendazole at any of their visits to the antenatal clinic with 63 % BP checks rates. All mothers were protected against tetanus and were tested for HIV at the antenatal clinic. Eight (15.4%) mothers were found HIV positive and were immediately started on ART. The study was unable to capture the number of VDRL and Urine protein done at the antenatal clinic, however, 2 mothers tested positive for syphilis and urine protein and VDRL.

Table 4: Core interventions during the antenatal care

Variable question		Response	Freq	Percent
Malaria prophylaxis	IPT1	Yes	25	48.1
	IPT2	Yes	15	28.8
	IPT3	Yes	12	23.1
Tetanus	TTV1	Yes	37	71.2
	TTV2	Yes	10	19.2
	TTV3	Yes	5	9.6
Albendazole	A1	Yes		
	A2	Yes		
	A3	Yes		
BP checks	BP1	Yes	23	44.2
	BP2	Yes	10	19.2
	BP3	Yes	10	19.2
Urine protein	Positive	Yes	2	3.8
HIV	Reactive	Yes	8	15.4
HAART		Yes	8	100.0
VDRL	Reactive	Yes	2	3.8

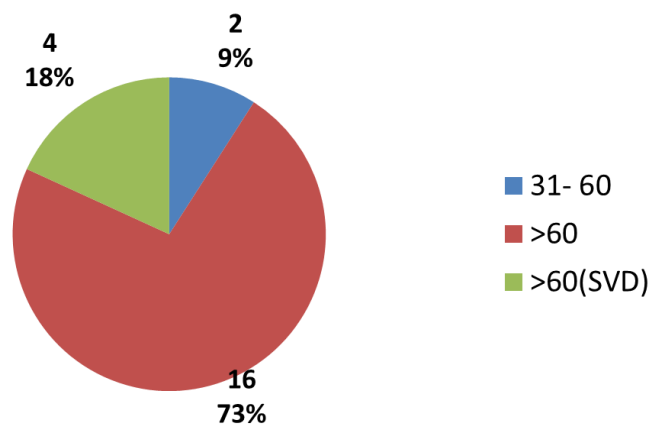
#### 4.1.3 Labour and Delivery

As per Table 5 below, the majority of the stillbirths resulted from spontaneous labour with 3 cases being elective caesarean section in mothers with 2 previous caesarean sections and

confirmed IUFD. Eighteen (34.6%) cases of the stillbirths were delivered through caesarean section (CS) with 15(83.3%) of them being FSB (Table 4). Fetal distress and ruptured uterus were the most common indications for the caesarean sections followed by abruption placenta, previous CS, cord prolapse respectively.

**Table 5: Labour and Delivery**

Variable		Number	Percent
Type of labour	Induced	8	15.4
	Spontaneous	41	78.8
	Elective	3	5.8
Fetal Activity	Yes	32	61.5
	No	20	28.5
Mode of delivery	SVD	34	65.4
	CS	18	34.6
Indication for CS	Fetal Distress	4	18.2
	Ruptured Uterus	4	18.2
	Abruptio Placenta	3	13.6
	Previous CS	3	13.6
	Cord Prolapse	2	9.1
	Retained twin	2	9.1
	Failed Induction	1	4.5
	Hand Prolapse	1	4.5
	Preeclampsia	1	4.5
	CPD	1	4.5



**Figure 1: Timing of CS**

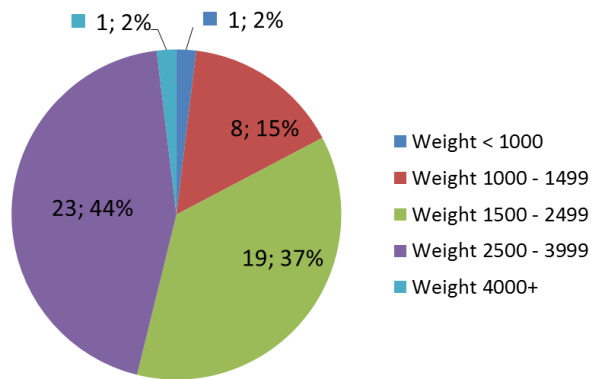
Figure 1 shows that out of the 22 caesarean sections ordered, 16(73%) were done after an hour from the time the decision was made with 4(18%) proceeding to deliver FSB per vagina .

#### 4.1.4 Investigation results (refer to Table 6)

None of the mothers had fasting blood sugar levels suggestive of diabetes mellitus and positive results for Malaria. Prior to delivery, anaemia was diagnosed in 52% mothers, with 17.3%, 28.9 % and 7.6% having mild, moderate and severe disease respectively (Table 5 below). 31% of the mothers had a blood group with Rhesus negative and 13.5% had a positive result for VDRL. This includes the 2 that were diagnosed at the antenatal clinic. Twenty five percent of the mothers had HIV with 5 cases having seroconverted during the antenatal period. There was no statistically significant difference between the macerated and the fresh stillbirths' distribution among the tests done.

**Table 6: Investigation results**

Variable	Category	Freq	Percent
<b>FBS</b>	<b>&lt;7mmol/</b>	<b>52</b>	<b>100.00</b>
<b>MRDT</b>	<b>Negative</b>	<b>52</b>	<b>100.00</b>
<b>Maternal Hemoglobin</b>	<b>&lt;7g/dl</b>	<b>4</b>	<b>7.6</b>
	<b>7.0 - 9.9</b>	<b>14</b>	<b>28.9</b>
	<b>10.0 - 10.9</b>	<b>9</b>	<b>17.3</b>
	<b>11+</b>	<b>25</b>	<b>48.1</b>
<b>Blood group</b>	<b>RH Positive</b>	<b>36</b>	<b>69.2</b>
	<b>RH Negative</b>	<b>16</b>	<b>30.8</b>
<b>VDRL</b>	<b>Positive</b>	<b>5(2)</b>	<b>9.6(13.5)</b>
	<b>Negative</b>	<b>45</b>	<b>86.5</b>
<b>HIV</b>	<b>Positive</b>	<b>5(+8)</b>	<b>9.8 (25)</b>
	<b>Negative</b>	<b>49</b>	<b>75.0</b>
<b>Urinalysis</b>	<b>Positive</b>	<b>4</b>	<b>7.7</b>
	<b>Negative</b>	<b>48</b>	<b>92.3</b>



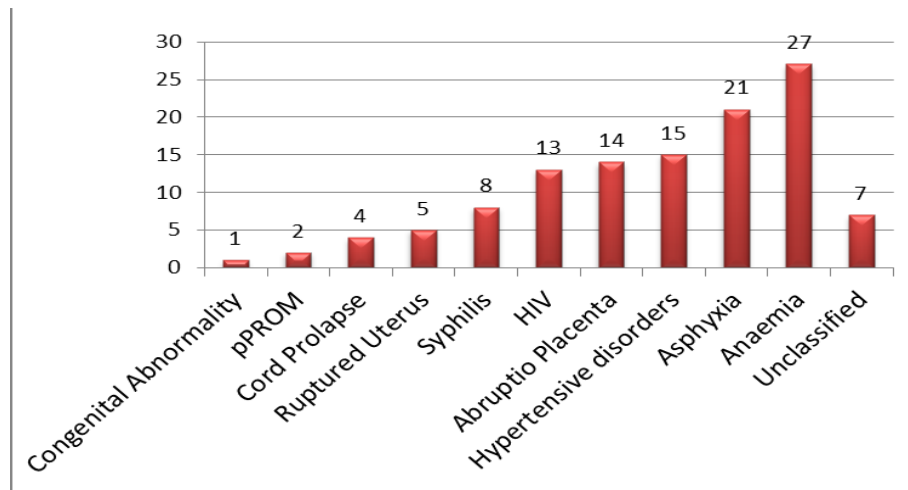
**Figure 2: Distribution of stillbirths according to birth-weight(grams)**

Figure 2 shows that 55% of the stillbirths had low birth weights with 15% being very low birth weights. One case had a macerated stillbirth weighing 4000grams and was delivered through caesarean section

#### **4.4.5 ReCoDe classification of the stillbirths**

With reference to Figure 3 below, Anaemia was the most common (52%) Relevant Condition at Delivery of the stillbirths; however, its frequency was reduced to 12 upon exclusion of ruptured uterus and abruption placenta which could have led to the acute anaemia making them cofounders. Birth asphyxia was found in 21(40%) of cases, attributed to intrapartum fetal distress which was diagnosed but emergency caesarean section could not be done due to shortage of theatre space. Severe pre-eclampsia occurred in 21(29%) of the cases with 66% of them leading to abruption placentae. Seven(13%) stillbirths (all MSB) could not be classified as the cause of death could not be ascertained. However, 2 of the unclassified cases were MSB with thick meconium upon delivery, and

2 had calcifications on the placenta suggestive of placental insufficiency. Placental histology could not be done to ascertain the diagnosis placental insufficiency.



**Figure 3: Distribution of the stillbirths according to ReCoDe**

#### **4.2 POOR OUTCOMES AND BIRTH ASPHYXIA**

During the second phase, there were 401 deliveries out of which 12 were stillbirths and 6 were early neonatal deaths representing a perinatal mortality rate of 44.9/1000births.

##### **4.2.1 Demographic characteristics of the mothers**

Majority of the births were to mothers above the age of 20 years with 19.8 % of all births born to mothers under the age of 20 years. Perinatal mortality was the same across the three age groups. 90% of the mothers had at least a primary school education level. Primiparas constituted 31% of the mothers with the majority (51%) in the Para2-4 group. 73% of the deliveries were at term with 8% being very preterm (<34 weeks). About 12% of the very preterm babies were stillbirths representing the largest proportion among the 3 gestation age groups for stillbirths (Table 7 below).



**Table 7: Demographic characteristics**

Variable	Category	Total Births		Live Births		Still Births		Perinatal Mortality(SB+ENN)	
		N	%	N	%	N	%	N	%
Total		401		389	97.01	12	2.99	18	4.49
Age	Below 20	82	20.45	79	19.70	3	0.75	4	1.00
	20 to 35	280	69.83	273	68.08	7	1.75	12	2.99
	Above 35	49	12.22	47	11.72	2	0.50	2	0.50
Parity	1	126	31.42	126	31.42	5	1.25	7	1.75
	Para 2-4	209	52.12	205	51.12	4	1.00	8	2.00
	>=5	66	16.46	63	15.71	3	0.75	3	0.75
Gestation	Below 34 weeks	39	9.73	34	8.48	5	1.25	7	1.75
	34 – 36 weeks	75	18.70	73	18.20	2	0.50	3	0.75
	Above 36 weeks	296	73.82	291	72.57	5	1.25	9	2.24
Education	none	44	10.97	43	10.72	1	0.25	1	0.25
	Primary	161	40.15	158	39.40	3	0.75	6	1.50
	Secondary	165	41.15	159	39.65	6	1.50	9	2.24
	Tertially	31	7.73	29	7.23	2	0.50	2	0.50

#### 4.2.2 Core ANC Interventions

The national program on Antenatal Clinic requires all women to be tested and treated for HIV, Syphilis, diabets, hypertension, malaria, anaemia and gastrointestinal and urinary tract infestation if found positive. Table 7 below shows that, 99.5% of the mothers in our study had at least one antenatal visit with 86.5%, 88.2 and 82.7% of them having received at least a single dose of malaria prophylaxis, tetanus toxoid vaccine and albendazole respectively. 51% got their BP checked at least once. HIV test was done in 98.8% of the mothers with 11.5% positive rate. All mothers who were found HIV positive were initiated on antiretroviral drugs. 83.5% of the mothers were tested for syphilis with 2.5% positive and all were treated. Urine protein was checked in 10% of the mothers with 8(2%) found

1+. Only 8 mothers were ever checked for blood sugar with none of them diagnosed with diabetes mellitus.

Hypertensive disorders were the most common conditions (9.7%) complicating the pregnancies of the mothers, followed by multiple gestation, urinary tract infections, Preterm prelabour rupture of membranes, anaemia and malaria (1.7%)

**Table 8: Core ANC Interventions**

Variable	Category	Total Births		Live Births		Still Births	
				N	%	N	%
<b>Total</b>		<b>401</b>		<b>389</b>	<b>97.01</b>	<b>12</b>	<b>2.99</b>
<b>Core ANC Interventions</b>	<b>At least 1 ANC</b>	<b>398</b>	<b>99.25</b>	<b>386</b>	<b>96.26</b>	<b>12</b>	<b>2.99</b>
	<b>At least 1 malaria prophylaxis</b>	<b>347</b>	<b>86.53</b>	<b>338</b>	<b>84.29</b>	<b>9</b>	<b>2.24</b>
	<b>At least 1 Tetanus prophylaxis</b>	<b>354</b>	<b>88.28</b>	<b>346</b>	<b>86.28</b>	<b>8</b>	<b>2.00</b>
	<b>At least 1 Albendazole prophylaxis</b>	<b>332</b>	<b>82.79</b>	<b>322</b>	<b>80.30</b>	<b>10</b>	<b>2.49</b>
	<b>At least 1 BP check</b>	<b>205</b>	<b>51.12</b>	<b>201</b>	<b>50.12</b>	<b>4</b>	<b>1.00</b>
<b>Medical Conditions</b>	<b>Malaria</b>	<b>7</b>	<b>1.75</b>	<b>7</b>	<b>1.75</b>	<b>0</b>	<b>-</b>
	<b>Anemia</b>	<b>13</b>	<b>3.24</b>	<b>13</b>	<b>3.24</b>	<b>0</b>	<b>-</b>
	<b>Hypertension</b>	<b>39</b>	<b>9.73</b>	<b>36</b>	<b>8.98</b>	<b>3</b>	<b>0.75</b>
	<b>UTI</b>	<b>28</b>	<b>6.98</b>	<b>28</b>	<b>6.98</b>	<b>0</b>	<b>-</b>
	<b>APH</b>	<b>11</b>	<b>2.74</b>	<b>10</b>	<b>2.49</b>	<b>1</b>	<b>0.25</b>
	<b>Multiple gestation</b>	<b>33</b>	<b>8.23</b>	<b>33</b>	<b>8.23</b>	<b>0</b>	<b>-</b>
<b>Maternal Test</b>	<b>PPROM</b>	<b>24</b>	<b>5.99</b>	<b>23</b>	<b>5.74</b>	<b>1</b>	<b>0.25</b>
	<b>VDRL Test</b>	<b>335</b>	<b>83.54</b>	<b>378</b>	<b>94.26</b>	<b>9</b>	<b>2.24</b>
	<b>VDRL reactive</b>	<b>10</b>	<b>2.49</b>	<b>9</b>	<b>2.24</b>	<b>1</b>	<b>0.25</b>
	<b>HIV Test</b>	<b>396</b>	<b>98.75</b>	<b>44</b>	<b>10.97</b>	<b>12</b>	<b>2.99</b>
	<b>HIV reactive</b>	<b>46</b>	<b>11.47</b>	<b>46</b>	<b>11.47</b>	<b>0</b>	<b>-</b>
	<b>Urine protein</b>	<b>40</b>	<b>9.98</b>	<b>39</b>	<b>9.73</b>	<b>1</b>	<b>0.25</b>
	<b>Random Blood Sugar</b>	<b>8</b>	<b>2.00</b>	<b>7</b>	<b>1.75</b>	<b>1</b>	<b>0.25</b>

### 4.2.3 Labour and Delivery

Of the 401 mothers, 370(92.3%) went into labour spontaneously, 20(5%) were elective caesarean sections and 9(2%) were induced (Table 9 below). The caesarean section rates were 33.1% and 33.3% among the women with spontaneous and induced labour respectively. The overall caesarean section rate was 36.5% of which 30% had lactate concentrations of equal to or above 5mmol/l. Vaginal delivery occurred in 63.5% of all deliveries with 7(1.8%) being breech, 244(60.8%) normal vaginal delivery and 4(1%) vacuum extraction. None of the vacuum extraction and breech deliveries resulted in

stillbirths or early neonatal deaths. There was 1 elective caesarean section that was done on a 3 previous scar mother with intrauterine death at 36 weeks of gestation age. During the study period, 56% of the babies born were males and 44% females with perinatal mortality of 48/1000births and 40/1000births respectively. Seventy eight % of the infants had births weights above 2500g with 1.5% having extremely low birth weight. The perinatal mortality was 92/1000 births and 32/1000births in underweights and normal birth-weights respectively. Fresh stillbirths (8) followed by early neonatal deaths (6) contributed the highest proportion to the perinatal mortality. Macerated still births (4) were the least common.

**Table 9: Labour and Delivery**

Variable	Category	Total Births		Live Births		Still Births	
		N	%*	N	%*	N	%*
<b>Total</b>		<b>401</b>		<b>389</b>	<b>97.01</b>	<b>12</b>	<b>2.99</b>
<b>Type of labour</b>	Induced	9	2.24	8	2.00	1	0.25
	spontaneous	370	92.27	361	90.02	10	2.49
	Elective CS	20	4.99	19	4.74	1	0.25
<b>Mode of Delivery</b>	Normal Vaginal	244	60.85	234	58.35	10	2.49
	Breech	7	1.75	7	1.75	0	-
	ER CS	125	31.17	124	30.92	1	0.25
	V/Extraction	4	1.00	4	1.00	0	-
	Elective CS	20	4.99	19	4.74	1	0.25
<b>Birth weight</b>	<1500	6	1.50	4	1.00	2	0.50
	1500-2499	81	20.20	76	18.95	5	1.25
	2500-3999	309	77.06	304	75.81	5	1.25
	>4000	5	1.25	5	1.25	0	-
<b>Infant gender</b>	Male	225	56.11	217	54.11	8	2.00
	Female	173	43.14	169	42.14	4	1.00
<b>CS Indications</b>	Brow pesentation	1	0.56	1	0.58	0	0
	Macrosomia	1	0.56	1	0.58	0	0
	Oblique lie	1	0.56	1	0.58	0	0
	Oligohydramnious	1	0.56	1	0.58	0	0
	Cervical dystocia	1	0.56	1	0.58	0	0
	Cord prolapse	1	0.56	1	0.58	0	0
	IUFD	2	1.11	1	0.58	1	25
	Ruptured uterus	1	0.56	0	-	1	25
	Obstructed labour	2	1.11	2	1.16	0	0
	APH	2	1.11	2	1.16	0	0
	Bad Obstetrics history	3	1.67	3	1.74	0	0
	Failed augmentation	4	2.22	4	2.33	0	0
	Fetal distress	7	3.89	7	4.07	0	0
	Eclampsia	8	4.44	8	4.65	0	0
	Multiple Gestation	10	5.56	10	5.81	0	0
	Breech	14	7.78	14	8.14	0	0
	Previous scars	56	31.11	54	31.40	2	50
	CPD	61	33.89	61	35.47	0	0

There were 180 caesarean sections that were ordered with 20% of them delivering vaginally. About half of the vaginal deliveries were in mothers for whom CS had been ordered for CPD, followed by previous scar (30.5%), fetal distress and breech in primigravida. Among these vaginal deliveries, the average lactate level was 4.46mmol/l with perinatal mortality of 194/1000 births. Of the 10 cases that had Lactate above 5mmol/L, 6 were mothers for whom CS had been ordered for CPD and the babies were born with a mean lactate concentration of 8.5mmol/L.

Among the caesarean sections undertaken as ordered, 33.9% were CPDs followed by previous scar (31.8%) breech in primigravida (8.1%), multiple gestation (7.4%) and hypertensive disorders (3.7%). Fetal distress was indication in 2.2% of the caesarean sections that were done.

#### 4.2.4 Investigation results

In 98.5% of all the mothers, the VDRL test was negative and one case among those with positive results had a still birth (Table 10 below).

**Table 10: Investigation Results**

Variable	Category	Total Births		Live Births		Still Births	
		N	%	N	%	N	%
VDRL	Negative	395	98.50	377	98.69	11	91.67
	Positive	6	1.50	5	1.31	1	8.33
HIV	Negative	349	87.03			12	2.99
	Positive	48	11.97	44	10.97	0	-
Hb	<7	6	1.50	6	1.50	0	-
	7-9.9	65	16.21	61	15.21	4	1.00
	10.0-10.9	77	19.20	77	19.20	0	-
	>=11	253	63.09	245	61.10	8	2.00
Lactate	<5mmol/L	275	70.69	274	70.98		-
	>=5mmol/L	114	29.31	109	28.24		-
UTI	Negative	367	96.33	350	96.42	11	91.67
	Positive	14	3.67	13	3.58	1	8.33

The HIV positive rate was 12% with 2 cases having seroconverted during the antenatal period. No stillbirths occurred among HIV positive mothers. Anaemia was present in about 37 % of all the mothers with a majority (19.2%) having mild anaemia (Hb 10.0-10.9g/dl). Severe anaemia (Hb less than 7g/dl) was diagnosed in 2% of the mothers. Urinary Tract Infection (UTI) was diagnosed when the mother's urine had white cells and nitrites. 14 mothers were found to have UTI with one of them having a stillbirth.

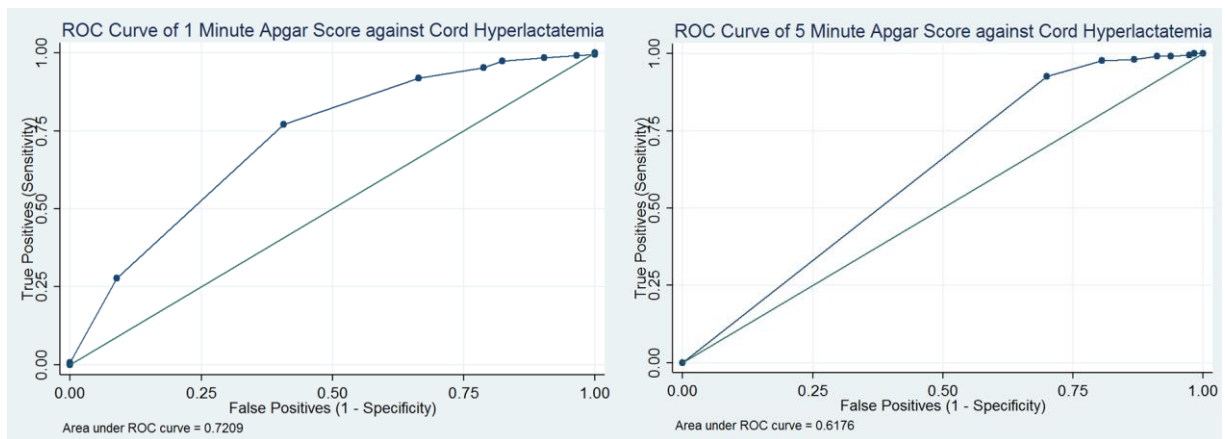
Nearly 30% of the babies had their lactate concentration above 5mmol/L with 13 cases having lactate above 9mmol/L. Maternal blood grouping and malaria tests were not done due to resource constraints at the hospital and strict guidelines on the use of MRDTs.

During this period there were 48 admissions to nursery and Birth Asphyxia (BA) was the leading documented cause of admission at 41.7%. Other indications for nursery admission were; respiratory distress syndrome (RDS) or transient tachypnea of new born (TTN)(21.9%), neonatal sepsis (16.6%) meconium aspiration, low birth weight and congenital abnormality. Birth asphyxia was diagnosed in 20(4.9%) infants of all deliveries basing on clinical picture of the infant and the Apgar scores at 5minutes. 10 infants were admitted in nursery basing on clinical picture upon reassessment despite having good Apgars at 5 minutes.

Umbilical blood Lactate testing was done on 389 infants. The twelve stillbirths were excluded. From cord blood sampling to testing, the median time was 2 minutes and the mean was 2.8 +-4.7minutes. There was a variation of lactate means according to the mode of delivery, with Vacuum extraction having the highest mean of 5.1+-1.1mmol/L; emergency caesarean section 4.6+-2.5mmol/L; vertex vaginal delivery: 3.9+-2.2mmol/L;

breech: 3.5+-1.8mmol/L and elective caesarean section 3.1+-1.1mmol/L. The lactate mean for vertex vaginal deliveries was higher (5.2mmol/L) in the cases that were diagnosed to have CPD and a caesarean section was ordered. All the five infants that had Lactate levels above 9mmol/L died with 48hours of birth.

Hyperlactatemia is an appropriate standard for the diagnosis of birth asphyxia. The relationship between the one and five-minute Apgar scores was examined using Receiver Operating Characteristics (ROC) curves (Figure 4).



**FIGURE 4:Receiver Operating Characteristics (ROC) curve for Apgar scores of 7 at 1minute(A) and 5 minutes(B) to diagnose birth asphyxia reflected as umbilical cord hyperlactatemia**

For Apgar scoring, the area under the curve was 0.721 at 1 minute and 0.618 at 5 minute. The Apgar score of 7 at 1 minute had 95.5% true positive rate and 67%false positive rate. While the Apgar of 7 at 5 minutes had 91.3% true positive rate and 70%false positive rate. This means that using Agpar scoring for initial assessment is performing its role in

identifying newborns in need of resuscitation (high rate of true positives) but at both time points there is a high false-positive rate

#### **4.2.5 Associations between birth asphyxia and different clinical and laboratory variables**

Using the Chi-Square Tests, associations were drawn between Hyperlactatemia (defined as the umbilical artery blood lactate of greater than 5mmol/L) and the different clinical variables. The following variables had a positive association with occurrence of hyperlactatemia (Table 11): emergency caesarean section ( $P=0.001$ ); vaginal delivery ( $P=0.019$ ), meconium stained liquor ( $P=0.005$ ) and maternal age ( $P=0.034$ ).

The study found no association between Hyperlactatemia and APH, gestation age, multiple gestation, PPRM, anaemia or malaria.

**Table 11: Association between hyperlactatemia and different clinical and laboratory factors**

		Total	Lactate >5	(*SD) or %	Lactate <5	(*SD) or %	pvalue
Variable		389	114	(*SD) or %	275	(*SD) or %	
Age			24.84	*6.7	26.41	*6.6	0.034
Parity			1.47	*1.7	1.74	*1.7	0.139
Gestation			37.79	*2.7	37.64	*2.7	0.665
Birth weight			2864.5	*549.6	2857.6	*545.1	0.91
At least 1 ANC	yes	386	114	29.5	272	70.7	0.559
	No	3	0	-	3	100.0	
Malaria	Yes	7	4	57.1	3	42.9	0.201
	No	382	110	28.8	272	71.2	
Anemia	Yes	13	3	23.1	10	76.9	0.763
	No	376	111	29.5	265	70.5	
Hypertension	yes	36	10	27.8	26	72.2	0.833
	No	353	104	29.5	249	70.5	
UTI	yes	28	7	25.0	21	75.0	0.673
	No	361	107	26.9	254	70.4	
APH	yes	10	5	50.0	5	50.0	0.65
	No	379	109	28.8	270	71.2	
Multiple gestation	yes	33	9	27.3	24	72.7	0.789
	No	356	105	29.5	251	70.5	
PPROM	yes	23	4	17.4	19	82.6	0.243
	No	366	110	30.1	256	69.9	
Liquor color	Muconium	40	20	50.0	20	50.0	0.005
	No Muconium	345	93	27.0	252	73.0	
VDRL	Reactive	5	1	20.0	4	80.0	0.998
	Non Reactive	383	113	29.5	270	70.5	
HIV status	Reactive	46	9	19.5	37	80.4	0.119
	Non Reactive	335	103	30.7	232	69.3	
SVD	yes	233	58	24.9	175	75.1	0.019
	No	156	56	35.9	100	64.1	
Elective CS	yes	19	2	10.5	17	89.5	0.065
	No	370	112	30.3	258	69.7	
Emergency CS	yes	124	50	40.3	74	59.7	0.001
	No	265	64	24.2	201	75.8	

A prognostic analysis was then undertaken to examine the influence of factors potentially affecting newborn survival associated with birth asphyxia. A binary neonatal outcome variable was constructed comprising early neonatal death or admission to the neonatal unit.



As admission is routine for babies weighing less than 2 kg these were excluded from the model as were newborns with identified congenital anomalies.

Independent variables were selected for inclusion in multiple regression modeling on the basis of univariate probabilities less than 0.20 so as to include those with potential significance once corrected for other variables: these were Hypertension (defined as any observed antenatal or intrapartum elevated blood pressure reading), Meconium stained liquor, HIV result, Age and Parity. Umbilical cord blood lactate concentration was included in the model as a categorical variable with a cut off of 5.0mmol/L so as to adjust the model for severe hyperlactatemia. Variables for mode of delivery were not included as the aim was to generate model reflecting antenatal and intrapartum status. The modeling revealed that the odds of the composite adverse outcome (early neonatal death or admission to the neonatal unit) were significantly elevated in the presence of maternal hypertension (OR=2.9, P=0.019) after correcting for the presence of hyperlactemia (Table 12, note that 'Exp(B)' corresponds to the Odds Ratio). Thus, hypertension contributed independently to adverse outcomes over and above birth asphyxia, perhaps reflecting reduced placental reserve and adverse circulatory conditions in hypertensive mothers.

**Table 12: Logistic regression analysis**

Variables in the Equation									
		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
								Lower	Upper
Step 1 <sup>a</sup>	Hypertension(1)	1.022	0.467	4.789	1	0.029	2.78	1.113	6.944
	Lactate level	0.801	0.337	5.672	1	0.017	2.229	1.152	4.31
	HIV_result	-0.258	0.572	0.203	1	0.652	0.773	0.252	2.369
	Meconium staining	0.396	0.463	0.731	1	0.393	1.486	0.599	3.686
	Age	-0.063	0.036	3.1	1	0.078	0.939	0.875	1.007
	Parity	0.266	0.151	3.119	1	0.077	1.305	0.971	1.753
	Constant	1.886	1.515	1.549	1	0.213	6.59		
Step 3 <sup>a</sup>	Hypertension(1)	1.077	0.461	5.461	1	0.019	2.936	1.19	7.246
	Lactate level	0.862	0.33	6.829	1	0.009	2.368	1.24	4.52
	Age	-0.064	0.036	3.211	1	0.073	0.938	0.874	1.006
	Parity	0.272	0.152	3.233	1	0.072	1.313	0.976	1.767
	Constant	1.674	0.918	3.322	1	0.068	5.333		

a. Variable(s) entered on step 1: Hypertension, lactate level, HIV result, Meconium staining, Age, Parity.

## **Chapter 5: Discussion**

### **5.1 Stillbirths**

At 39.8/1000 births, the stillbirth rate is higher than the current national stillbirth rate of 34/1000[31] and what was found QECH in 2005 (34/1000) by Metafaria and colleagues [7]. This could be attributed to the prospective nature of the study which resulted in reduced missing data. The difference may also be due to the short duration of the study, making the study's sample size unrepresentative. It is also noted that the proportion of the fresh stillbirths (FSB) was higher (61%) than that of macerated stillbirth (MSB)(35%). This was also noted by Lawn[2], and signifies the existence of deficiencies in the intrapartum and emergency obstetric care, in the unit. The proportions of stillbirths is however different from what Ferusi and colleagues found in a study done in Zimbabwe in 1998 where the stillbirth rate was 56/1000 and the proportion of MSB was higher than that of FSB[4].

In this study, it was observed that 34.6% of the stillbirths were delivered through caesarean section, out of which 73% were done after more than an hour from decision to undertake the procedure. as per indication. All delays were attributed the lack of theatre space for caesarean section. Theatre space unavailability could be attributed to the structural absence of space or unavailability of human resource like anaesthetist, theatre midwives or obstetrician and gynaecologist, all of which the study was unable to evaluate.

The majority of the stillbirths (70%) occurred to mothers of the 20-35 years age group, with parity group of 2-4 (60%). All mothers had antenatal visits with majority having attended at least twice. These are mothers that are expected to deliver healthy babies without difficulties. However, 35(67%) of the still births were preterm with 34.6% being

late (34 weeks to 36<sup>6/7</sup>) and 32.7% early preterm (<34 weeks). Upon delivery, 55% had low birth weight which could be attributed to the high rates of hypertensive disorders, antepartum haemorrhage, HIV and anaemia [32]. Other studies have supported the general occurrence of high prematurity rates in stillbirths [33]. The low birth weights can also be attributed to intrauterine growth failure as found by Gardosi and co-workers [26]. Stillbirth is strongly related to impaired fetal growth. However, the relationship between fetal growth and stillbirth is difficult to determine because of uncertainty in the timing of death and confounding characteristics affecting normal fetal growth[34].

To reduce the incidence of malaria and anaemia, the Ministry of health recommends the provision of albendazole, Ferrous sulphate and sulfadoxine pyrimethamine (SP). It is noted in this study that none received albendazole and 12 mothers got the full prescription of SP due to short supply of the drugs in the health centres. It is therefore not surprising that anaemia was the most frequent determinant (52%) present at delivery. Other key observation was the antenatal BP checks which were done in 63% of all mothers with most of them (44%) having a single check despite having attended the clinic more than once. The MDHS 2015-2016 reported a higher BP measurement rate of 83%. Better documentation in our study could account for the difference unlike the population based estimates used in the MDHS. The low BP measurement rates signify the health system's failure to provide the basic important services to the mothers in the antepartum period. BP check is a single most important tool in the initial diagnosis and management of hypertensive disorders in pregnancy. Hypertensive disorders are highly associated with poor outcomes for both the mother and the baby [35].

The HIV prevalence in the mothers to stillborn babies (25.5%) was higher than the national (8.8%) and the urban (14.6%) rates with a sero-conversion rate of 11.3% [21]. Different studies have demonstrated the positive association between preterm stillbirths and HIV [36].

Studies support that diabetes mellitus and malaria are associated with stillbirth [8-10,37]; however, none of the stillbirth mothers had malaria or diabetes mellitus. Kupka and co-workers stated that, “only active placental malaria increases the risk of stillbirths” [36]. In this study, placental histology was not done, however, the mothers did not have any clinical symptoms suggestive of malaria.

Anaemia has been shown to increase the risk of low birth-weight, preterm labour and stillbirth. Upon analysing the data, anaemia had the prevalence rate of 52% which dropped to 23% upon exclusion of cofounders (acute events) like ruptured uterus and abruption placenta.

Using the ReCoDe system of stillbirth classification, attributable causes were found in 86.5% of the stillbirths. Thus, our unexplained stillbirth proportion (13.5%) was slightly lower than what Gardosi (15.5%) and Spong described [26, 38]. With placental histology, lower proportions of unexplained stillbirths are expected.

In Malawi, like other Sub Saharan countries, the burial of the stillbirths does not follow the adult rituals as the stillborn is not considered to be human yet. Depending on the parents' tribe, new-borns are not given names for up to a week or until the umbilical cord remnant falls off the navel. During this waiting period, the infant remains indoors to avoid being bewitched [39]. Traditionally, a new born only becomes human after the foliage of the umbilical cord remnant and hence any new-born that dies prior is considered an object. For

those who deliver in hospitals, the postpartum care is incomplete as the grief counselling is usually omitted. The mothers are discharged and go home without knowing the cause of death and with many unanswered questions like; did I do something wrong? Will it happen again [40]? This poor practice continues despite the evidence that empathic attitudes of care providers and targeted interventions may moderate the negative effects of the stillbirth [37].

## **5.2 Poor outcomes and birth asphyxia**

The stillbirth rate in this data set mirrors the national rate of 34/1000births. The perinatal mortality, defined as the number of stillbirths and deaths of infants in the first week of life per 1,000 total births, was 44.9/1000 births which is higher than the national rate of 35/1000births[31]. The mortality was high among the male infants than the female infants, the trend observed by different authors [41-43]. As per findings from the phase 1 of this study, fresh still births constituted the majority of the stillbirths (66.7%). The risk factors associated with the occurrence of the stillbirths have been discussed in the stillbirth section.

Birth asphyxia (BA) is the most common documented cause of nursery admission seconded by RDS and TTN combined. There was a positive association of birth asphyxia diagnosis, and emergency caesarean sections ( $P<0.0001$ ) and vertex vaginal deliveries ( $P=0.016$ ). This could be attributed to the prolonged waiting time from decision to do caesarean section to actual delivery of the baby. It was also noted that shortage of theatre space led to 20 vaginal deliveries in mothers diagnosed with CPD. Infants that were born to these mothers had higher mean lactate levels which can be explained by the prolongation of pushing period as observed by Dessolle L and co-workers [44]. There could be under diagnosis of birth asphyxia due to the failure to follow up the infants that were noted to

have high lactate levels but were never admitted to nursery. Babies born to mothers through vaginal delivery are usually discharged with their mother within 24 hours of delivery. It would therefore be difficult to know what happened to the babies that had high lactates at delivery and were discharged without following up. There was one case of birth asphyxia that was admitted to nursery 24 hours post-delivery as the mother was still recovering from caesarean section.

In this study, a cut off of 5mmol/L was used, above which the infant is more likely to be asphyxiated. There is no consensus regarding the level of lactate at which birth asphyxia can be diagnosed. Suidan and Young in 1984 used a cut off of 3.69mmol/L while Westgren and colleagues used 3.2mmol/L [45]. In 2005, Gjerris and colleagues used 8mmol/L which was notably high and could have been due to the differences in the test strips they used. However, ranges between 3 and 7 have been used in different studies [46]. There was a variation of lactate means according to the mode of delivery with Vacuum extraction having the highest mean of 5.1+-2.11mmol/L; caesarean sections had 4.37+-3.2mmol/L; vertex vaginal deliveries had 3.88+-2.2mmol/L and breech deliveries had 3.5+-2.3mmol/L.

These variations were also noted in 2015 by Mishra and colleagues in India [47]. The lactate mean for vertex vaginal deliveries was increased to 5.2mmol/L among cases that were diagnosed to have CPD and caesarean section was ordered but could not be done due to shortage of theatre space. Theatre space unavailability was also noted to have contributed to the occurrence of stillbirths in the phase one of the study.

Hyperlactatemia (lactate >5mmol/L) was diagnosed in 29.6% of all live births. It was associated with emergency caesarean sections, spontaneous vaginal deliveries and any grade of meconium liquor staining. The study found no association between

Hyperlactatemia and APH, multiple gestation, PPROM, anaemia, gestation age, HIV or malaria. These conditions are associated with the occurrence of stillbirth as found in phase one. However, low case volumes could have contributed to the absence of the association. There was no association between gestation age and hyperlactatemia, contrary to what Wiberg and colleagues found in Sweden in 2008[14].

For Apgar scoring, the true positive rates were higher at one minute (95.5%) than at five minutes (91.3%). The false positive rates were slightly lower at five minutes (67%) than at one minute (70%). This means that using Apgar scoring for initial assessment is performing its role in identifying newborns in need of resuscitation (high rates of true positives) but at both time points there is a high false-positive rate

The modeling revealed that the odds of the composite adverse outcome (early neonatal death or admission to the neonatal unit) were significantly elevated in the presence of maternal hypertension (OR=2.9, P=0.019) after correcting for the presence of hyperlactatemia. Thus, hypertension contributed independently to adverse outcomes over and above birth asphyxia, perhaps reflecting reduced placental reserve and adverse circulatory conditions in hypertensive mothers.

## **Chapter 6: Conclusion and Recommendation**

### **6.1 Conclusion**

This study has highlighted the risk factors for stillbirths at QECH, many of which are in agreement with other studies done outside Malawi. These include preeclampsia, abruption placenta, anaemia, syphilis, HIV and most importantly asphyxia. Poor intrapartum care



attributed to lack of theatre space was the single most important cause of fresh stillbirths. None of the mothers had diabetes mellitus and malaria both of which are highly associated with increased risk of stillbirth in other studies.

The antenatal care coverage is excellent however, the quality of care provided in the centres needs improvement in terms of Blood Pressure measurement, syphilis, urine, blood sugar testing and administration of prophylactic drugs.

It is further noted that birth asphyxia is the commonest cause of admission to the nursery and high perinatal mortality. The Apgar score at 1 minute is a good predictor of hyperlactaemia. However, it has a challenge of high false positive rates (not very good specificity), thus it over diagnoses acidosis. When used together with lactate, there will be reduction of false positive diagnosis of birth asphyxia, and potentially reduce unnecessary nursery admissions.

Adjusted for age and parity, hypertensive mothers had higher risk of having poor neonatal outcome for any given level of umbilical artery blood lactate. This means that newborns of mothers with hypertension should receive careful assessment in the early neonatal period as is the case with low Apgar score and low birth weight infants.

## **6.2 Limitations**

The phase one study did not have a comparison group for the stillbirths due to lack of funds at the time. This limited the analysis of the data to frequencies only. For the same reasons, placental and membrane histology were not done as originally planned. The results of the

study may be unique to the hospital as it was done at a tertiary hospital, within the urban area that does not have a secondary public health care service.

In phase two of the study, there was no follow-up for the babies that were born with high lactate levels after discharge from both the neonatal ICU and postnatal ward. This could have led to underestimation of birth asphyxia rates.

### **6.3 Recommendation**

The study revealed a high incidence rate of Rhesus negative blood group which was not well evaluated regarding its association with stillbirth occurrence. We recommend a further study that would objectively advocate for routine Rhesus blood group testing for every mother during the first pregnancy. We further recommend for creation of more theatre space for Chatinkha labour ward for both elective and emergency caesarean sections. This is in terms of structural space, anaesthetists, theatre midwives and equipment. The HIV sero-conversion rate was very high among the stillbirth mothers, therefore, we recommend HIV testing for every mother (regardless of a negative test result at ANC) upon admission in the labour ward in order to reduce the HIV transmission from mother to child. This study can serve as a feasibility study for bigger study that would have a bigger sample size, comparison group and placental histology both of which this study did not have.

Further study to examine the outcomes in babies with lactate more than 3.2mmol/L but less than 5mmol/L is recommended. These babies are likely to have 'mild' birth asphyxia but it is not known whether it is clinically significant, so a follow up for that group might be informative as to whether they need more attention or not.

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