Maternal and neonatal mortality in Moi Teaching and Referral hospital in Kenya

Faith Yego
MSc, BSc

This thesis is submitted in fulfilment of the requirements for the Degree of Doctor of Philosophy (Gender and Health)

School of Medicine and Public Health
University of Newcastle, NSW 2308
Australia

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Statement of Originality

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to this copy of my thesis, when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968. **Unless an Embargo has been approved for a determined period.

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I hereby certify that this thesis is submitted in the form of a series of published papers of which I am a joint author. I have included as part of the thesis a written statement from each co-author; endorsed by the Faculty Assistant Dean (Research Training), attesting to my contribution to the joint publications.

13/7/2015

Faith Yego Date

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List of manuscripts to be submitted

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Statement of collaboration

I hereby certify that the work embodied in this thesis has been done in collaboration with other researchers, or carried out in other institutions. I have included as part of the thesis a statement clearly outlining the extent of collaboration, with whom and under what auspices.

As author of this thesis I conducted the work presented under the supervision of three supervisors: Professors Catherine D'Este and Julie Byles and Dr. Jennifer Stewart Williams

Dr. Paul Nyongesa and Dr. Wilson Aruasa were also instrumental advisors and contributed in some of the publications. I was a major contributor to all aspects of the study: planning, literature review, data collection, analysis and statistical modeling, interpretation of results, writing of manuscripts for peer-reviewed journals and writing of thesis.

13/7/2015

Faith Yego Date

Dedication

I dedicate this thesis to all women who have died as a result of childbirth or lost a child during childbirth

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List of Abbreviations

ANC: Antenatal Care

APH: Antepartum Haemorrhage

BBA: Born Before Arrival

BP: Blood Pressure

EmOC: Emergency Obstetric Care

EMR: Electronic Medical Record

END: Early Neonatal Death

ENMR: Early Neonatal Mortality Rate

HDU: High Dependency Unit

HIV: Human Immunodeficiency Virus

HREC: Human Research Ethics Committee

ICD: International Classification of Disease

ICU: Intensive Care Unit

IREC: Institutional Research Ethics Committee

KNH: Kenyatta National Hospital

LND: Late Neonatal Death

MDGs: Millennium Development Goals

MMR: Maternal Mortality Rate

MMR: Maternal Mortality Ratio

MOH: Ministry of Health

MTRH: Moi Teaching and Referral Hospital

NMR: Neonatal Mortality Rate

NMR: Neonatal mortality Ratio

NBU: Newborn Unit

PAC: Post Abortal Care

PE: Preeclamspia

PPH: Postpartum Haemorrhage

PROM: Premature rupture of membranes

RA: Research Assistants

RAMOS: Reproductive Age Mortality Survey

RDS: Respiratory Distress Syndrome

SMI: Safe Motherhood Initiative

UN: United Nations

WHO: World Health Organization

Synopsis

The idea for this thesis originated while I was attending weekly mortality meetings at the Moi Teaching and Referral Hospital (MTRH) coupled with high maternal and neonatal mortality rates in Kenya. I shared the idea with two obstetricians who provided their support and willingness to help understand the problem. With support from the University of Newcastle and The Ministry of State for Public Service in Kenya, I received a scholarship to undertake my PhD at the University of Newcastle in Australia.

This thesis by publication is composed of seven chapters including: an introduction, methodology, four papers (each a separate chapter), and conclusion. All papers relate to factors surrounding maternal and neonatal mortality at a tertiary hospital in Kenya. At the time of submission three papers have been published and one is under review.

The first paper is a retrospective review of the incidence of maternal and neonatal mortality at MTRH and a description of characteristics of maternal and neonatal deaths at this hospital. The study identifies a range of socio demographic, clinical and health system factors as possible contributors to high maternal and neonatal mortality in Kenya. This paper was published in the Reproductive Health Journal.

The second paper is a case-control study following a manual review of maternal records at MTRH. The study identified antenatal care and maternal education as risk factors for maternal mortality at MTRH. This paper was published in BMC Pregnancy and Childbirth.

Paper Three is a case-control study of neonatal records at MTRH. Results showed that some risk factors for early neonatal mortality included: number of antenatal visits, gestational age, qualification of birth attendant, mother's complication at birth, and low Apgar scores at five minutes, and congenital malformations. This paper has been published in BMC Pregnancy and Childbirth.

The fourth paper presents an assessment of completeness of maternity data at MTRH including factors associated with missing data. The results showed that a range of maternal neonatal and health system factors were associated with missing data in the maternal and neonatal sample. This paper will be submitted for publication in a reputable journal.

The support I received from my supervisors was overwhelming in terms of making the project more realistic. We prepared all the necessary documents and obtained necessary approvals and permission to undertake the study. I personally was involved in the data collection process which was the bulk of this thesis because we had to go through paper records to obtain data for this study. I also did the data analysis with the guidance of my supervisors.

The outcomes of this study have had a huge audience globally as well as health system policy implications for the hospital and nationally. More specifically, one of the obstetricians in the hospital who was the study advisor (PN) had this to say about the study. "This study has had an impact in more revision and development of new protocols in the maternity unit on pre-eclampsia, triage of patients at admission, involvement of paediatricians in management of newborns, establishment of High

Dependence Unit (HDU) in addition to the existing Intensive Care Unit (ICU), involvement of physicians in management of medical disorders in pregnancy and increased staffing of labour ward with more doctors. More population based studies of the same are underway to help clarify the study findings".

Thesis Overview

This thesis by publication contains an introduction; a chapter providing an overview of maternal and neonatal mortality including burden of disease, causes of and risk factors for mortality, and a conceptual framework for the thesis; a methods chapter; four papers and a conclusion chapter. The four papers focus on findings on maternal and neonatal mortality at the Moi Teaching and Referral Hospital (MTRH) in Kenya from 2004-2011. The papers are based on data collected from the maternity ward records at this hospital. Chapter Four presents the first of the journal articles (Paper One) which describes incidence and characteristics associated with maternal and neonatal mortality at MTRH. Paper Two presents a case-control study to examine risk factors associated with maternal mortality. A case-control study examining factors associated with fetal and early neonatal mortality at MTRH is provided in Paper Three. The final paper examines record completeness at MTRH and factors associated with missing data. The final chapter (Chapter 8) provides an overall conclusion to the work, discussing the directions for future research, study strengths and limitations. The appendices contain the publications, statements of contribution of authorship, study questionnaire, ethics approval, and a letter from MTRH.

Chapter 1 Introduction

Maternal and child health is an important area of concern globally. Every minute in the world a woman dies as a result of pregnancy or childbirth, and every three seconds a child dies from preventable causes.[1] These deaths are not just isolated medical occurrences. Maternal and child deaths have impacts beyond the immediate family to the broader society. The greatest disparities in maternal and child mortality are seen between developed and developing regions with the highest burden in the developing countries.[2] Because of these disparities maternal and child mortality is a core priority for international development efforts.

In 2000 the United Nations (UN) and other partners set Millennium Development Goals (MDGs) as a roadmap for the implementation of the Millennium Declaration.[3] The MDGs seek to inspire development of universal efforts to improve the livelihoods of people around the world, and in particular the rights of women to give birth without risking their lives and those of their children. The UN and its partners have identified eight priority areas for development, with two of the eight goals specifically targeting maternal and child mortality.[3] Goal Four is to reduce under-five mortality by two thirds between 1990 and 2015, and Goal Five is to reduce maternal mortality by three quarters and achieve universal access to reproductive health by 2015.[4] The achievement of these goals by 2015 is dependent upon each country's developmental strategies, and specifically upon the policies and programmes put in place to address the MDGs. Since 1990, maternal and child deaths have reduced by about 40% worldwide.[5] However, not all countries have made improvements. A recent report

showed that Kenya, for example, has made insufficient progress towards reducing maternal and child mortality and meeting the MDGs.[3]

Maternal mortality is defined by the World Health Organization (WHO) as "the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes".[6] Lifetime risk of maternal death is defined as "the probability that a 15-year-old female will die at some time from a maternal cause if she experiences throughout her lifetime the prevailing risks of maternal death and the overall levels of fertility and mortality that are observed for a given population".[6]

The lifetime risk of maternal death derives from estimates of the maternal mortality ratio (MMR) and maternal mortality rate. The MMR is defined as "the ratio of the number of maternal deaths during a given time period per 100,000 live births during the same time-period," and the maternal mortality rate is defined as "the number of maternal deaths in a population divided by the number of reproductive women per 1000 women".[5] A woman's lifetime risk of maternal death is one in 3800 in developed countries versus one in 150 in developing countries.[5]

The Kenyan population has more than tripled over the past four decades -increasing from 11 million in 1969 to about 40 million in 2009, with 51% of the current population aged 15-64 years.[7] Kenya continues to experience poor pregnancy outcomes. The MMR is 488 per 100,000 live births, compared with the current global MMR of 287 per 100,000 live births.[3, 7] More than half of the births in Kenya (56%) still take place at home,

especially among older women, women from rural areas, and for multiparous births.[7] Home births can result in complications that are not appropriately addressed and are often combined with delayed referral to hospital facilities; home births can result in adverse outcomes for the mothers and neonates.[8]

Stillbirth is a term that refers to a dead born fetus, whereby intrauterine death occurs either before onset of labour - known as antepartum death, or during labour - also known as intrapartum death.[9] Fetal death is s any fetus born without a heartbeat, respiratory effort or movement, or any other sign of life.[10] Fetuses may die intra utero before onset of labour because of pregnancy complications or maternal diseases.[9] Neonatal death is defined as death of a live born baby within 28 days of life, and can be further divided into: early neonatal death (END) defined as death of a live born baby within the first seven days of life, and late neonatal death (LND) defined as death of a live born baby after the first seven days of life but within 28 days of life.[9] Live birth is "the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached; each product of such a birth is considered live born".[11]

Over three million neonatal deaths and over two million stillbirths or fetal deaths occur globally every year.[12] In Africa, the average neonatal mortality rate (NMR), defined as the number of neonatal deaths per 1000 live births, is 35 per 1000 live births compared to developed countries where it is seven per 1000 live births.[3] In Kenya the NMR is

lower, at 28 per 1000 live births.[7] This difference can be partly attributed to the birth decline in Kenya to four children per woman in recent years, and to tetanus immunization during the antenatal period.[13] The 2012 MDG report showed that there has been a 35% overall reduction in under five mortality globally over the past decade.[14] This is largely attributed to the introduction of programs that target malaria and immunizations for neonates beyond the first month of life.[14] However it is concerning that the proportion of deaths occurring within the first month of life relative to under five deaths, increased by about 11% from 2000-2010.[3]

Potential causes of maternal and neonatal deaths have been widely researched, and these vary from one region to another. Overall, the leading causes of maternal death in developing countries are indirect causes, haemorrhage, hypertensive disorders, and sepsis, whereas in developed regions the major causes of maternal death are indirect causes and other direct causes.[15] Factors contributing to maternal mortality also vary among countries. These factors include rural residence, poverty, poor education, younger age, birth order, antenatal care, contraceptive use, gestational age, and health system factors, such as lack of skilled staff, equipment, supplies and inadequate quality of care.[16-19]

The leading causes of neonatal deaths include preterm birth, intrapartum related deaths and infections.[20] Some of the known maternal risk factors that have been shown to contribute to neonatal mortality include: lack of skilled attendants at birth; multiparity and maternal complications such as haemorrhage, hypertensive disorders, obstructed labour, prolonged labour, rupture of membranes, malpresentation, malaria, Human Immunodeficiency Virus (HIV), and meconium staining.[21, 22]

There is evidence that the most effective interventions for reducing maternal and child mortality are those that target an overlap between maternal and neonatal health outcomes.[10, 12] Examples of these programs are those directed at antenatal care such as the presence of skilled birth attendants, counselling, family planning, hygienic practices during delivery, the management and treatment of infections including malaria and HIV, good maternal nutrition, post-natal care and screening and the management of maternal illness during pregnancy.[10, 12] However in order to be successful these interventions must be tailored to the health system within which the women seek care.

1.1 Significance of the study

This research investigates maternal and early neonatal mortality in Kenya. The work was undertaken at the Moi Teaching and Referral Hospital (MTRH). The MTRH is Kenya's second largest hospital and is located in rural Western Kenya. This region is important since it comprises a large human resource population as well as agricultural, livestock and natural resources which provide micronutrients and food sources that are important determinants of mothers and newborn survival.[23] This is the first study of its kind and the findings have both local and national significance given Kenya's slow progress towards meeting the MDGs Four and Five.

More specifically, the outcomes of this study will provide information on health system and other factors that contribute to maternal and early neonatal mortality. This information can help identify interventions to strengthen the health system and encourage more hospital births. The role of referrals in contributing to mortality is

explored here in order to identify the reasons for, and outcomes of, pregnancy related referrals to the MTRH.

It is also important to understand the reasons for the increase in neonatal deaths given the declining proportion of under five deaths. This research will not only examine the incidence of maternal and early neonatal mortality, but also a range of contributing factors.

The findings will shed light on issues related to completeness of maternal and neonatal data and highlight strengths, weakness and areas for improvement in record keeping in a national teaching hospital that still relies heavily on paper records for data storage.

Mortality is an important indicator of maternal and neonatal health in populations. At a global level, the outcomes of this study will provide vital information to inform the monitoring of progress towards achieving MGDs Four and Five.

The next chapter discusses maternal and neonatal mortality, highlighting the causes, global burden and risk factors associated with maternal and neonatal mortality.

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Chapter 2 Overview of maternal and neonatal mortality

This chapter has three main sections. The first section discusses maternal mortality with respect to the burden of maternal mortality, clinical features and definitions of causes of maternal mortality, and risk factors for maternal mortality. The second section discusses fetal deaths and early neonatal deaths, including the global burden of fetal and neonatal deaths, clinical features and causes of fetal and early neonatal deaths, and risk factors for fetal and early neonatal deaths. The final section discusses the areas of maternal and neonatal mortality where there is limited knowledge, introduces the conceptual framework used in this thesis, and states the objectives.

2.1 Maternal mortality and contributing factors

2.1.1 Burden of maternal death

A comparison of maternal mortality ratios in different regions of the world is shown in Table 2.1. From the table it is evident that maternal mortality varies from 16 per 100,000 live births in the developed regions to 500 per 100,000 live births in the developing regions; 99% of maternal deaths occur in Sub-Saharan Africa.[1]

Table 2-1 Estimates of Maternal Mortality Ratio and lifetime risk of death by regions in 2010. Adapted from a report by WHO, UNICEF, UNFPA and The World Bank estimates[1]

Region	Maternal Mortality Ratio (per 100,000 live births)	Lifetime Risk of Maternal Death, 1 in:
Developed Regions	16	3800
Developing Regions	240	150
Sub-Saharan Africa	500	39
Southern Asia	220	160
Latin America	72	580

2.1.2 Causes of maternal mortality

Globally, the causes of maternal mortality are divided into direct causes or indirect causes. Direct causes are defined as "those causes that result from obstetric complications of the pregnancy state (pregnancy, labour or puerperium), from interventions, omissions, incorrect treatment, or from a chain of events from any of the above".[2] Indirect causes are "infections, cardiovascular diseases, psychiatric illnesses, and other chronic diseases that result from previous existing diseases or diseases that develop during pregnancy and are aggravated by physiological effects of pregnancy".[2] The five leading causes of maternal death in the developed regions[3] are: indirect causes (24%); other direct causes (20%); haemorrhage (16%); embolism (14%) and hypertension (13%). These are shown in Figure 2.1.

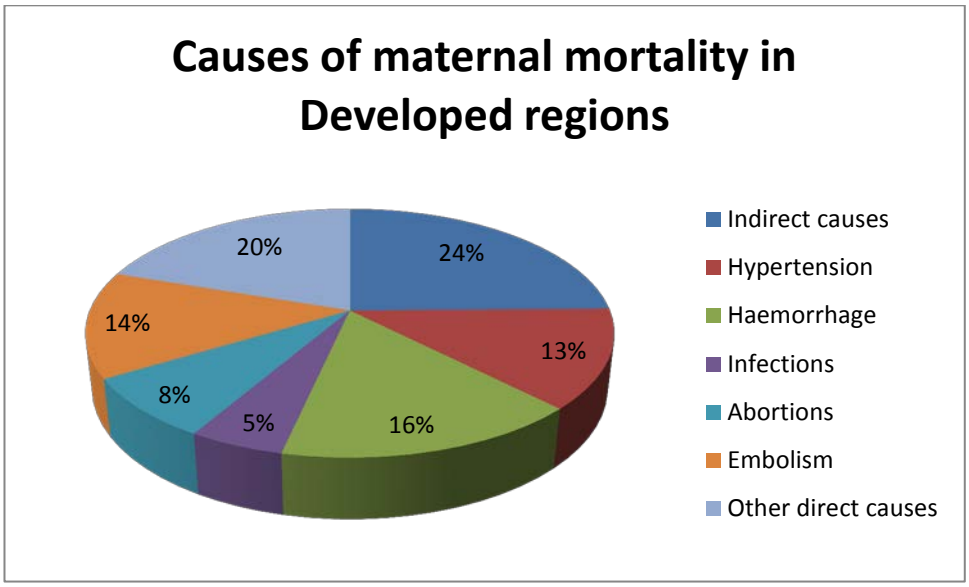

Figure 2-1 Distribution of causes of maternal mortality in developed regions. Adapted from Say et al[3]

The top five leading causes of maternal deaths in developing regions are: haemorrhage (27%); indirect causes (27%); hypertensive disorders (14%); infections (11%), and other direct causes (10%). These are shown in Figure 2.2.

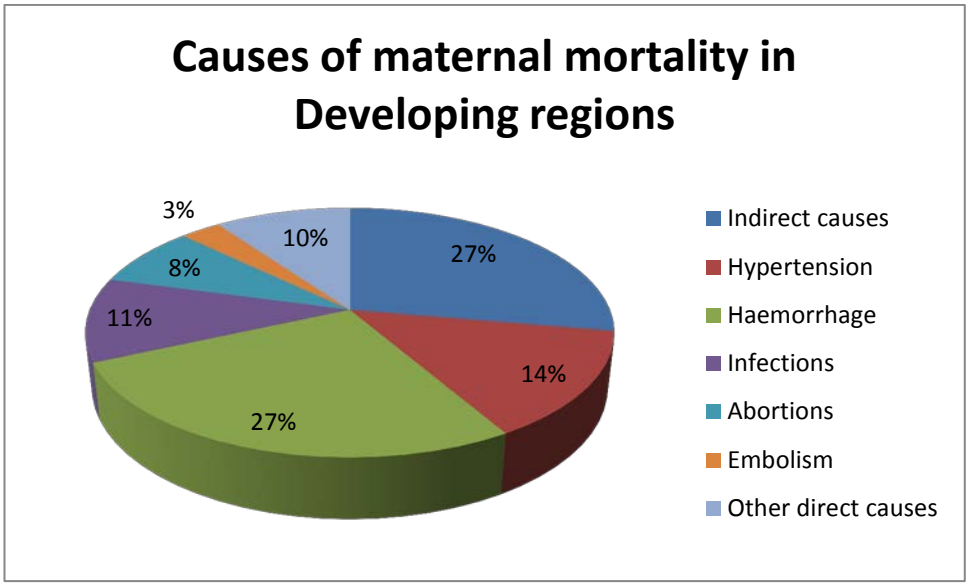

Figure 2-2 Distribution of causes of maternal mortality in developing regions. Adapted from Say et al[3]

Indirect causes of maternal death in developing countries include HIV, malaria, tuberculosis, and cardiovascular disease. These factors also have enormous impact on maternal and fetal outcomes during pregnancy. A systematic review found that pregnant women living in areas with endemic malaria were more likely to become infected than non-pregnant women.[4] Antenatal anaemia can also result in slow fetal growth, and both of these conditions are harmful to the mother and baby.[4] A study undertaken in Malawi using the Demographic and Health Survey data from 1999 to 2004, found that children born to HIV infected mothers were more than twice as likely to die during infancy as those born to uninfected mothers.[5] There is evidence that pregnant women with type one or type two diabetes are not only at greater risk of adverse outcomes, such as gestational hypertension and preterm births, but also diabetic complications that can be aggravated by pregnancy.[6]

2.1.3 Definitions and clinical criteria for direct causes of maternal death

The following section describes the operational definitions and clinical manifestations for the five leading causes of maternal death in Africa - being haemorrhage, eclampsia, hypertensive disorders, obstructed labour and sepsis. These definitions are based on WHO guidelines for monitoring obstetric care, literature searches, and the WHO handbook on pregnancy, childbirth, postpartum and newborn care.[2, 7]

Haemorrhage refers to excessive bleeding from the vagina either when pregnant (after 22 weeks) or immediately after delivery.[2] There are two kinds of haemorrhage in childbirth, ante-partum that occurs before delivery, and post-partum that occurs after delivery. Ante-partum haemorrhage (APH) is severe bleeding that occurs before and during labour. The primary causes of APH are abruptio placenta (premature separation of the placenta), placenta previa (placenta implanted in the lower segment of the uterus), uterine rupture and lower genital tract lesions.[2] Significant APH may result in severe fetal morbidity, for example preterm birth, asphyxia and even fetal death. Excessive blood loss may lead to severe maternal anaemia, coagulation and bleeding problems and eventually maternal death.[2]

Post-partum haemorrhage (PPH) is defined as excessive bleeding, that occurs after delivery of approximately 500 millilitres (mls) after vaginal delivery and 1000mls after caesarean section.[2] PPH is further divided into two types: Primary or Immediate PPH that occurs within 24 hours of delivery, and Secondary or Late PPH that occurs between 24 hours and six weeks postpartum.[2] PPH is the world's leading cause of maternal mortality accounting for a third of all maternal deaths.[8] A mother with PPH is

usually predisposed to infection, severe anaemia, bleeding tendencies and even death.[9] In developing countries 25% of maternal deaths are due to haemorrhage. Globally, APH accounts for approximately 40% of maternal deaths while PPH accounts for the remaining 60%, the majority of which occur within four hours of delivery.[8, 9]

Sepsis is defined as a rise in temperature equal to or above 38 degrees Celsius (ºC) sustained for more than 24 hours or recurring between the end of the first and 10th day after childbirth, miscarriage, or termination of pregnancy.[10] Sepsis is defined by the presence of both infection and a systemic inflammatory response accompanied by more than one of the following: temperatures equal to or greater than 38°C, tachycardia >90 beats per minute (bpm), rapid breathing, alteration in white blood cell count >12,000 cubic millimetres (cu mm) or <4,000 cu mm, or immature neutrophils of 10% or above.[11] The clinical features of sepsis include lower abdominal pain, high temperatures more than 24 hours after delivery, general malaise, anorexia, sub involution of the uterus and in severe cases, septic shock with low blood pressure (< 90/60 Millimetres of Mercury (mm Hg)) and a high pulse of 100 bpm.[2] There is also a higher risk of infection due to exposure to pathogens following delivery by caesarean section.[12] If not treated well, or if patients present late, sepsis can result in severe morbidity such as kidney and liver failure and in some cases death. Sepsis accounts for 10% of maternal deaths worldwide, with the greatest burden in Africa and Southeast Asia.[12]

As previously mentioned, hypertensive disorders in pregnancy are one of the leading causes of maternal death in developing countries. Hypertensive disorders in pregnancy are characterized by high blood pressure i.e. BP > 140/90 mm Hg with or

without excessive proteins in urine.[2] Preeclampsia (PE), is manifested by diastolic blood pressure ≥ 110 mm Hg or proteins of more than three after 20 weeks gestation.[2] Signs and symptoms of PE include headache, blurred vision, oliguria, epigastric pain, pulmonary oedema, and hyperflexia.[2] Patients may also have convulsions, with risk of this increased for those with diastolic blood pressure ≥ 90mm Hg after 20 weeks gestation or proteinuria equal to or above two.[2] In severe cases of preeclampsia diagnoses may be complicated by the presence of low platelets, decreased urine output, excessive protein loss in urine, liver failure, bleeding tendencies, convulsions, difficulty in breathing secondary to pulmonary oedema, visual disturbance or even blindness secondary to retinal detachment, fetal growth retardation, abruptio placenta and fetal demise.[13-15] All of these risks and complications make the pregnancy "high-risk" usually necessitating early delivery to avoid both maternal and fetal morbidity and even mortality. In developing countries the incidence of preeclampsia is seven times higher than developed countries.[16]

Prolonged or obstructed labour (dystocia) is defined as any of the following: prolonged established first stage labour (>12 hours); prolonged second stage of labour (above two hours); cephalic-pelvic disproportion including scarred uterus, and mal-presentation.[9] Dystocia is further defined as failure of descent of the fetal head into the birth canal due to mechanical obstruction.[17] This occurs in about one to three percent of pregnancies.[17] Some of the causes of obstructed labour are mal-position or mal-presentation of the fetus and/or having a small inadequate pelvis.[17] Obstructed labour can lead to adverse fetal and maternal outcomes if not well managed. Outcomes resulting from obstructed labour include: maternal infection; uterine rupture; and

haemorrhage; formation of fistula (abnormal communication between either bladder and vagina or vagina and rectum, causing uncontrollable leakage of either urine or faecal matter or both); maternal death; birth asphyxia; neonatal sepsis and fetal death.[17]

2.1.4 Risk factors for maternal mortality

Previous research has been undertaken to investigate risk factors for maternal mortality in developed countries. A study conducted in Australia between 2003 and 2005 found that the majority of maternal deaths were a result of embolism, hypertensive disorders and indirect causes. The risk factors identified were age below 30 years, primiparity, gestational age below 20 weeks and transfer from other hospitals.[18] A case-control study undertaken in France between 2001 and 2006 identified risk factors for maternal mortality as haemorrhage, embolism, and hypertensive disorders.[19] In the United States a review of birth and death certificates conducted from 1998 to 2005 identified an increased risk of maternal death among women of African American origin and women with cardiovascular disease.[20] A retrospective cohort study in Denmark conducted on women with a first singleton delivery from 1978 to 2007 reported that preterm delivery and small size for gestational age were associated with maternal complications of diabetes and cardiovascular disease.[21]

Some studies of risk factors for maternal mortality have been conducted in middle-income countries. A case-control study of 300 women undertaken in Brazil in 2001-2005 found that maternal death was associated with health system factors, such as birth by caesarean section, and having fewer than four antenatal visits.[22] There is evidence that antenatal care links the women to the health system, hence increasing their

knowledge of the pregnancy continuum and emergency obstetric care which increases their probability of utilizing the health facility for birth.[23] A community based case-control study in India showed that risk factors for maternal mortality were illiteracy, high parity, lack of antenatal care, distance to health facility, and complications such as jaundice, retained placenta, haemorrhage and anaemia.[24] In Mexico a matched case-control study conducted from 1992-2004 reported that age, being unmarried, a high number of antenatal visits (which was protective), pre-existing medical conditions (such as cardiovascular disease), obstetric complications in previous pregnancies and delivery by caesarean section, were risk factors for maternal mortality.[25] In Syria, the Reproductive Age Mortality Survey (RAMOS) undertaken in 2003 through home interviews and verbal autopsies found that the determinants of mortality were factors associated with the health system, such as poor clinical skills by hospital staff and lack of clinical competency by health personnel.[26]

Several studies have been conducted to examine the risk factors for maternal mortality in Africa. In Senegal, a case-control study undertaken over a year at three major hospitals found that the leading causes of death were sepsis, haemorrhage and preeclampsia.[27] The factors associated with maternal mortality in Senegal included low education, history of complications, late referrals, lack of antenatal care, lack of personnel at the time of admission, and maternal status on admission including the presence of complications, elevated blood pressure, elevated temperature and low haemoglobin levels.[27] A case-control study in Guinea concluded that lower family income, the presence of infection, having anaemia or hypertension or dystocia, and delivery by caesarean section were associated with maternal mortality.[28] In Ghana, an

audit undertaken using maternal death notifications revealed that deaths of mothers were linked to delays in receiving care and also non-adherence to treatment protocols.[29] A retrospective study in Nigeria from 2003-2007 found that nulliparity, lack of antenatal care, and illiteracy were the most significant factors associated with maternal mortality.[30] A prospective analysis of maternal mortality conducted in Nigeria from 2001-2007 reported a high-risk of maternal death among nulliparous adolescents, with the leading cause of maternal death being eclampsia followed by haemorrhage.[31] In Malawi, a case review identified several determinants of maternal mortality, including health workers who performed inadequate resuscitation, lack of obstetric skills, lack of proper monitoring of patients, delay in initiating treatment, inadequate monitoring of staff, lack of blood transfusion, shortage of staff, poor data quality and lack of sufficient resources.[32] A cohort study in Tanzania (2000-2007) reported that having a formal referral system helped identify high-risk births compared to self-referred women who had higher caesarean section rates due to complications and poor neonatal characteristics.[33] Additionally, formal referral was associated with rural residence, level of education and obstetric risks during pregnancy.[33]

In summary, the risks for maternal mortality for developed and developing countries are different. The most common risk factors for developed countries include hypertensive disorders and cardiovascular disease in pregnancy. Risks for developing countries include a range of individual, obstetric/reproductive and health system factors.

2.2 Fetal and early neonatal mortality and contributing factors

2.2.1 Burden of fetal and early neonatal death

Every year, over four million babies die in the first four weeks of life and three million of these are early neonatal deaths. It is estimated that more than three million babies are stillborn every year and that one in three of these deaths occur during delivery and can largely be prevented.[34] For every baby who dies within the first week of birth, another is born dead.[34]

Table 2.2 below shows the global burden of stillbirth and early neonatal deaths in the various regions of the world. The highest rates of stillbirths and neonatal deaths are in Africa (32 stillbirths and 31 neonatal deaths per 1000 live births) and the lowest rates are in developed regions (six stillbirths and four neonatal deaths per 1000 live births).[34]

Table 2-2: Stillbirth rates and early neonatal mortality rates in different regions in 2000 Adapted from WHO[34]

Region	Stillbirth rate (per 1000 live births)	Early neonatal mortality rate (per 1000 live births)
World	24	23
Developed regions	6	4
Developing regions	26	25
Africa	32	31
Asia	27	24
Europe	8	4
Oceania	23	19

2.2.2 Causes of fetal and early neonatal deaths

Figure 2.3 shows the leading global causes of neonatal death including preterm birth (29%), asphyxia (22%), and sepsis (15%).

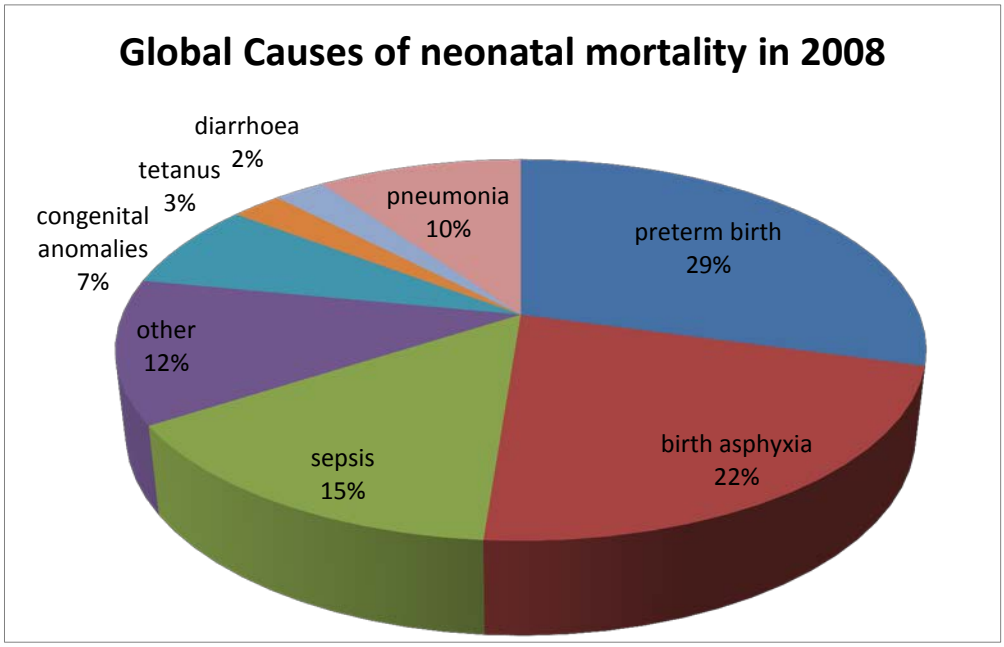

Figure 2-3 Global causes of neonatal deaths. Adapted from Liu et al [35]

There is evidence that the highest number of early neonatal deaths in Africa result from infections.[7, 34, 36] Obstetric complications, particularly those that occur in labour, represent more than half (58%) of stillbirths and early neonatal deaths. Almost 30% of neonatal deaths are the result of injuries sustained during delivery.[34, 37] Three percent of neonatal deaths are due to congenital anomalies in developing countries, especially those caused by diseases such as syphilis, or by nutrient deficiency, which leads to neural tube defects and cretinism.[34] Safe childbirth and effective neonatal care are essential for the prevention of neonatal deaths.

2.2.3 Definition, clinical criteria for the leading causes of deaths in the perinatal period

Preterm birth is defined as any delivery occurring before 37 completed weeks.[10] A baby born before 37 completed weeks is premature and the condition itself is termed as prematurity. Births that occur after 37 completed weeks are considered term babies.[10] Five percent of births are delivered preterm and contribute to almost 50% of neonatal

morbidity and mortality.[38] A developing fetus requires the last weeks and months of pregnancy to develop various vital organs including the brain, liver and lungs and being born earlier poses a serious risk of death and disability. These risks include breathing problems, feeding difficulties, cerebral palsy, developmental delay, vision problems, hearing impairment and even death.[38] Premature rupture of membranes (PROM) occurs when there is rupture of membranes prior to term and prior to the onset of labour, and predisposes the pregnancy to risk of preterm labour.[39] Respiratory Distress Syndrome (RDS) is a condition that makes it hard for the baby to breathe and is a result of complications of preterm birth. This is the primary cause of early neonatal death and disability and RDS primarily affects low birth weight babies.[40] There is evidence that where women are at risk of preterm delivery, PROM and hypertensive disorders, and are given antenatal corticosteroids, the risks of complications occurring between 26 to 35 weeks gestation with subsequent newborn death is reduced substantially.[40]

Birth asphyxia is an intra-partum related condition that affects the neonate and is caused by the lack of oxygen to the fetal brain causing brain injury.[41] According to the WHO, birth asphyxia is defined as the failure to establish breathing at birth and causes about a million deaths a year, especially in the first week of life.[42] Birth asphyxia has also been previously defined as the failure to initiate spontaneous respiration with an Apgar score of less than seven at five minutes, though this is not the standard indicative measure of asphyxia and the definition has come under a lot of criticism.[43] Asphyxia is usually characterized by profound acidemia (pH of less than seven) determined on an umbilical cord arterial blood sample, persistent five minute Apgar

score of zero to three, and evidence of neonatal neurological sequelae such as seizures, coma, or hypotonia; or dysfunction in one or more of the following systems: cardiovascular; gastrointestinal; haematological; pulmonary, or renal.[41] Birth asphyxia can be classified as mild, moderate and severe, with symptoms ranging from restlessness, jitteriness and hyper-alertness to severe cases of seizures, poor responsiveness, coma, cardiac, renal and neurological abnormalities and even death.[41] In general, infants with mild birth asphyxia have good prognosis, but those with severe asphyxia and permanent brain damage develop motor deficits and cerebral palsy.[41] Some known risk factors for birth asphyxia include preeclampsia, placenta abruption, fetal anaemia, intrauterine growth restriction, post maturity, malpresentation and abnormal labour.[44]

Neonatal sepsis is by consensus defined as blood infection that occurs in an infant younger than 90 days old.[11] Early-onset neonatal sepsis often appears within 24 hours of birth with the baby acquiring the infection from the mother before or during delivery, while for late-onset neonatal sepsis the infection is contracted after delivery.[11] The definition of neonatal sepsis remains vague and flexible to physician interpretation. Neonatal sepsis is mostly caused by infection of the neonate by microorganisms acquired from the mother such as Group B Streptococcus and Haemophilus Influenzae, or from organisms acquired from the care giving environment, for example E Coli and Candida.[45] Infants with neonatal sepsis can have the following symptoms: difficulty breathing; irritability; lethargy; cyanosis; acidosis; poor feeding; vomiting; unexplained jaundice; petechiae; changes in body temperature or glycaemic state; pulmonary hypertension; hypotonia, or seizure.[11] With prompt

treatment and birth under hygienic conditions many babies with septic infections recover completely. However, inappropriate treatment of the infant results in various complications, disability and death. Neonatal sepsis is one of the leading causes of infant death. There is evidence that preterm delivery, low birth weight, prolonged rupture of membranes, intrapartum fever, labour complications and birth asphyxia are risk factors for early-onset neonatal sepsis.[46]

Low birth weight is also associated with the death of many newborn infants, even though it is not considered a direct cause. A neonate weighing less than 2500 grams at birth is considered as being low birth weight.[34] It has been estimated that about 15% of newborn infants weigh less than 2500 grams, with the proportion ranging from six percent in developed countries to more than 50% in countries such as India, Nigeria, Pakistan, China and Philippines.[34] Maternal health, nutrition, and presence of infections such as malaria, HIV and syphilis at conception are important determinants of baby weight at birth.[47]

2.2.4 Risk factors for fetal and early neonatal mortality

It has been widely documented that newborn deaths can be averted by the following interventions: mothers receiving the tetanus toxoid immunization; skilled care and hygienic conditions at birth; exclusive breastfeeding; clean cord care, and proper management of infections among newborns.[48] There is evidence that interventions such as syphilis screening and treatment, malaria prevention using insecticide treated nets, and medical therapies for certain maternal indications, can reduce stillbirths.[49]

It is well established that maternal factors including the mother's social and nutritional status, early childbearing, too many closely spaced pregnancies, and not taking care of the newborn well may have effects on the health and outcomes of the newborn.[34] Furthermore, the lack of adequate antenatal care, lack of skilled attendants at birth, low socioeconomic status, and poor nutrition are characteristics associated with stillbirths.[23] Exposure to harmful substances (e.g. tobacco, alcohol, drugs, cooking fires (biomass fuel) and environmental toxins) has also been associated with stillbirths.[50]

In all regions of the world, stillbirths have been associated with advanced maternal age, rural residence, low socioeconomic status, lack of education, single marital status, increased parity, primiparity, and short pregnancy intervals.[23] Caesarean delivery is protective for stillbirths in high-risk cases. Caesarean delivery rates in developed countries are about 24% compared to about one percent in developing countries.[23, 51] Reports indicate that caesarean delivery rates of less than five percent are a marker for lack of emergency and neonatal intensive care especially in rural areas.[51] In middle-income countries cigarette smoking and cooking with biomass fuels have been associated with stillbirths, primarily because of emissions from these substances that are harmful to the fetus.[23] In developing countries neonatal deaths and stillbirths also occur as a result of poor maternal health, lack of adequate care during pregnancy, mismanagement of complications during pregnancy and delivery, lack of proper hygiene practices during delivery or within the first critical hours after birth, and lack of adequate newborn care.[34] Other contextual factors, contributing to neonatal deaths in developing regions, include: lack of access to care; low maternal education; religious and cultural practices such as female circumcision that can cause reproductive

complications that can be harmful to the baby; distance to health facility, and financial barriers which result in women not being able to afford costs for antenatal care and birth by skilled personnel.[50]

Pre-existing maternal illnesses such as diabetes, hypertensive disorders, liver disease and thrombophilia, and maternal complications also predispose the neonate to morbidity and mortality risks.[50] A systematic review found that pre-existing diabetes is associated with increased risk of stillbirths, neonatal mortality and congenital anomalies, and that diabetic babies are usually larger than normal babies.[6] In a Canadian cohort study conducted in 2003-2009,[52] preeclampsia was found to increase the risk of RDS, smaller gestational age at birth and neonatal death. For about six percent of pregnancies globally, eclampsia results in poor fetal growth and hypoxia.[23] Maternal infections also contribute to 25-50% of stillbirths globally, with syphilis, malaria and HIV, being the leading infections in developing countries.[23]

Health systems also play an important role during the neonatal period through interventions by skilled personnel and efficient management of the newborn to improve the chances of survival in the first month of life. Worldwide, nearly one in ten infants require basic resuscitation which involves observing the infant for response, establishing if mask or bag ventilation is needed, checking heart rate and assigning an Apgar score if an infant fails to establish respiration at birth.[7] In the absence of necessary equipment to facilitate immediate resuscitation, the infant is at risk of death, even if the person attending to the neonate has formal training.

Studies of mortality during the neonatal period are not widely available, primarily because of the difficulty in defining etiology and also because healthcare providers evaluate these outcomes differently in different settings. However there is some literature from developed countries. For example, in the USA a review of New Jersey data from 1997-2005 revealed that risk factors associated with stillbirth were advanced maternal age (over 35 years), absence of antenatal care, "non-black" Hispanic ethnicity, placenta abruption, eclampsia and diabetes mellitus.[53] In a multi-ethnic population in England a cohort study conducted from 2009 to 2011 reported that the risk factors for stillbirth were maternal obesity, smoking in pregnancy and fetal growth restriction.[54] Among Indigenous Australians, the majority of stillbirths and early neonatal deaths resulted from conditions such as birth trauma, disorders related to length of gestation and fetal growth, while conditions related to the mother included complications of the placenta, cord or membranes.[55] In Brazil a case-control study undertaken between 2004 and 2005 showed that fetal malformations, less than six antenatal visits, haemorrhage, referral, advanced maternal age (above 35 years) and less than eight years of school were factors associated with perinatal mortality.[56] In developing countries a case-control study at the Nigeria University Hospital conducted from 2006-2007, reported that the major causes of stillbirths were abruption placenta, hypertensive disorders and maternal HIV infection.[57] Risk factors for mortality in Nigeria included lack of antenatal care and late presentation for complicated pregnancy at the health facility.[57] Another prospective study conducted in Central Africa in 2005 to 2007 found that the highest odds of fetal and early neonatal death occurred amongst neonates who were premature and had low birth weight, and neonates born to mothers who had no antenatal care and experienced economic difficulties.[58]

In summary risk factors for neonatal mortality vary among countries and differ between developed and developing regions. Factors common to all countries include maternal conditions that pre-dispose the neonate to high-risk of mortality. They include hypertensive disorders and haemorrhage, advanced maternal age and lack of antenatal care.

2.3 Study Justification

As shown in the literature, the causes and risk factors for maternal and early neonatal mortality are well established in the world although they differ among individual countries and settings. In developed countries, most studies investigating risk factors for mortality focus on high-risk complications that cause the highest incidence of maternal and neonatal mortality and report mortality estimates for the entire country. Some studies also focus on specific populations that have higher mortality rates, for example Aboriginal and Torres Islander women in Australia whose death rates are more than twice as high as other women.[18] With the exception of cause-specific mortality studies, a limited number of studies of maternal and neonatal mortality in developed countries rely on hospital data alone. One reason for this is that developed countries have more efficient vital registration systems compared with developing countries. In middle-income countries, most studies of mortality have been community based cohort studies or surveys of maternal and neonatal mortality. Recommendations described in these studies are therefore generally applicable to these settings and not necessarily generalizable. In Africa, the majority of studies of maternal and neonatal mortality rely on data from health facilities as the primary source of routine information used to compare trends and monitor progress in maternal and neonatal

characteristics.[59] In Kenya, studies of maternal and neonatal mortality have been undertaken in the city of Nairobi,[60-64] but the results may not necessarily be generalizable to the broader population hence the reason for choosing MTRH in Eldoret.

Research shows that maternal and newborn care is closely linked.[65] A few studies have examined maternal factors that contribute to newborn mortality. There is some evidence that integrated packages can improve maternal and neonatal health outcomes by focusing on maternal health throughout pregnancy,[48, 66, 67] even though no such studies apply specifically to Kenya or other African countries. There is a need to understand how to improve the functioning of health systems in these countries in order to provide essential newborn care within existing maternal and child health programs that produce the most effective outcomes.

There is also a need to conduct studies on the quality of maternal and newborn care in the intrapartum and postpartum period in health facilities in developing countries. The role of referrals in contributing to maternal and neonatal mortality in these countries must be understood in order to improve and develop formal referral systems to help avert mortality. There is very little literature on the association between behavioural factors, beliefs and practices and the use of skilled birth attendants in Kenya.

2.4 Theoretical framework for assessing the risk factors for maternal and early neonatal mortality

A theoretical framework can be useful way of assessing risk factors for mortality. In 1984 Mosely and Chen proposed an analytical framework suitable for studies on child

health that combined biological and social exploratory models into a single conceptual framework that categorises independent variables into distal or proximate determinants (see Figure 2.4).[68] The distal determinants include culture, religion education and the economy, while proximate determinants are maternal, health system, neonatal and delivery factors, as well as post-natal care.[68]

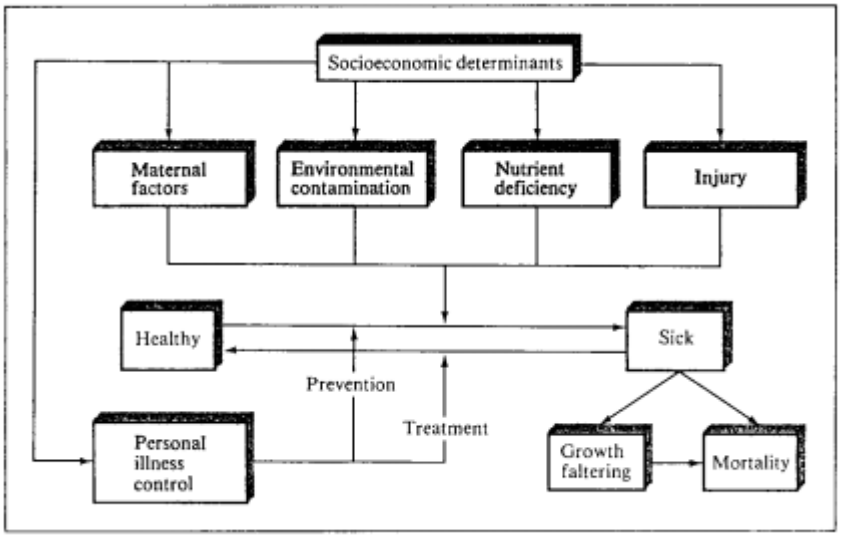

Figure 2-4 Theoretical framework by Mosely and Chen of the five groups of proximate determinants on the health dynamics of a population

The Delay Model by Thaddeus and Maine proposes that there are three delays that contribute to high maternal mortality - the delay in the decision to seek care, the delay in arriving at a health facility and the delay in receiving adequate care.[69] The Model by Gabrysch and Campbell (Figure 2.5),[70] which is based on the Delay Model, classifies delays related to the seeking of emergency care based on socio-cultural and economic factors, physical accessibility, the quality of preventative care and the quality of emergency care.[70]

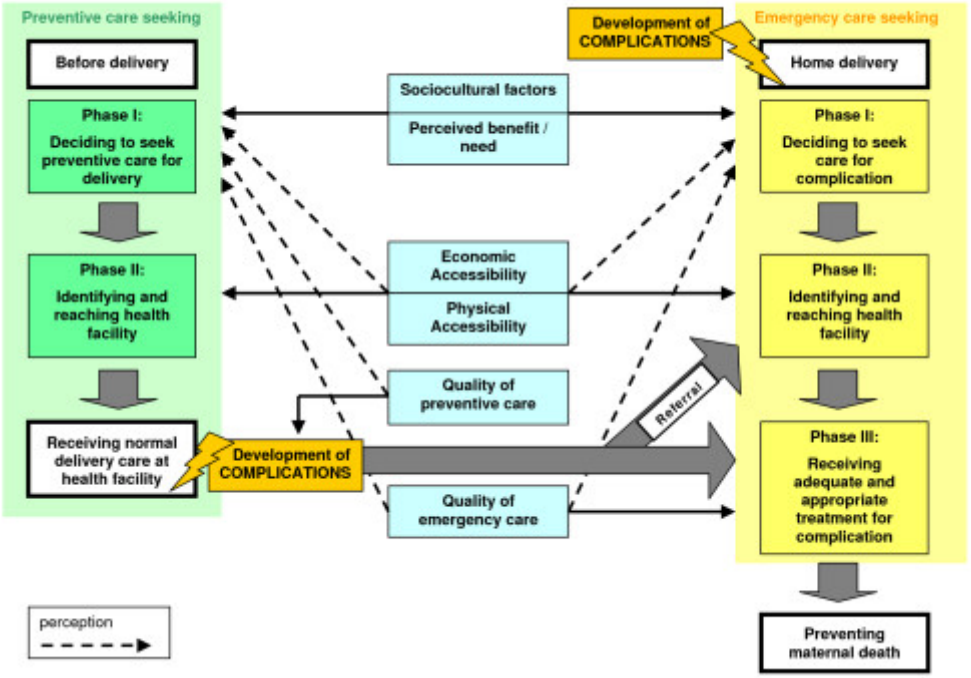

Figure 2-5 Delay phases and factors affecting use of delivery care and maternal mortality by Gabrysch and Campbell, 2006.

This thesis will use a combined model, adapted from the frameworks by Mosley and Chen, and Gabrysch and Campbell in order to capture a wide range of risk factors associated with maternal and neonatal mortality. The components used from the Mosely model include: socio-economic determinants, maternal factors, prevention, treatment and mortality. From the McCarthy model components used include: sociocultural factors, health system factors affecting quality of preventative and emergency care and economic accessibility. The model used for this study categorises determinants of mortality into individual and socioeconomic factors and distal factors. Factors contributing to delay in decision to seek and access care were classified as individual and socioeconomic determinants and all other factors were classified as proximate determinants as outlined in the model by Mosely and Chen as shown in Figure 2.6

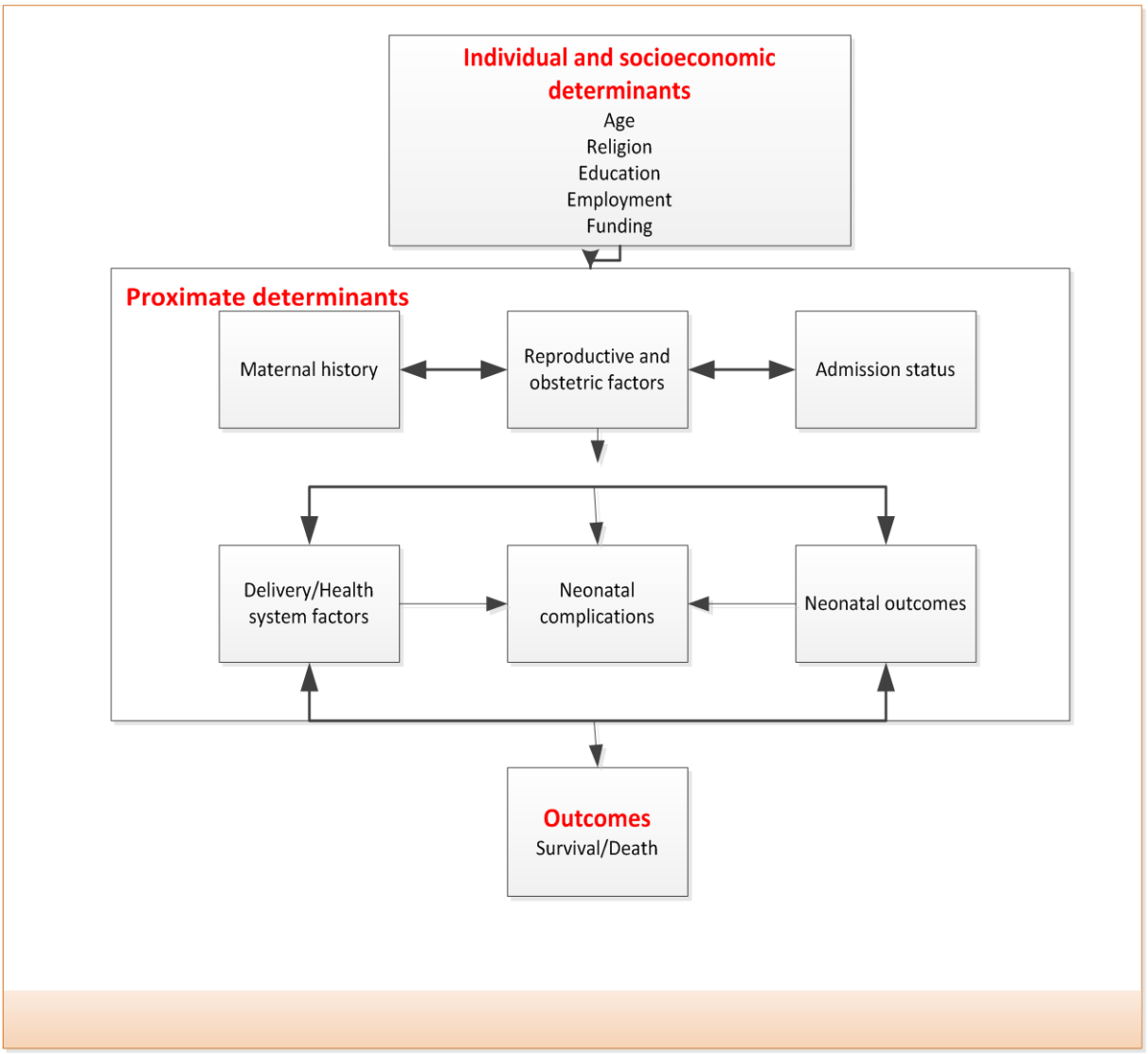

Figure 2-6 A Conceptual Framework for assessing risk factors for maternal and early neonatal mortality. Adapted from Mosley and Chen 1984 and McCarthy and Maine 1992

The model for this study model categorizes the determinants of maternal and neonatal mortality into individual and socioeconomic factors that include mother's age, religion education, occupation, spouse's education, and the source of funding for healthcare. Proximate determinants include: maternal history (smoking, alcohol, contraceptives previous abortions, twins, and underlying medical conditions), reproductive and obstetric factors (gravida pregnancy stage, and labour stage), admission factors (comorbid conditions, clinical causes of death, systolic blood pressure, diastolic blood pressure, haemoglobin, pulse, temperature, and hospital booking status), delivery or

health system factors (mode of delivery, qualification of birth attendant, number of ANC visits, and place of ANC attendance), neonatal complications (clinical cause of death) and neonatal characteristics (gestational age, condition of baby at birth, birth weight, five minute Apgar score, and sex).

2.5 Study objectives

The main objectives of this research are to measure incidence and assess risk factors associated with maternal and early neonatal mortality at MTRH in Kenya.

Specific objectives are:

- To measure incidence of maternal and early neonatal mortality at MTRH
- To investigate risk factors for maternal mortality at MTRH
- To investigate risk factors for early neonatal mortality at MTRH

The next chapter includes a detailed description of the methodology including the study setting, sampling strategies, data collection and analysis procedures and ethical approvals.

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Chapter 3 Methodology

The aim of the research was to determine the incidence of mortality at MTRH and examine risk factors for maternal and early neonatal mortality at MTRH. This chapter describes the study design, setting, sampling, study variables, training, data collection, data analysis and ethical approval process.

3.1 Study design

This study was undertaken in three phases. The first phase was a retrospective audit of all maternal and early neonatal admissions from January 2004 to December 2011 at MTRH to estimate the incidence of mortality. This was done by reviewing hospital records of mothers and neonates. The second phase was a case-control study on a sample of 450 maternal records to identify risk factors associated with maternal mortality at MTRH. The third phase was a case-control study on a sample of 600 records to examine risk factors for early neonatal mortality (including fetal deaths) at MTRH. A retrospective case-control study design was used because recruiting adequate numbers of neonatal deaths for a prospective study would have required a lengthy time period for data collection.

3.2 Setting

Kenya is located in Eastern Africa and has a population of about 38 million people.[1] Health services in Kenya are provided through a network of over 4,700 health facilities countrywide, with the public sector system accounting for about 51% of these facilities.[2] The public health system is a pyramidal structure (see Figure 3.1), consisting of the following levels of health facilities: tertiary hospitals at national level; secondary

hospitals at provincial level; primary hospitals at district level; a fourth level consisting of health centres, maternities, and nursing homes; and at the community level households, families and individuals.[2] The referral system in Kenya is designed such that rural patients move up the pyramidal structure starting at the base, in the community dispensaries and clinics, all the way up to the national or referral level. A referral from a lower level facility is undertaken when the type of illness or its severity supersedes the training and experience of the staff and availability of equipment at the first point of contact between the patient and the health care facility.[3]

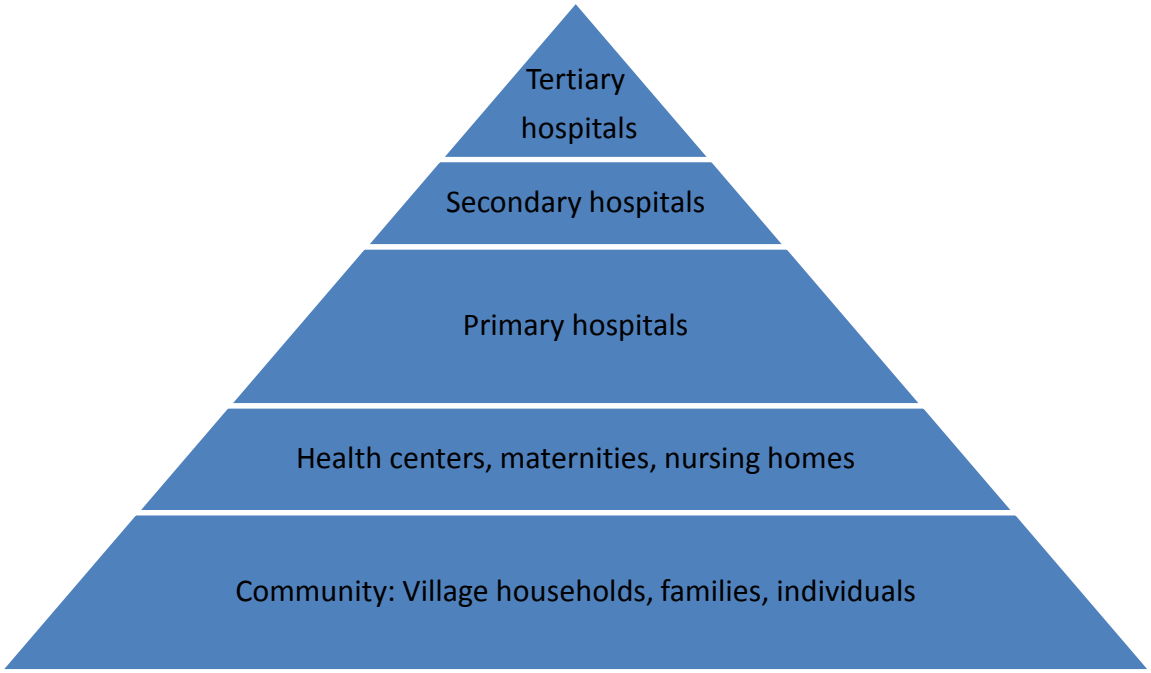

Figure 3-1 Levels of care in the Kenya Health System. Adapted from the Ministry of Health[2]

According to the Kenya National Bureau of Statistics, in 2009 there were 7549 doctors and 32,941 nurses in Kenya.[4] These figures represent about 19 doctors per 100,000 population and about 85 nurses per 100,000 population, who are registered with the Medical Board of Kenya.[4] The figures can be compared to countries like Australia that has a physician to patient ratio of 380 per 100,000 population, and the United States

where the ratio is 280 per 100,000 population.[5] Traditional Birth Attendants (TBAs) in Kenya attend about 59% of the births that occur at home and estimates show that about 2 in 10 TBAs have undergone any kind of formal training.[6]

Private facilities in Kenya consist of large tertiary-level hospitals and private clinics located primarily in urban areas, and run by individual providers.[6] Obstetric care in Kenya is mostly provided by doctors who are employed by the government as specialists and medical officers, about 20 of whom not only run their own specialist clinics, but are also employed to offer consultant services to the referral hospital.[6] Private care in Kenya is very expensive and unaffordable to many Kenyans, while the public hospitals are scarce and usually lack adequate stock of medical supplies due to an overwhelming number of patients.[6]

MTRH is the second largest national referral hospital in Kenya and is located in a rural setting of the Western region in Rift Valley province. Figure 3.2 shows the location of Eldoret town where MTRH is located.[7] The hospital provides a range of health services in three categories namely: curative, preventive and rehabilitative.[7] The hospital catchment covers an area of about 400,000 inhabitants. In addition the hospital accepts referrals from the large indigent population (13 million) in Northern and Western Kenya.[8]

The Mother and Baby Unit at MTRH at has an antenatal ward, post-natal ward (2), labour ward, Newborn Unit (NBU), two theatres dedicated for obstetrics, and other theatres within the hospital that offer assistance when all other theatres are in use. The

bed capacity is approximately 20 for the antenatal and labour wards, and about 50 for the post-natal wards.[7]

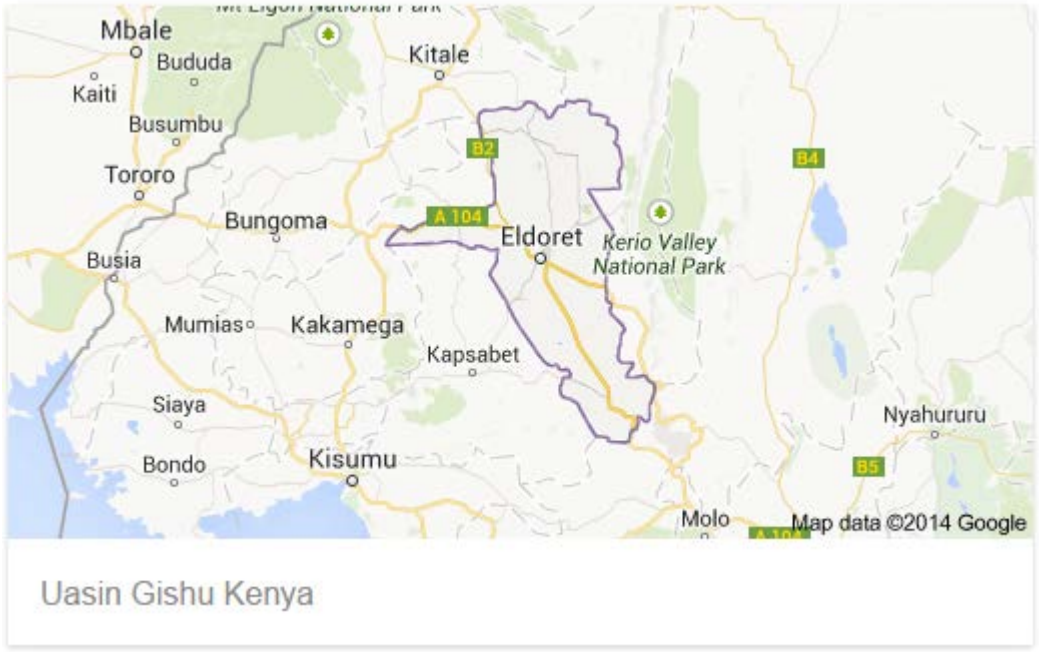

Figure 3-2 Map of Eldoret, Kenya

Source: Google images, 2014

There are approximately 450 maternal admissions per month at MTRH.[7] Activities undertaken in the obstetrics and gynaecology wards include: admission, management and care of mothers in labour, management of referrals and complications of pregnancy, labour and gynaecological emergencies, care of post-natal mothers and their babies, management and care of gynaecological cancer conditions, provision of comprehensive post abortal care (PAC) services, and clinical instruction of medical and nursing students.[7]

Patient flow to the obstetric wards is such that all obstetric patients bypass the emergency department and go directly from the referral facility to the labour and delivery wards at MTRH. They are seen by an admissions clerk who generates a file

number and medical admission form. They are then seen by a nurse for assessment of triage, followed by a medical officer for admission. The consultant or gynaecologist on call is then consulted to confirm the diagnosis and the decision to admit the patient.[7]

3.3 Sampling and sample size determination

Information for the three studies was obtained from the hospital records department. All mothers aged 15-49 years who were pregnant and delivered at MTRH maternity wards and all neonates who were born dead (fetal deaths) or died within seven days of birth, and those who were alive within seven days of birth and admitted to the neonatal wards were included in the first study, which aimed to estimate the incidence of mortality at MTRH.

For the maternal case-control study, cases were defined as women who were certified dead because of complications attributable to pregnancy, throughout birth or the post-partum period. Two controls were selected per case, these being women who gave birth immediately before and following the case. In the neonatal study, cases were neonates who were born dead (fetal deaths) or born alive but died within seven days of birth (early neonatal deaths). Controls were surviving neonates born immediately preceding and following the cases.

The deaths were determined by the physician's report and records in post mortem reports as those that were attributable to pregnancy. The complications reported are those that were attributable to pregnancy, throughout birth or the post-partum period, based on patient records interpretation by the abstractors. All the deaths were identified from the registers in the maternity wards, thereafter these were examined to

see if they met the inclusion and exclusion criteria and hence included or excluded from the study. The diagnosis provided in the patients records as the final cause of death were used to determine the cause of death.

For both case-control studies, the cases were selected retrospectively and sequentially from the most recent delivery until the desired sample size was achieved. The sequential selection process was appropriate because using more recent cases would have reduced the study period and impact of changes over time which did not affect the selected demographic variables at the time. It was not possible to blind the data abstractors to case or control status because deaths were clearly identifiable in medical records.

The PS power program was used to calculate the sample sizes.[9] The mortality rate at MTRH was expected to be higher than the national average because this is a tertiary referral hospital and thus women with more difficult births and complications were likely to present at hospital. To estimate the sample size for the incidence study in Chapter 4, an estimate of 50% was used in sample size calculations. This gave a very conservative estimate of the precision of the study. For the case-control study on risk factors for maternal mortality in Chapter 5, assuming the probability of exposure i.e. risk factor prevalence in controls was 40% and the ratio of cases to controls was 1:2, with 80% power and a 5% level of significance, a sample of approximately 450 women (150 cases and 300 controls) was needed to detect an absolute difference in risk factor prevalence of at least 15%, or an odds ratio of approximately 0.5 or 1.8. For a ratio of cases to controls of 1:2, 80% power, a 5% significance level and 40% probability of exposure in controls, a sample of 600 neonates (200 cases and 400 controls) was

required to detect an absolute difference in risk factor prevalence of at least 12%, or an odds ratio approximately 0.6 or 1.7 (Chapter 6). The probability of exposure varied substantially among the risk factors of interest; and using 40% prevalence was expected to provide adequate power for risk factors. The reason for the 1:2 ratio is because the number of cases was expected to be small and increasing the number of controls per case would increase the power for the study.

3.4 Study variables

The overall outcome of the study was maternal death for the mothers and fetal or early neonatal death for the neonates. A modification of the conceptual model designed by Mosley and Chen[10] in 1984 combined with the delay model used by McCarthy and Maine in 1992[11] was used to identify risk factors for maternal and early neonatal mortality based on individual/ socioeconomic, and proximate determinants (Figure 2.6).

Individual and socioeconomic determinants included: mother's age (15-24 years; 25-34 years; or 35-45 years), marital status (never married; married (de facto relationships do not exist legally); divorced; separated), education (none; primary; secondary; tertiary), employment categories based on KDHS (unemployed; trader, farmer; public servant; other), spouse's education (none; primary; secondary; tertiary), spouse's employment (unemployed; trader; farmer; public servant; other), and source of funding for treatment (self; health insurance; waiver/fees waived by the hospital).

Proximate determinants were categorised into maternal history; reproductive and obstetric factors; admission status; delivery factors; neonatal characteristics and neonatal complications, and are listed below in the different categories.

Maternal history included information relating to the mother's gravidity categorised as: primigravida (1); multigravida (2-4) or grandmultigravida (above 5); mother's history of smoking (yes/no); alcohol use(yes/no); contraceptive use (yes/no); previous abortion (yes/no); previous twins (yes/no); and pre-existing medical conditions (malaria, cardiovascular disease, HIV, diabetes, rheumatic heart disease, epilepsy, other), and the number of antenatal care (ANC) visits.

Reproductive and obstetric factors included: booking status on admission (yes=attended ANC at MTRH or no=did not attend ANC at MTRH); the presence of common causes of death, as documented in the patient records and post mortem reports; premature rupture of membranes (PROM); dystocia (prolonged or obstructed labour); pre-eclampsia; haemorrhage, and other complications (cardio respiratory diseases, previous scar, Human Immunodeficiency Virus or HIV, malaria, retained placenta, anaemia, abortion). A complication was considered as present if there was an indication to this effect in the notes, and absent if there was no mention in the notes.

Maternal admission factors included: gestational age (less than 37 weeks, 37-42 weeks or above 42 weeks); diastolic blood pressure (mm Hg); systolic blood pressure (mm Hg); haemoglobin level (g/dL); pulse rate (beats per minute/bpm); and temperature (ºC).

Delivery factors are those factors that influenced delivery outcomes and included qualification of birth attendant (doctor, or midwife) and mode of delivery (spontaneous vertex delivery, assisted vaginal delivery, caesarean section, other/did not deliver).

Neonatal complications included the presence or absence of causes of newborn death as documented in the records, including asphyxia, congenital malformation, sepsis, Respiratory Distress Syndrome (RDS), and other complications (hypothermia, diarrhoea, jaundice, hypoglycaemia, meconium aspiration syndrome, and HIV).

Neonatal characteristics included fetal outcome at birth (dead or alive); discharge date; condition on discharge; sex; Apgar score at five minutes and weight in grams.

A structured data collection instrument was used to obtain data from medical records. The primary cause of death was identified using the information from medical records and post mortem reports. Where interpretation was required, the information on the cause of death was verified by the study physicians. The data were coded and double entered into two separate password protected databases that were later compared for consistency.

3.5 Logistics and Research Staff Training

Prior to commencement of data collection in February 2011, the PhD Candidate met with the hospital administration to notify them of the study objectives and research plan and officially obtain approval to proceed with the research. The Candidate provided copies of approvals from the University of Newcastle Human Research Ethics Committee (HREC) and the Institutional Research and Ethics Committee (IREC)

in Kenya to the hospital administrator. The hospital administration informed all departments and staff about the study and posters (with contact information) were displayed in the hospital notice boards to increase public awareness of the research.

Data were extracted from hospital records by hospital staff trained for the study. Four potential study research assistants (RAs) were initially recruited and provided with formal training on data collection. The RAs were first familiarized with the questionnaire and the kind of information that was required. They were then each given 10 records randomly selected from the obstetric wards to enter to assess their competence and accuracy for data collection. The completed test questionnaires were reviewed and rated for accuracy and competence by the two study obstetricians and the candidate, who provided written comments followed by a meeting to compare and discuss test results. Two research assistants with the highest accuracy scores for the test records were selected to undertake data collection for the main study, and provided with additional feedback. This data collection pilot also provided the team with an indication of the availability of data. Research assistants were trained on issues relating to death and emotional sensitivity arising from dealing with death and their impartial role in the data collection process. Two research advisors who were senior obstetricians in the hospital based on their clinical expertise and interest in the study outcomes were also invited to join the study team. The Candidate proposed their names and contribution to development of their protocol to the study researchers who agreed to include them as part of the research team.

The data collection team was composed of two obstetricians, two research assistants, one medical records officer, one biostatistician (hospital), and one data entry clerk and

the Candidate. The team underwent two days of training in order to become familiar with the research plan and discuss study logistics. Training materials for discussion included the research protocol, confidentiality statement, data collection instruments, and a statement of roles and responsibilities for each team member. As the study relied on secondary data from medical records, patient consent was not necessary; however patients usually sign a form to indicate that their records can be accessed for research being a teaching and referral hospital. In addition, the team discussed the code of conduct expected during the research process, ethical requirements and protocols, the hospital records systems and procedures and remuneration issues. It was emphasized that if a particular condition, procedure, treatment or factor of interest was not in the medical record then the item was to be recorded on the data collection form as "not present". On completion of training, each member of the study team signed a form confirming their participation and adherence to all procedures and maintaining patient privacy, as outlined in the ethics and code of conduct for the study.

Although it was necessary for data collection staff to have access to information that could potentially be used to identify mothers and babies, explicit patient identifiers were not available to the researcher. The confidentiality of participants was maintained by excluding names and addresses from the study database. Individuals were identified only by unique study numbers. Participants were not intentionally identified or re-identified by the researcher and every effort was taken to ensure that the privacy of participants was protected at all times.

3.6 Statistical Methods

Statistical analysis was performed using STATA 11.[12] Exploratory data analysis involved checking the data for implausible relationships, outliers and errors, using frequency distributions, tables and graphs. Checks involved visualizing the distributions by use of graphics including histograms overlaid with a normal curve, normal probability plots and box plots to identify potential errors. Bar charts were also used to compare distributions between groups.

Initial analysis involved estimating the incidence of maternal and early neonatal mortality and descriptive analysis of maternal and neonatal cases. With information on total number of deaths and total number of live births, the annual incidence rates were augmented by data provided by the records department on the total number of maternal deaths and total number of fetal and early neonatal deaths for each year. Information on total number of deliveries for each year was also provided. This was used to estimate the number of live births, this being the denominator for calculating the maternal mortality ratio (MMR) and the early neonatal mortality rate (ENMR). The MMR was calculated as the number of maternal deaths divided by the number of live births for that year multiplied by 100,000. This was done for each year and the overall number was obtained by adding up all the deaths for each year, divided by the total number of live births for the study period multiplied by 100,000. The ENMR was calculated by dividing the number of newborn deaths, including fetal deaths, per year, by the total number of live births for that year and multiplying by 1000. The overall ENMR was the sum of all neonatal deaths, divided by the sum of all the live births for the study period, multiplied by 1000. These mortality ratio estimates were displayed

graphically together with their respective 95% confidence intervals (see Chapter 4, Paper One for figures).

All variables were tabulated to investigate the proportion of missing values and to identify categorical variables with low cell sizes. Cut-points were used to covert mother's age, gravida and gestational age (expressed continuously) to categorical variables. Frequency distributions were described for all variables for cases and controls. The distribution of missing data was examined overall and for each variable, by cases and controls, in order to investigate possible bias. Tables were used to demonstrate frequencies and percentages. (Chapter 4, Paper One). Further work regarding missing data involved undertaking regression analyses to examine factors associated with missingness for variables missing data for 20% or more observations for either cases or controls within the maternal and neonatal sample. The examination of missing data is provided in Paper Four (Chapter 7).

Analyses for the case-control studies in Chapter 5 and Chapter 6 included undertaking chi-squared tests to compare the characteristics of the cases and controls. Logistic regression was undertaken to investigate risk factors for mortality (case or control status) while adjusting for confounders. The reference group for each variable was the category with the lowest risk. Initial modelling was undertaken by including all variables with $p<0.2$ for the chi-square analysis in a separate model for each of the four groups of potential risk factors (maternal and obstetric characteristics, neonatal complications, maternal and obstetric complications and neonatal characteristics). Four sets of multiple regressions were undertaken to examine each group of potential risk factors. A backward stepwise regression method was used whereby variables with a p-

value of 0.1 or more on the likelihood ratio test were removed. The variables included in each of these four models were then combined in a final overall model. Unadjusted and adjusted odds ratios, confidence intervals and p-values were reported for all models.

3.7 Ethical approval

Ethical approval was provided by the University of Newcastle Human Research Ethics Committee and the Institutional Research and Ethics Committee in Kenya. Permission was sought from the hospital administration prior to undertaking the study (See appendices).

The next chapter is a published paper that presents the incidence of maternal and neonatal mortality at MTRH describes characteristics and circumstances surrounding these mortalities.

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Chapter 4 Paper One

A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya

This study provides important information about maternal and early neonatal mortality in Kenya's second largest tertiary hospital. A range of socio demographic, clinical and health system factors are identified as possible contributors to Kenya's poor progress towards reducing maternal and early neonatal mortality. The study has been published as:

Yego, F[1]., Stewart Williams, J[2]., Byles, J[3]., Nyongesa, P[4]., Aruasa, W[4]., D'Este, C[5]. (2013). *"A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya."* Reprod Health 10:13. doi:10.1186/1742-4755-10-13

The authors' affiliations are:

[1]Moi University, P.O. Box 4606 Eldoret, Kenya 30100

[2]Research Engineer, Umeå Centre for Global Health Research, Unit of Epidemiology and Global Health, Department of Public Health and Clinical Medicine, Faculty of Medicine, Umeå University, Umeå, Sweden.

[3]Director, Research Centre for Gender Health and Ageing, University of Newcastle, Hunter Medical Research Institute building, New Lambton Heights, NSW

[4]Department of Reproductive Health, Moi University College of Health Sciences, Eldoret, Kenya 30100

[5]Chair in Biostatistics, National Centre for Epidemiology and Population Health, Research school of Population Health, the ANU College of Medicine Biology and Environment, the Australian National University, Canberra, ACT

Tables and figures have been renumbered for consistency with the thesis.

4.1 Abstract

Objective

To measure the incidence of maternal and early neonatal mortality in women who gave birth at Moi Teaching and Referral Hospital in Kenya (MTRH) and describe clinical and other characteristics and circumstances associated with maternal and neonatal deaths following deliveries at MTRH.

Methods

A retrospective audit of maternal and neonatal records was conducted with detailed analysis of 150 maternal deaths and 200 neonatal deaths. Maternal mortality ratios and early neonatal mortality rates were calculated for each year from January 2004 to March 2011.

Results

Between 2004 and 2011, the maternal mortality ratio was 426 per 100,000 live births and the early neonatal mortality rate (< 7 days) was 68 per 1000 live births. The Hospital record audit showed that half (51%) of the neonatal mortalities were for younger mothers (15-24 years) and 64% of maternal deaths were in women between 25 and 45 years. Most maternal and early neonatal deaths occurred for multiparous women, in referred admissions and when the gestational age of the mother was under 37 weeks and in latent stage of labour. Indirect complications accounted for the majority of deaths. Where there were direct obstetric complications associated with the delivery, the leading cause of maternal death was eclampsia and the leading cause of early neonatal death was pre-mature rupture of membranes. Pre-term birth and asphyxia

were leading early neonatal complications. In both series the majority of deliveries was vaginal and performed by midwives.

Conclusion

This study provides important information about maternal and early neonatal mortality in Kenya's second largest tertiary hospital. A range of socio demographic, clinical and health system factors are identified as possible contributors to Kenya's poor progress towards in reducing maternal and early neonatal mortality.

Keywords: Maternal mortality, Early neonatal mortality, Determinants, Referral hospital, Kenya, Maternal mortality ratio, Early neonatal mortality rate

4.2 Background

In developing countries more than nine million infants die every year before birth and in the first week of life as a result of complications occurring during pregnancy. Many of these deaths are preventable.[1] In 2000 the United Nations (UN) made a declaration to include maternal and child mortality reduction as a target in its Millennium Development Goals (MDGs).[2] Maternal mortality is high throughout Africa, yet the rates are particularly high in Kenya, where a woman's lifetime risk of dying is one in 38 compared to one in 2000 in the developed world.[1] The World Health Organization (WHO) reported that Kenya's progress towards improving maternal and neonatal health is presently "insufficient" with little or no progress having been made over the past decade.[3]

Of the more than 500,000 women who die each year as a result of complications arising during pregnancy, half live in sub-Saharan Africa.[4] Yet death is not the only outcome

resulting from pregnancy complications. For every woman who dies, at least 30 others are injured and disabled. Globally seven million women are affected by health problems related to childbearing.[5] Despite the inauguration of the Safe Motherhood Initiative (SMI) in Nairobi in 1987, Kenya has made limited progress towards improving maternal mortality.

Between 1980 and 2010, the national maternal mortality ratio (MMR) was 400-560 per 100,000 live births.[1, 6, 7] The ratios are higher in the major teaching and referral hospitals where obstetric complications are concentrated. For example, the MMR in Kenya's largest referral hospital, Kenyatta National Hospital (KNH), was 922 per 100,000 live births in 2004.[8] In Kilifi hospital in Kenya, the MMR was 250 per 100,000 live births between 2008 and 2010.[9] In nearby sub-Saharan African countries, MMRs in teaching hospitals are also high. For instance, in Adeoyo Hospital in Nigeria, the MMR was 963 per 100,000 live births between January 2003 and December 2004.[10] The Neonatal Mortality Rate (NMR) in KNH from January to December of 2000 was 215/1000 live births.[11]

Newborn deaths represent 38% of all deaths among children under five year of age.[12] One in five women in Africa risks losing a newborn baby during her lifetime.[13] Pre-term birth accounts for 29% of neonatal deaths globally and approximately 14% of babies are born with low birth weight.[12] Early neonatal characteristics can be affected by nutrition, lifestyle and socio-economic status of their mothers. "The best care in the world cannot save a woman's life if she cannot reach it, cannot afford it, does not know it is there when to seek it, or is not permitted to use it".[14]

The Delay Model by Thaddeus and Maine[15, 16] provides a suitable conceptual framework for understanding risk factors associated with maternal mortality at a tertiary referral hospital. The Model identifies three types of delays. They are: delay in decision to seek care, delay in arrival at a health facility and delay in provision of adequate care.[15] Some risk factors that have been linked to the delay model are: lack of funding, inaccessibility, poor infrastructure, inadequate staffing, inadequate equipment and supplies, lack of information, cultural issues, social vulnerability, and low socioeconomic status.[17]

Ensuring the continuum of care throughout pregnancy is an important requirement for the reduction of maternal and early neonatal deaths. There is evidence that a significant number of stillbirths and neonatal deaths could be prevented if all women were adequately nourished and received good quality care during pregnancy, delivery, and in the postpartum period.[13, 18] The antenatal period helps the mother to assess risks and treat conditions that could affect both the mother and baby.[19]

It is essential that during delivery, obstetric emergencies are effectively managed to prevent complications which account for up to 58% of stillbirths and early neonatal deaths.[20] Countries such as Thailand, Sierra Leonne, Libera, Pakistan, Sudan, Liberia, Bosnia, Uganda, Tanzania, and Northern Kenya have established intervention projects to improve the availability of emergency obstetric care (EmOC).[21] These projects include the use of signal funtions to asses whether their health facilties adhere to international standard operating procedures for management of emergencies during pregnancy.

In the post-partum period the provision of family planning advice after delivery is of vital importance, especially in settings where the birth rate is high an multiparous women are at repeated risk of pregnancy complications and adverse birth outcomes.[19]

Health care infrastructure in Kenya includes two national tertiary teaching and referral hospitals as well as provincial hospitals, district and sub-district hospitals, health centres and dispensaries, or chemists. The private sector provides about one third of outpatient care and 14% of inpatient care. High-risk patients are managed in the tertiary hospitals where clinical resources are more specialized. A number of measures have been introduced to help meet the MDGs in Kenya. For example, Kenya's second largest referral hospital, the Moi Teaching and Referral Hospital (MTRH) has initiated 24 hour maternal and perinatal death reviews and monthly maternal mortality reviews for all maternal deaths. Over the past two years the MTRH has also established some standard operating procedures for managing both direct and indirect maternal complications in pregnancy. Yet more work is needed to achieve progress in this area.

While there have been many maternal health studies in Kenya, little has been published specifically on maternal and early neonatal mortality.[8, 11, 22-26] The aim of this study is to measure the incidence of maternal and neonatal mortality in women who gave birth at MTRH and describe clinical and other characteristics and circumstances associated with maternal and early neonatal deaths following deliveries at MTRH. As one of two teaching and referral hospitals in Kenya, the MTRH serves an important role in the country's health system. The MTRH is also the largest hospital in the rural western region of Kenya. High maternal and early neonatal mortality at MTRH has local and national implications and therefore requires investigation.

4.3 Methods

A retrospective audit of maternal and neonatal records at MTRH between January 2004 and March 2011 was conducted for this study. Detailed information was independently extracted from hospital records for the most recently hospitalized 150 women aged 15-49 years, who were classified as maternal deaths, and the most recently hospitalized 200 neonates, who died during delivery or within seven days of delivery. Record numbers were based on the sample size needed for a subsequent case-control study of maternal and early neonatal deaths at MTRH. This was obtained by assuming the probability of exposure was 40% and the ratio of deaths to survivors was 1:2. A sample of approximately 450 women (120 cases and 300 controls) was sufficient to detect an absolute difference in risk factor prevalence of at least 15% (80% power, 95% significance). These calculations were made using PS power software.[27] Standard definitions of maternal mortality, early neonatal mortality, neonatal mortality, and direct causes of death were used.[28] Non-pregnancy related deaths are not included.

4.3.1 Data source and setting

The MTRH is located in Kenya's Rift Valley province[29] providing a range of curative, preventive and rehabilitative services. The catchment covers a population of over seven million inhabitants[6] and the MTRH also accepts referrals from Kenya's 13 million indigent population in the north and west.[29] The reproductive health department at MTRH has 17 obstetrician-gynecologists, five medical officers, two clinical officers, 100 nurses who are either trained midwives or have basic training in midwifery.[29] The reproductive health department has four medical wards, and a Mother/Baby Hospital with a capacity of 150 beds.[29]

Patients at MTRH are referred either from other hospitals or the community, usually following evidence of complications.[29] Deliveries at MTRH occur in labour wards where women are delivered in maternity couches and attended by midwives, but in cases of complications attended by doctors.[29] The hospital provides gloves and linen necessary for delivery.[29]

4.3.2 Descriptive variables

Information extracted from the mothers' hospital records included: age, parity, gestational age, maternal complication on admission, stage of labour, pregnancy stage, birth attendant at delivery, and booking status. Patients who were referred i.e. from other lower level clinical facilities or from home or by a traditional birth attendant were classified here as "unbooked". All other patients who attended antenatal clinics at MTRH and had been scheduled to deliver at MTRH were classified as "booked". Information extracted from neonates' hospital records included: outcome at birth, Apgar score, birth weight, sex, complication at birth, and mothers' and neonates' condition at discharge. All definitions of causes of death were based on WHO International Classification of Diseases Version 10 (ICD-10). Where multiple causes of death were recorded, the primary cause was identified using available documentation and post mortem reports.

4.3.3 Statistical Analyses

The retrospective audit at MTRH, which covered the period January 2004 and March 2011, provided descriptive information on mothers and babies and pregnancy and birth outcomes. This was determined by data available at the time the study was undertaken. The annual incidence estimates were augmented by data provided by the

records department at the MTRH, giving the total numbers of live births and maternal and neonatal deaths per year between 1st January 2004 and 31st December 2011. These data were used to calculate the annual maternal mortality ratios and early neonatal mortality rates. STATA version 11 was used for all statistical analyses. The study was approved by the University of Newcastle Human Resource and Ethics Committee (HREC) and the Institutional Research and Ethics Committee (IREC) in Kenya.

4.4 Results

Figure 4.1 and Figure 4.2 show annual changes in MMRs and NMRs with 95% confidence intervals. The overall MMR was 426 per 100,000 live births and the overall NMR was 68 per 1,000 live births. There were wide variations between 2004 and 2011. For example in 2010, the MMR was the lowest and the NMR was second highest for the period. Despite different point estimates, year-to-year differences in maternal mortality were not statistically significant as seen by the overlapping 95% confidence intervals. However, neonatal mortality rates were significantly different between 2005 and 2006, 2008 and 2009 and 2010 and 2011.

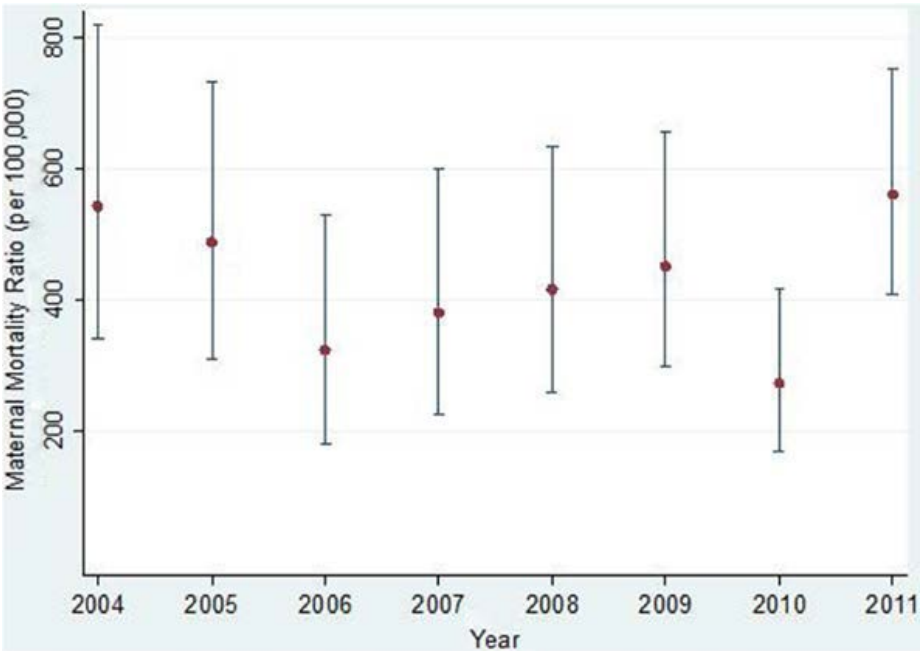

Figure 4-1 Annual neonatal mortality rates with 95% confidence intervals from January 2004 - to December 2011

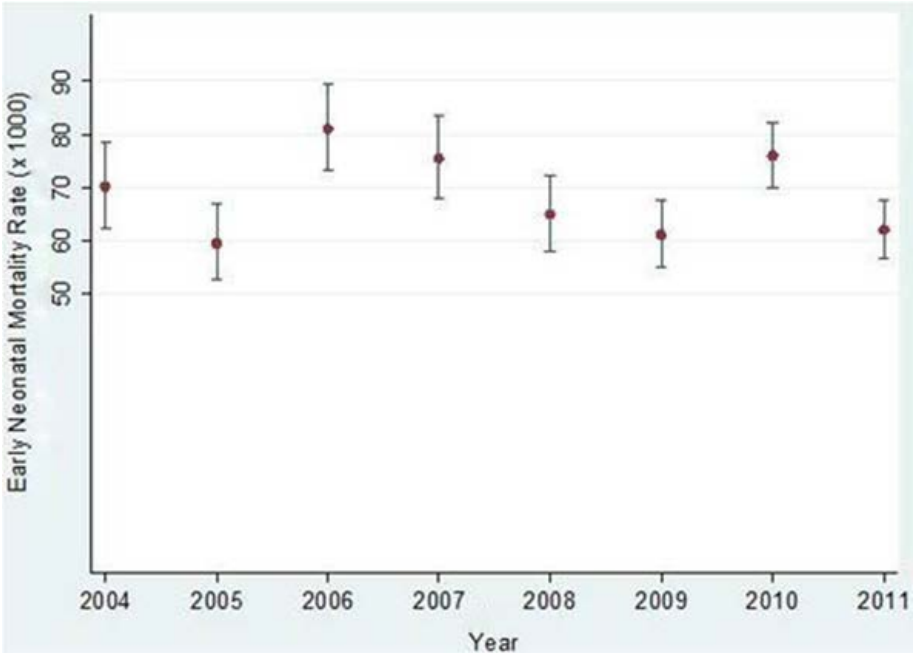

Figure 4-2 Annual neonatal mortality rates with 95% confidence intervals from January 2004 - to December 2011

Table 4.1 shows the maternal and obstetric characteristics for the 150 maternal deaths and the 200 early neonatal deaths. Half (51%) of the early neonatal mortalities were for younger mothers (15-24 years) and 64% of maternal deaths occurred for women aged between 25 and 45 years. For both the maternal and early neonatal deaths, high

proportions (49%) of mothers were multigravida. The majority of birth attendants were midwives for both maternal and early neonatal deaths (53% and 71% respectively). The majority of mothers with early neonatal deaths (56%) were admitted at the intrapartum stage of pregnancy (which is the period from start of labour to delivery). A high proportion of mothers who died (42%) were also admitted at the intrapartum stage. The labour stage at admission was mostly active (87%) for the neonatal deaths. The labour stage for the maternal deaths was mostly latent (42%). This is the early or slow phase of labour. The gestational age was commonly less than 36 weeks. A high proportion of these deliveries were vaginal (43% for the maternal deaths and 73% for the neonatal deaths). Most mothers (58%) were not pre-booked at the MTRH but referred from home and other facilities while most neonates (79%) were referrals.

Table 4-1 Maternal and obstetric characteristics of maternal and early neonatal deaths

Characteristic	Maternal deaths n=150		Neonatal deaths n=200	
	n	%	n	%
Age (years)				
15-24	54	36%	97	51%
25-34	66	44%	68	35%
35-45	30	20%	27	14%
Gravida				
Primigravida (1)	34	23%	58	29%
Multigravida (2-4)	73	49%	108	54%
Grandmultigravida (5-7)	32	21%	26	13%
Grandgrandmultigravida (>8)	11	7%	8	4%
Birth attendant				
Doctor	61	47%	50	26%
Midwife	70	53%	136	71%
Pregnancy stage on admission				
Antepartum	53	37%	73	37%
Intrapartum	61	42%	110	56%
Puerperium	30	21%	14	7%
Labour stage on admission				
Latent	42	42%	16	9%
Active	37	37%	156	87%
Second stage	20	20%	7	4%
Gestational Age				

Characteristic	Maternal deaths n=150		Neonatal deaths n=200	
	n	%	n	%
<36 weeks	78	59%	116	58%
37-41 weeks	37	28%	39	19%
<42 weeks	3	2%	5	2%
Post-partum	14	11%	40	20%
Mode of delivery				
Vaginal	64	43%	146	73%
Caesarean	51	34%	45	22%
Assisted delivery	27	18%	9	5%
Other (did not deliver)	8	5%	0	0%
Booking status				
Booked	63	42%	38	21%
Unbooked (referral)	87	58%	139	79%

*Denominators vary for each item depending on missing data

The highest number of deliveries by a single mother at the MTRH was 13

Pregnancy complications associated with maternal and early neonatal deaths at MTRH are shown in Table 4.2. Eclampsia (22%) was the leading direct complication for maternal death, followed by dystocia (14%), and haemorrhage (13%). For neonatal deaths the leading maternal complication was premature rupture of the membrane (PROM) (26%) followed by dystocia (22%).

Table 4-2 Pregnancy complications for maternal and early neonatal deaths

Pregnancy complication	Maternal deaths n=150		Neonatal deaths n=200	
	n	%	n	%
Eclampsia	33	22%	13	7%
Dystocia	21	14%	44	22%
Haemorrhage	20	13%	17	8%
Sepsis	10	7%	0	0%
Post abortal	10	7%	5	3%
Premature rupture of membrane (PROM)	2	1%	52	26%
Post datism	1	1%	3	1%
Other (indirect)†	53	35%	66	33%

*Denominators vary for each item depending on missing data

†Indirect causes include: HIV, malaria and cardiovascular diseases

Table 4.3 shows the leading neonatal complications among the maternal and early neonatal deaths were asphyxia (17% of maternal deaths and 25% of early neonatal deaths) and pre-term birth (13% of maternal deaths and 38% of neonatal deaths).

Table 4-3 Neonatal complications for maternal and early neonatal deaths

Neonatal complication	Maternal deaths n=150		Neonatal deaths n=200	
	n	%	n	%
None	84	56%	0	0%
Pre-term birth	16	13%	75	38%
Asphyxia	20	17%	51	25%
Sepsis	1	1%	29	14%
Congenital malformation	2	2%	21	11%
Other	12	10%	24	10%

*Denominators vary for each item depending on missing data

Neonatal characteristics for both maternal and early neonatal deaths at MTRH are given in Table 4.4. Among the neonatal deaths, majority of the neonates (86%) were alive at birth. Among the maternal deaths, 45% of the neonates were alive at birth but only 25% were discharged alive. There was a high proportion of missing information for the neonates born to mothers who died for weight (55%), sex (38%), and Apgar score (39%). There was missing information for Apgar score for 21% of neonatal cases.

Table 4-4 Early neonatal and maternal characteristics

Outcome	Maternal deaths n=150		Neonatal deaths n=200	
	N	%	n	%
Baby's outcome at birth				
Alive	66	45%	172	86%
Stillbirth	61	41%	28	14%
Early neonatal death	20	14%	0	0%
Missing	4	2%	0	0%
Baby's weight at birth				
0-2499gms	31	20%	133	67%
2500-4499gms	36	24%	49	25%
Missing	82	55%	18	9%

Outcome	Maternal deaths n=150		Neonatal deaths n=200	
	N	%	n	%
Apgar score at 5 mins				
0-6	61	41%	78	39%
7-10	31	20%	79	40%
Missing	58	39%	43	21%
Baby's sex				
Male	41	27%	105	52%
Female	52	35%	85	43%
Missing	57	38%	10	5%
Baby's condition on Discharge				
Alive	38	25%	0	0%
Neonatal death	96	64%	200	100%
Missing	15	10%	0	0%
Mothers condition on Discharge				
Alive	0	0%	186	98%
Death	150	100%	4	2%
Missing	0	0%	0	0%

*Denominators vary for each item depending on missing data

4.5 Discussion

This study provides important information about maternal and early neonatal mortality in Kenya's second largest tertiary hospital. The MTRH draws referrals from a large catchment area and a high proportion of admissions are for women with obstetric complications. By conducting a secondary analysis of records in a large tertiary referral hospital with high-risk obstetrics admissions, we were able to measure the incidence of maternal and early neonatal mortality in women who gave birth at the hospital and describe clinical and other characteristics and circumstances surrounding maternal and early neonatal deaths following deliveries at MTRH. It is intended that this information will be used to inform changes in policies and practices that can lead to improvements in maternal and early neonatal mortality.

The findings are in agreement with other studies in developing countries in which, like Kenya, progress in reducing maternal and early neonatal mortality has been slow.[30, 31]

The MMR and NMR are best estimates based on available data from a major referral hospital. The peaks in maternal and early neonatal mortality at MTRH in 2011 and 2010 may be explained in part by industrial strikes at the hospital during this time. The strikes reduced staffing levels placing pressure on hospital resources at a time when birth numbers were fairly high. Birth rates have increased in Kenya over the past decade leading to a tripling in population.[32] These trends may also have contributed to the higher mortality ratios seen here.

The study found that half (51%) of the early neonatal mortalities were for younger mothers (15-24 years) and 64% of maternal deaths were in women between 25 and 45 years. Evidence from other studies in developing countries also shows that high proportions of early neonatal deaths are among teenage mothers and maternal deaths occur among women who are multigravida.[33-36] In this study most maternal and early neonatal deaths occurred for multiparous women and in unbooked women whose gestational age was under 37 weeks. Morality occurred among women who were admitted in the latent stage of labour. This could be due to for example, delayed labour ward admission, and lack of strict criteria for admission into labour wards.

Indirect obstetric complications accounted for about one third of the maternal and early neonatal deaths, with direct complications accounting for two thirds, possibly reflecting poor diagnosis and treatment of diseases that developed during pregnancy. However, other studies have shown that direct pregnancy complications contribute to a higher proportion of maternal deaths than indirect complications.[3, 37, 38] In this study the majority of maternal and early neonatal deaths were among women whose babies were at lower gestational age. Lower gestational age increases risk of death[34, 35] and

other studies have reported similar findings. Babies born below 37 weeks gestation are at higher risk of pre-mature birth and hence adverse birth outcomes.[3, 33, 39]

Compared with assisted or caesarean delivery, the majority of the maternal and early neonatal deaths followed vaginal deliveries. Studies show that maternal and early neonatal deaths are associated with the mode of delivery and also medical practices. For example, some doctors may be unwilling to intervene aggressively on behalf of the fetus.[34] Access to skilled birth attendants (including doctors and midwives) is essential for the prevention of maternal and early neonatal deaths and this is still an issue in Sub-Saharan Africa. In Kenya the majority of deliveries are managed by traditional birth attendants in the communities. Many such attendants lack appropriate skills which can contribute to high maternal and early neonatal morbidities and mortalities.

Of the maternal and early neonatal deaths at the hospital, more than half were referred admissions. Studies in Africa have shown that of the women who are referred to hospitals for delivery, many have severe or life threatening complications.[10] There is evidence that newborn deaths are higher in cases where best practice for newborn care is limited.[36, 39]

While there are a number of areas that could be followed up, some key points are noted here. There is a need to improve hospital referral policies, and also review clinical guidelines and management protocols for at-risk mothers. There is also need for attendance at antenatal clinics in order to screen for underlying illnesses and ensure proper management of complications that can occur in pregnancy.

This work has strengths and limitations. This is the first study of its kind to be conducted at a major tertiary teaching and referral hospital in Kenya. The MTRH allowed access to individual patient records. This provided a means for describing characteristics and circumstances surrounding maternal and early neonatal deaths associated with deliveries at MTRH. Importantly this study provides a platform for identifying a range of issues that could be addressed in efforts to reduce maternal and early neonatal deaths in other similar hospitals. The fact that detailed hospital level data were analysed also makes it possible to suggest changes in hospital policies, practices and procedures that may ultimately reduce maternal and early neonatal mortality. Although undertaken from a hospital perspective, the work contributes more generally to understanding some of the reasons for Kenya's lack of progress towards achieving MDGs Four and Five by 2015.

A possible limitation is that the work is not generalizable at national level. The data comprise only hospital births. Both nationally and in the MTRH catchment, approximately 40-43% of births are in hospitals. This proportion is similar for the MTRH and its catchment.[6] A second limitation was the difficulty in estimating MMR and NMR due to small numbers in the denominators as shown in the overlapping confidence intervals. A further limitation is that high proportions of the medical records collected for the study were incomplete or had missing data. It was impossible to say how much data were missing, and it is not known to what extent the missing data may have biased the results. The huge proportion of missing data in neonatal variables highlights the need to link maternal and neonatal records so that information

can be easily retrieved for both mothers and babies, especially when there are adverse outcomes.

4.6 Conclusion

Maternal and early neonatal mortality remains high in MTRH despite the efforts to achieve MDGs Four and Five. Using data collected in a large tertiary referral hospital, this descriptive study identified a range of socio demographic, clinical and health system factors as possible contributors to Kenya's poor progress towards reducing maternal and early neonatal mortality. Further research is needed in order to understand other possible contributors, such as those found in the community, and factors associated with quality of care.

List of abbreviations

MTRH: Moi Teaching and Referral Hospital; UN: United Nations; WHO: World Health Organization; MDGs: Millennium Development Goals; SMI: Safe Motherhood Initiative; ICD: International Classification of Diseases; ENMR: Early Neonatal Mortality Rate; MMR: Maternal Mortality Ratio; PROM: Premature rupture of membranes

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FY participated in all stages of the study including design, implementation, data collection, analysis and writing. JSW contributed input to the study design, analysis and interpretation, and assisted in drafting and editing the manuscript. JB contributed

to the study design and provided intellectual input at all stages of the research. PN assisted with the design of the study, data collection, interpretation and manuscript preparation. WA provided input regarding study design and data interpretation. CD advised on all statistical issues and also provided intellectual input at all stages of the study. All authors read and approved the final manuscript.

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The next chapter is a case-control study that describes risk factors associated with maternal mortality at MTRH in Kenya.

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Chapter 5 Paper Two

Risk factors for maternal mortality in a Tertiary Hospital in Kenya: a case-control study

This paper assesses the risk factors associated with maternal mortality at MTRH in Kenya. The paper was published as:

Yego F[1], D'Este C[2], Byles J[3], Stewart Williams J[4], Nyongesa P[5]. Risk factors for maternal mortality in a tertiary hospital in Kenya: a case-control study. BMC Pregnancy and Childbirth, 2014;14:38. doi:10.1186/1471-2393-14-38. Online: http://www.biomedcentral.com/1471-2393/14/38/abstract

The authors' affiliations are:

[1]Moi University, P.O. Box 4606 Eldoret, Kenya 30100

[2]Chair in Biostatistics, National Centre for Epidemiology and Population Health, Research school of Population Health, the ANU College of Medicine Biology and Environment, the Australian National University, Canberra, ACT

[3]Director, Research Centre for Gender Health and Ageing, University of Newcastle, Hunter Medical Research Institute building, New Lambton Heights, NSW

[4]Research Engineer, Umeå Centre for Global Health Research, Unit of Epidemiology and Global Health, Department of Public Health and Clinical Medicine, Faculty of Medicine, Umeå University, Umeå, Sweden.

[5]Department of Reproductive Health, Moi University College of Health Sciences, Eldoret, Kenya 30100

Tables and figures have been renumbered for consistency with the thesis

5.1 Abstract

Background

Maternal mortality is high in Africa, especially in Kenya where there is evidence of insufficient progress towards Millennium Development Goal (MDG) Five, which is to reduce the global maternal mortality rate by three quarters and provide universal access to reproductive health by 2015. This study aims to identify risk factors associated with maternal mortality in a tertiary level hospital in Kenya.

Methods

A manual review of records for 150 maternal deaths (cases) and 300 controls was undertaken using a standard audit form. The sample included pregnant women aged 15-49 years admitted to the Obstetric and Gynaecological wards at the Moi Teaching and Referral Hospital (MTRH) in Kenya from January 2004 and March 2011. Logistic regression analysis was used to assess risk factors for maternal mortality.

Results

Factors significantly associated with maternal mortality included: having no education relative to secondary education (OR 3.3, 95% CI 1.1-10.4, p=0.0284), history of underlying medical conditions (OR 3.9, 95% CI 1.7-9.2, p=0.0016), doctor attendance at birth (OR 4.6, 95% CI 2.1-10.1, p=0.0001), having no antenatal visits (OR 4.1, 95% CI 1.6-10.4, p=0.0007), being admitted with eclampsia (OR 10.9, 95% CI 3.7-31.9, p<0.0001), being admitted with comorbidities (OR 9.0, 95% CI 4.2-19.3, p<0.0001), having an elevated pulse on admission (OR 10.7, 95% CI 2.7-43.4, p=0.0002), and being referred to MTRH (OR 2.1, 95% CI 1.0-4.3, p=0.0459).

Conclusions

Antenatal care and maternal education are important risk factors for maternal mortality, even after adjusting for comorbidities and complications. Antenatal visits can provide opportunities for detecting risk factors for eclampsia, and other underlying illnesses but the visits need to be frequent and timely. Education enables access to information and helps empower women and their spouses to make appropriate decisions during pregnancy.

Keywords: maternal mortality, tertiary hospital, risk factors, Kenya

5.2 Background

The maternal mortality ratio (MMR) is defined as "the ratio of the number of maternal deaths during a given period per 100,000 live births during the same time-period". The global MMR is 210 per 100,000 live births.[1] Despite worldwide declines since 1990, the MMR is 15 times higher in developing than developed regions.[1] Sub-Saharan Africa has the highest MMR at 500 per 100,000 live births. In developed regions the MMR is 16 per 100,000 live births.[1] The target for Millennium Development Goal (MDG) Five is to reduce the global MMR by three quarters and to achieve universal access to reproductive health by 2015.[2] In Kenya, the MMR has remained at 400-600 per 100,000 live births over the past decade - resulting in little or no progress being made towards achieving MDG Five.[1, 3]

The main direct causes of maternal death in developing countries include haemorrhage, sepsis, obstructed labour and hypertensive disorders.[4] The risk of death from haemorrhage is one in 1,000 deliveries in developing countries, compared with

one in 100,000 in developed countries, and accounts for one third of the maternal deaths in Africa.[5] A study in Canada found increased risk of eclampsia among women with existing heart disease and anaemia.[6] A retrospective study undertaken at a tertiary hospital in Nigeria in 2007 found that the most common risk factors for maternal mortality were primaparity, haemorrhage, anaemia, eclampsia and malaria.[7] Risk factors for complications arising from infections include birthing under unhygienic conditions, poor nutrition, anaemia, caesarean section, membrane rupture, prolonged labour, retained products and haemorrhage.[8]

In developing countries, indirect causes of maternal death include both previously existing diseases and diseases that develop during pregnancy. These include HIV, malaria, tuberculosis, diabetes, and cardiovascular disease, all of which and have an enormous impact on maternal and fetal outcomes during pregnancy.[4]

Many individual and socioeconomic factors have been associated with high maternal mortality. These include lack of education, parity, previous obstetric history, employment, socioeconomic status, and types of care seeking behaviours during pregnancy. There is also evidence of increased risk of death among women who are less than 24 and older than 35 years.[9] A study in Tanzania found that low level of spouse education was a risk factor for maternal mortality.[10] Lack of knowledge regarding the need for skilled attendants is a barrier to women seeking care, especially during birth emergencies. A survey conducted in Kenya in 2006 showed that 15% of pregnant women were not informed of the importance of hospital deliveries.[11] In Nigeria, a cross-sectional survey revealed that the most common risk factors for maternal death were primigravidity (19%), and unbooked status (19%).[12] Poverty has

also been associated with adverse maternal outcomes, not directly, but as a contributor to maternal ability to access and utilise care where complications occur.[13, 14] There is also evidence that contraceptive use is efficient for the primary prevention of maternal mortality in developing countries by about 44%.[15]

Antenatal care (ANC) is very important during pregnancy. International organizations recommend a minimum of four visits, the administration of two doses of tetanus toxoid and folic acid supplementation during ANC attendance.[16] When women receive good care during the pre-partum period, they have been shown to be at less risk of maternal morbidity and mortality, since they had a higher likelihood of using a professional health facility during birth.[10, 17]

In the Kenya Demographic and Health Survey (2008-2009), it was reported that 92% of women received ANC from a skilled provider (doctor, nurse, or midwife), especially those who were more educated and resided in urban areas.[3] The report further showed that 83% of women who visited public hospitals were required to pay for antenatal services, which may explain why only 47% of antenatal women attended the recommended four visits.[3] Women had also been required to pay for delivery services until June 2013, when the Kenyan government rolled out a program where pregnant women can receive free maternity services in public hospitals.

Health systems functioning with adequate equipment, resources and trained personnel to handle maternal complications can reduce the risks of mortality. In Africa maternal deaths are associated with delayed referrals for women from lower level facilities, and where referral systems are not well equipped to handle emergency obstetric care.[18] The

presence of skilled attendants during birth is also important in managing life threatening complications. In Kenya, the use of skilled attendants at delivery is currently 50%.[19]

The Delay Model by McCarthy and Maine is a conceptual framework that has been used to assess factors contributing to maternal mortality in developing countries.[20] This framework attributes mortality to certain determinants that contribute to the delay in deciding to seek care, the delay in reaching a health facility, and the delay in receiving quality care upon reaching a health facility. In Kenya there has been insufficient progress made towards achieving MDG Five. The aim of this study is to identify risk factors associated with maternal mortality in a tertiary level hospital in Kenya. Using a framework adapted from the Delay Model, this study analyses four sets of determinants: individual and socio-demographic, maternal history, reproductive or obstetric, and hospital admission/health system.

5.3 Methods

An unmatched case-control study of women who delivered between January 2004 and March 2011 was conducted at Moi Teaching and Referral Hospital (MTRH) located in the Western region of the Rift Valley Province, Kenya.[21] As the second largest national hospital in Kenya with over 800 beds, MTRH provides a range of curative, preventive and rehabilitative health services to a population of about 400,000 inhabitants, and an indigent referral population of 13 million from Northern and Western Kenya.[21] The Mother and Baby Unit at MTRH at has an antenatal ward, post-natal ward, labour ward, Newborn Unit (NBU) and two theatres dedicated for obstetrics. The bed capacity

is approximately 20 for the antenatal and labour wards, and 50 for the post-natal wards.[21]

Cases (n=150) were maternal deaths identified from a manual review of hospital records. Two controls (n=300) were selected per case. Controls were surviving women who were admitted immediately preceding and following cases. Cases were selected retrospectively and sequentially from the most recent delivery until the required sample size was achieved. Trained staff collected information using a standard audit form. Abortion related deaths were excluded from the study.

Maternal hospital death was the outcome. This was a clearly defined adverse event certified by medical personnel. The data collection form included: mother's age, mother's marital status, mother's education, spouse's education, mother's occupation, spouse's occupation, and the source of funding for the delivery. Information relating to the mother's medical history included: smoking, alcohol use, contraceptive use, previous abortion, previous twins, gravida, and pre-existing medical conditions. Obstetric or reproductive factors were pregnancy stage, labour stage, number of ANC visits, and place of ANC care. Health system factors included mode of delivery, qualification of birth attendant, and referral from another facility (yes/no). Information on the mother's admission factors comprised: clinical cause of death or diagnosis on admission (e.g. eclampsia, dystocia haemorrhage, or comorbid causes), diastolic blood pressure (millimetres of mercury/ mm Hg), systolic blood pressure (mm Hg), haemoglobin level (grams per decilitre g/dL), pulse rate (beats per minute/bpm), and temperature (degrees Celsius/ºC). The primary obstetric cause of death was that documented in the patient hospital and post mortem records.

5.3.1 Statistical Analyses

Analyses were performed using Stata version 10.0 (Stata- Corp, College Station, TX, USA). Following initial data checking and exploratory analysis, univariable logistic regression analysis was conducted for each potential risk factor. The multivariable models initially included all variables with $p < 0.2$ in the univariable models. Backward stepwise multiple logistic regression was undertaken separately for the four groups of risk factors in the framework adapted from the Delay Model, (individual and socio-demographic; maternal history; reproductive or obstetric; and admission). Variables were removed from the models where p-values >=0.1 on the Likelihood Ratio Test. The variables in each of the final models were then included in a combined model and removed where p-values >=0.1 in order to derive a final parsimonious model. Odds ratios (ORs), 95% confidence intervals and p-values are reported for all models. The reference group was the category with the lowest expected risk of death, or if there were few cases in this category, the group with the majority of respondents.

Assuming the probability of exposure in controls was 40% and the ratio of cases to controls was 1:2, with 80% power and a 5% level of significance, a sample of approximately 450 women (150 cases and 300 controls) was needed to detect an odds ratio of approximately 0.5 or 1.8.

Ethical approval was provided by the University of Newcastle Human Research Ethics Committee (HREC) and the Institutional for Research and Ethics Committee (IREC) in Kenya.

5.4 Results

Table 5.1 shows the demographic factors associated with maternal mortality. In this model, mother's age and mother's education were significantly associated with mortality. Relative to controls, cases had three times the odds of being aged 35-45 years rather than 15-24 years (OR 3.1, 95% CI 1.5- 6.2; p<0.0001). Cases had eight times the odds of having no education versus secondary education compared with controls (OR 8.0, 95% CI 4.0-16.3; p<0.0001).

Table 5-1 Individual and Socio-demographic risk factors for maternal mortality

Risk Factor	Cases n=150 n (%)	Controls n=300 n (%)	Unadjusted OR (95% CI)	Adjusted OR (95%CI)[a]	P-value[†]
Individual and socio-demographic characteristics					
Age					<0.0001
15-24 years	66(44)	147(49)	1	1	
25-34 years	54(36)	129(43)	1.1(0.7-1.6)	1.4(0.9-2.4)	
35-45 years	30(20)	24(8)	3.0(1.6-5.6)	3.1(1.5-6.2)	
Marital status					
Married	111(74)	240(80)	1		
Single	39(26)	60(20)	1.4(0.9-2.2)		
Mother's education					<0.0001
None	31(23)	17(6)	8.5(4.3-17.0)	8.0(4.0-16.3)	
Primary	66(50)	108(37)	2.9(1.8-4.6)	2.9(1.8-4.7)	
Secondary	36(27)	168(57)	1	1	
Spouse's education					
None	20(22)	14(6)	5.9(2.8-12.7)		
Primary	30(33)	46(20)	2.7(1.5-4.8)		
Secondary	40(44)	166(74)	1		
Occupation of mother					
Unemployed	106(71)	176(59)	1		
Formal employment	28(19)	88(29)	0.5(0.3-0.9)		
Informal employment	15(10)	35(12)	0.7(0.4-1.4)		
Occupation of spouse					
Informal employment	59(41)	124(42)	1		
Formal employment	47(32)	114(38)	0.9 (0.5-1.3)		
NA	39(27)	60(20)	1.4(0.8-2.3)		
Funding for delivery					
Self	105(70)	210(70)	1		
Insurance	16(11)	47(16)	0.7(0.4-1.3)		
Hospital Waived	28(19)	43(14)	1.3(0.8-2.2)		

* Spouse's education was not included in the multiple regression model due to high cases of missing data and correlation with mothers education

[a]Adjusted for variables included in the final demographic model

[†] P- value for Likelihood Ratio Test in the adjusted model

Reference category for logistic regression represented by 1

Numbers may not add to total sample due to missing values

Table 5.2 shows the association between maternal history of prevailing conditions and obstetric and reproductive factors with maternal mortality. After adjusting for all other factors in the model, cases had higher odds than controls of having a history of maternal alcohol use (OR 2.5, 95% CI 1.2-5.3; p =0.0018), more than five previous pregnancies (OR 2.6, 95% CI 1.4-4.8; p=0.0049), and a history of pre-existing illnesses (OR 3.0, 95% CI 1.7-5.3; p<0.0001). Contraceptive use was protective (OR 0.3 95% CI

0.1-0.6; p=0.0007). Table 5.2 also shows obstetric and reproductive characteristics associated maternal mortality. Compared to controls, cases had higher odds of assisted or caesarean deliveries (OR 3.0 95% CI 1.5-5.6; p<0.0006). Cases had higher odds than controls of having a doctor, rather than a nurse or midwife attend the birth (OR 4.1 95% CI 2.2-7.6; p<0.0001). Relative to controls, cases had almost nine times the odds of arriving at hospital at the puerperium stage (OR 8.9, 95% CI 3.5, 22.7; p<0.0001), and almost six times the odds of lack of antenatal care (OR 5.7, 95% CI 2.6-12.4; p<0.0001).

Table 5-2 Mother's history of prevailing conditions and obstetric characteristics associated with maternal mortality

Risk factor	Cases n=150 n (%)	Controls n=300 n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI) [a]	P-value†
History of prevailing medical conditions					
Smoking					
Yes	2(1)	7(2)	0.6(0.1-2.7)		
No	148(99)	286(98)	1		
Alcohol					0.018
Yes	16(11)	20(7)	1.6(0.8-3.2)	2.5(1.2-5.3)	
No	134(89)	273(93)	1		
Contraceptives					0.0007
Yes	17(11)	74(25)	0.4(0.2-0.7)	0.3(0.1-0.6)	
No	133(89)	220(75)	1		
Abortion					
Yes	11(7)	20(7)	1.1(0.5-2.4)		
No	139(93)	279(93)	1		
Twins					
Yes	10(7)	17(6)	1.2(0.5-2.7)		
No	140(93)	283(94)	1		
Gravida					0.0049
Primigravida	34(23)	104(35)	1		
Multigravida	73(49)	153(51)	1.5(0.9-2.4)	1.5(0.9-2.5)	
Grandmultigravida	43(29)	43(14)	3.1(1.7-5.4)	2.6(1.4-4.8)	
Underlying medical conditions*					<0.0001
Yes	41(27)	29(10)	3.5(2.1-5.9)	3.0(1.7-5.3)	
No	109(73)	271(90)	1		

Risk factor	Cases n=150 n (%)	Controls n=300 n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI) [a]	P-value†
Obstetric and reproductive characteristics					
Mode of delivery					0.0006
Normal	64(43)	230(77)	1		
Assisted	27(18)	13(4)	7.5(3.6-15.3)	4.4(1.7-11.2)	
Caesarean	51(34)	57(19)	3.2(2.0-5.1)	3.0(1.5-5.6)	
Did not deliver	8(5)	0	omitted	omitted	
Birth attendant					<0.0001
Nurse/midwife	70(53)	264(89)	1	1	
Doctor	61(47)	31(11)	7.4(4.5-12.3)	4.1(2.2-7.6)	
Pregnancy stage					<0.0001
Intrapartum	61(42)	259(86)	1	1	
Antepartum	53(37)	29(10)	7.8(4.6-13.2)	3.0(1.5-6.2)	
Puerperium	30(21)	12(4)	10.6(5.1-21.9)	8.9(3.5-22.7)	
Labour stage					
Latent	42(42)	68(24)	1		
Active	37(37)	180(63)	0.3(0.2-0.6)		
Second stage	20(20)	34(12)	1.0(0.5-1.9)		
Number of ANC visits					<0.0001
1 to 3	71(50)	199(67)	1	1	
None	59(42)	14(5)	11.8(6.2-22.5)	5.7(2.6-12.4)	
Above 4	11(8)	83(28)	0.4(0.2-0.7)	0.6(0.3-1.2)	
Place of ANC attendance ††					
Health centre	41(28)	122(41)	1		
Hospital	26(18)	60(20)	1.3(0.7-2.3)		
MTRH	19(13)	100(34)	0.6(0.3-1.0)		
None	59(41)	14(5)	12.5(6.3-24.8)		

*These include: HIV, malaria, rheumatic heart disease, cardiovascular disease, and diabetes

† P- value for Likelihood Ratio Test in the adjusted model

[a]Adjusted for variables included in the final demographic model

Reference category for logistic regression represented by 1

††Did not include ANC place because of high correlation with number of ANC visits

Numbers may not add to total sample due to missing values

Table 5.3 shows maternal admission factors associated with mortality. Admission from comorbid complications (OR 6.7, 95% CI 3.8-11.8; p<0.0001), eclampsia (OR 4.7, 95% CI 1.6, 13.7; p=0.0038), non-normal blood pressure (OR 7.5, 95% CI 1.5-37.7; p=0.0039), tachycardia (OR 16.5, 95% CI 4.8-57.3; p<0.0001), and being referred to MTRH (OR 3.3, 95% CI 1.9-5.7; p<0.0001) were all statistically significant risk factors for maternal mortality.

Table 5-3 Maternal admission factors associated with maternal mortality

Risk Factor	Cases n=150 n (%)	Controls n=300 n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	P-value[††]
Admission factors					
Comorbid complications					<0.0001
Yes	93(62)	63(21)	0.2(0.1-0.3)	6.7(3.8-11.8)	
No	57(38)	237(79)	1	1	
Eclampsia					0.0038
Yes	33(22)	16(5)	5.0(2.7-9.4)	4.7(1.6-13.7)	
No	117(78)	284(95)	1	1	
Dystocia					
Yes	21(14)	51(17)	0.8(0.5-1.4)		
No	129(86)	249(83)	1		
Haemorrhage					
Yes	20(13)	15(5)	2.9(1.5-5.9)		
No	120(87)	285(95)	1		
Diastolic blood pressure (mm Hg)**					0.0039
Normal	102(72)	280(96)	1	1	
Low	16(11)	2(1)	22.0(5.0-97.2)	7.5(1.5-37.7)	
High	24(17)	10(3)	6.6(3.0-14.3)	3.2(0.9-10.6)	
Systolic blood pressure (mm Hg)**					
Normal	93(65)	271(93)	1		
Low	33(23)	6(2)	16.0(6.5-39.5)		
High	17(12)	15(5)	3.3(1.6-6.9)		
Haemoglobin [†]					
<10g/dL	63(52)	43(20)	4.2(2.6-6.9)		
>=10g/dL	59(48)	171(80)	1		
Pulse					<0.0001
<110bpm	103(71)	283(99)	1	1	
>=110bpm	41(28)	4(1)	28.2(9.8-80.6)	16.5(4.8-57.3)	
Temperature[†]					
<37.5ºC	110(82)	205(95)	1		
>=37.5ºC	24(18)	11(5)	4.1(1.9-8.6)		
Referral					<0.0001
No	63(42)	234(78)	1	1	
Yes	87(58)	66(22)	4.9 (3.2-7.5)	3.3(1.9-5.7)	

**Diastolic blood pressure was used as a proxy for systolic because of high correlation

[†] Temp and haemoglobin were omitted in the adjusted model because of too many missing values

[††] P- value for Likelihood Ratio Test in the adjusted model

[a]Adjusted for variables included in the final demographic model

Reference category for logistic regression represented by 1

Numbers may not add to total sample due to missing values

Table 5.4 shows the multivariable analysis combining all factors from the previous models. Statistically significant risk factors for maternal mortality included: no education, relative to secondary education (OR 3.3, 95% CI 1.1-10.4, p=0.0284), history of pre-existing medical conditions (OR 3.9, 95% CI 1.7-9.2, p=0.0016), doctor attendance

at birth (OR 4.6, 95% CI 2.1-10.1, p=0.0001), having no antenatal visits (OR 4.1, 95% CI 1.6-10.4, p=0.0007), being admitted with eclampsia (OR 10.9 95% CI 3.7-31.9, p<0.0001), having comorbid complications on admission (OR 9.0, 95% CI 4.2-19.3, p<0.0001), having elevated pulse (OR 10.7, 95% CI 2.7-43.4, p=0.0002), and being referred to MTRH (OR 2.1, 95% CI 1.0-4.3, p=0.0459).

Table 5-4 Multivariable model showing risk factors for maternal mortality

Risk Factor	Cases n=150 n (%)	Controls n=300 n (%)	OR (95% CI)	Likelihood Ratio Test X^2 (df), p-value
Final multivariable model				
Mothers education				
Secondary	36(27)	168(57)	1	
None	31(23)	17(6)	3.3(1.1-10.4)	
Primary	66(50)	108(37)	2.4(1.1-5.3)	7.13(2), 0.0284
Underlying medical conditions				
No	109(73)	271(90)	1	
Yes	41(27)	29(10)	3.9(1.7-9.2)	9.95(1), 0.0016
Birth attendant				
Nurse/midwife	70(53)	264(89)	1	
Doctor	61(47)	31(11)	4.6(2.1-10.1)	14.41(1), 0.0001
Number of ANC visits				
1 to 3	71(50)	199(67)	1	
None	59(42)	14(5)	4.1(1.6-10.4)	
Above 4	11(8)	83(28)	0.5(0.2-1.2)	14.56(2), 0.0007
Comorbid complications†				
No	57(38)	237(79)	1	
Yes	93(62)	63(21)	9.0(4.2-19.3)	36.33(1), <0.0001
Eclampsia				
No	117(78)	284(95)	1	
Yes	33(22)	16(5)	10.9(3.7-31.9)	21.29(1), <0.0001
Pulse				
<110bpm	103(71)	283(99)	1	
>=110bpm	41(28)	4(1)	10.7(2.7-43.4)	13.58(1), 0.0002
Referral				
No	63(42)	234(78)	1	
Yes	87(58)	66(22)	2.1(1.0-4.3)	3.98(1), 0.0459

* Final model included all variables with P-value of 0.1 or less on the likelihood ratio test

Reference category for logistic regression represented by 1

†These include: HIV, malaria, rheumatic heart disease, cardiovascular disease, and diabetes

Numbers may not add to total sample due to missing values; the final model included 367 observations

5.5 Discussion

In the multivariable analysis of each of the four groups of risk factors (socio-demographic, maternal history, reproductive/ obstetric and admission factors) variables significantly associated with maternal mortality included: age, education, alcohol use, contraceptive use, gravida, pre-existing medical conditions, mode of delivery, type of birth attendant, pregnancy stage, number of ANC visits, having comorbid complications on admission, eclampsia, diastolic blood pressure, elevated pulse, and referral status. However, in the final model combining only significant factors from the four separate sets of analyses into a parsimonious model, only education, underlying medical conditions, birth attendant, number of ANC visits, having comorbid complications, eclampsia, having an elevated pulse on admission, and referral status were significant risk factors for maternal mortality.

Cases had three times the odds of having no education versus secondary education compared with controls. This is in agreement with another study that also reported a higher risk of mortality among illiterate women.[22] This finding is important since it emphasizes the role of education for both the mother and her spouse in obtaining and understanding the benefits of good health and being able to make appropriate decisions during pregnancy. It is important to note that despite the woman's weaker role in decision-making in African settings, education has a strong influence on mortality. In this study, we used mother's education as a proxy for the husband's education. Although there was considerable missing data for spouse's education there was correlation between these two education variables.

Having no antenatal care during pregnancy was associated with mortality in this study, a finding which corresponds with those of other studies.[22, 23] Antenatal care is important in screening for pre-existing illnesses and complications in the early stages of pregnancy that could impact adversely during pregnancy and childbirth.[24] Since ANC coverage is high in Kenya, there is a need to scale up interventions that empower women to make at least four visits during pregnancy as recommended by international organizations.[16, 19]

The findings here were that comorbid conditions including HIV, malaria, rheumatic heart disease, cardiovascular disease, and diabetes contributed to maternal deaths. This is contrary to other research showing that direct pregnancy complications are the leading causes of maternal deaths.[4] However, other research shows that the significant increases in MMRs in Sub-Saharan Africa are predominantly due to increasing HIV prevalence in that region.[25] The finding that the odds of comorbid conditions were higher in cases than controls also demonstrates the importance of ANC for screening, detection and management of underlying illnesses that could potentially pose a threat to the mother during pregnancy and childbirth.

Contraceptive use was protective for maternal mortality, which coincides with findings from another study that found that maternal mortality would be 77% higher globally in the absence of family planning programs and contraceptive use.[15] The role of contraceptives in tackling maternal mortality has been through reducing exposure to incidence of pregnancy, lowering hazards of fragility from high parity pregnancies, reducing vulnerability to abortion risks, and postponing pregnancies, especially in countries with high fertility rates.[15]

Alcohol use was also associated with mortality in the individual model but not in the final model, possibly due to the small numbers and potential confounding. After adjusting for other factors, haemorrhage was not significantly associated with mortality possibly as a result of hospital protocols for management of haemorrhage.

However, in this study, hypertensive disorders during pregnancy were higher among cases than controls. Our study demonstrated increased odds of eclampsia in cases, which is in agreement with another study that found that the delay in diagnosis, triage, transport and treatment of eclampsia increases the risk of maternal death.[26] There is evidence that screening for hypertensive conditions during the antenatal period plays a significant role in reducing the risk of death to the mother.[13] This study also found higher odds of elevated pulse amongst cases, which could explain the increased risk of death due to eclampsia.

This study found health care system related factors that identified cases as being at risk including doctor attendance at birth and referrals. Cases had higher odds than controls of a doctor attending their delivery, potentially because they were diagnosed with the most difficult complications. This has been previously reported, especially in low resource settings where uptake of professional birth attendants is low hence women only seek help when the condition is critical or too late for the doctor to save their lives.[4] Cases had twice the odds of referral relative to controls, potentially because the number of referrals represented over half of the cases who were referred following complications of birth.

This study provides information that is important for the identification of risk factors that contribute to maternal mortality in the second largest referral hospital in Kenya. It also provides information that will aid in identifying areas of improving health facilities locally and nationally in terms of referrals, antenatal care, and the availability of skilled birth attendants who are able to manage pregnancy related complications. This study is timely given the free maternity program roll out in Kenya since June 2013. Importantly, these findings will inform policy makers about ways of strengthening the health system and promoting more hospital births.

This study has some limitations. Firstly, it only includes deaths that occurred during the hospital admission and therefore the risk factors identified here were specifically associated with in-hospital mortality. Pregnancy related mortality that occurs outside hospital may have other risk factors that were not identified here. Secondly, bias may have resulted from the misclassification of causes of death data and missing information in some fields.

5.6 Conclusions

This study highlights risk factors for mortality at a tertiary hospital in Kenya showing the importance of antenatal care and maternal education in preventing maternal mortality. The findings are timely given Kenya's limited progress towards achieving MDG Five by 2015. Antenatal visits provide opportunities for the detection of risk factors for eclampsia and other underlying illnesses that may put a mother at risk during birth. There is need to focus on integrated care throughout the pregnancy by improving women's knowledge and empowering them to take an active role in their own health as well as gaining access to skilled care at birth and during pregnancy.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FY conceived the study. FY, CD, JB, JSW, and PN all contributed to the protocol design, questionnaire design and ethics application process. FY contributed in data collection and extraction. PN contributed in providing consultation and advice during data extraction. FY, CD and JB contributed to data analysis and writing of the paper. CD, JB, FY and JSW contributed to the drafting and editing the paper. All authors contributed to reviewing the paper and approved the final version for publication.

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List of abbreviations

MDG: Millennium Development Goal; MMR: Maternal Mortality ratio; ANC: Antenatal Care; MTRH: Moi Teaching and Referral Hospital; NBU: Newborn Unit; WHO: World Health Organization; HIV: Human Immunodeficiency Virus.

The next chapter presents a paper that has been submitted for publication that describes the risk factors associated with fetal and early neonatal mortality at MTRH.

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Chapter 6 Paper Three

A case-control study of risk factors for fetal and early neonatal deaths in a tertiary hospital in Kenya

Yego F[1], D'Este C[2], Byles J[3], Nyongesa P[4], Stewart Williams J[5].

The authors' affiliations are:

[1]Moi University, P.O. Box 4606 Eldoret, Kenya 30100

[2]Chair in Biostatistics, National Centre for Epidemiology and Population Health, Research School of Population Health, the ANU College of Medicine Biology and Environment, the Australian National University, Canberra, ACT

[3]Director, Research Centre for Gender Health and Ageing, University of Newcastle, Hunter Medical Research Institute building, New Lambton Heights, NSW

[4]Department of Reproductive Health, Moi University College of Health Sciences, Eldoret, Kenya 30100

[5]Research Engineer, Umeå Centre for Global Health Research, Unit of Epidemiology and Global Health, Department of Public Health and Clinical Medicine, Faculty of Medicine, Umeå University, Umeå, Sweden.

Tables and figures have been renumbered for consistency with the thesis.

6.1 Abstract

Background

It is important to understand the risk factors for fetal and neonatal mortality which is a major contributor to under five deaths globally. Fetal and neonatal mortality is a sensitive indicator of maternal health in society. This study aimed to examine the risk factors for fetal and early neonatal mortality at the Moi Teaching and Referral Hospital in Kenya.

Methods

This was a case-control study. Cases were fetal and early neonatal deaths (n=200). The controls were infants born alive immediately preceding and following the cases (n=400). Bivariate comparisons and multiple logistic regression analyses were undertaken.

Results

The odds of having 0-1 antenatal visits relative to 2-3 visits were higher for cases than controls (AOR= 4.5; 95% CI: 1.2-16.7, p=0.03). There were lower odds among cases of having a doctor rather than a midwife, as a birth attendant (AOR=0.2; 95% CI: 0.1-0.6; p<0.01). The odds of mothers having Premature Rupture of Membranes (AOR=4.1; 95% CI: 1.4-12.1; p=0.01), haemorrhage (AOR=4.8; 95% CI: 1.1-21.9; p=0.04) and dystocia (OR=3.6; 95% CI: 1.2-10.9; p=0.02) were higher for the cases compared with the controls. The odds of gestational age below 37 weeks (AOR=7.0; 95% CI 2.4-20.4) and above 42 weeks (AOR=16.2; 95% CI 2.8-92.3) compared to 37-42 weeks, were higher for cases relative to controls (p<0.01). Cases had higher odds of being born with congenital

malformations (AOR=6.3; 95% CI: 1.2-31.6; p=0.04) and with Apgar scores of below six at five minutes (AOR=26.4; 95% CI: 6.1-113.8; p<0.001).

Conclusion

Interventions that focus on educating mothers on antenatal attendance, screening, monitoring and management of maternal conditions during the antenatal period should be strengthened. Doctor attendance at each birth and for emergency admissions is important to ensure early neonatal survival and avert potential risk factors for mortality.

Keywords: early neonatal mortality, fetal death, risk factors, maternal, tertiary hospital

6.2 Background

Neonatal death is defined as newborn death occurring within the first four weeks after birth.[1] Neonatal deaths represent 40% of under-five deaths worldwide.[2, 3] Despite the reduction in overall under five mortality in developing regions from 97 deaths per 1000 live births in 1990 to 63 per 1000 live births in 2010, there has been little change in neonatal deaths as a proportion of under five deaths.[2, 3] In Sub-Saharan Africa, for example, the proportion of neonatal deaths among under five deaths increased from 37% in 1990 to 40% in 2010.[2, 3] Neonatal mortality rates in the developing world are generally high, for example, there were 32 deaths per 1000 live births in Central Africa in 2009;[4] and in Somalia the estimated neonatal mortality rate was 52 per 1000 live births in 2012.[5] In comparison, the neonatal mortality rate in Kenya is currently 28 per 1000 live births and there has been no progress towards achieving the Millennium Development Goal (MDG) Four for child survival.[2, 6] The main direct causes of neonatal deaths globally are preterm births (27%), severe infections (26%), asphyxia (23%), and neonatal tetanus (7%).[3, 7, 8]

Early neonatal death is defined as all deaths of live-born infants occurring on or before the first seven days of life.[9] There is evidence that there has been no measurable reduction in early neonatal mortality over the past decade.[2] Most programs addressing childhood mortality focus on pneumonia, malaria, diarrhoea and vaccine preventable conditions, which are geared towards improving child survival after the first four weeks of life.[5, 6] There is evidence that the highest numbers of early neonatal deaths in Sub-Sahara Africa are due to infections.[10, 11]

Fetal death is defined as any fetus born without a heartbeat, respiratory effort or movement, or any other sign of life.[9] It is estimated that globally 2.9 million babies experience fetal death or die within the first week of life, with 99% of these deaths occurring in developing countries.[12] Studies have shown that 50% of maternal deaths occur within the first day after childbirth and approximately 30% of stillbirths occur during labour.[5]

The health and survival of newborns has been shown to be closely linked to that of their mothers, since inadequate maternal care during the pregnancy and postpartum period can also affect the neonate.[13] It has been suggested that access to antenatal care and emergency obstetric care could reduce neonatal mortality by 10-15%.[5, 14] There is evidence that 10 % of intrapartum-related and preterm deaths can be reduced by immediate assessment and stimulation of newborns.[15] Treatment with antenatal corticosteroids has been associated with a decrease in overall neonatal deaths, especially for women with premature rupture of membranes (PROM).[16]

Health system factors have been associated with newborn deaths, especially in low resource settings where quality of care is generally poor and inadequate.[17] An assessment of six African countries showed that less than 12% of personnel working in health facilities were trained to conduct neonatal resuscitation and no more than 22% of the facilities had sufficient equipment for neonatal resuscitation.[18]

Due to these high mortality rates it is important to understand the risk factors for fetal and neonatal mortality which are major contributors to high under five deaths globally. Fetal and neonatal mortality is also a sensitive indicator of maternal health in

society because healthy mothers give birth to healthy babies. This study was undertaken to assess maternal and neonatal risk factors associated with fetal and early neonatal deaths in the second largest tertiary hospital in Kenya in order to provide insights into the circumstances surrounding fetal and early neonatal deaths.

6.3 Methodology

This retrospective case-control study was conducted in Moi Teaching Referral Hospital (MTRH) in Kenya, the second largest referral hospital. The study was undertaken in Uasin Gishu County which is in the Rift Valley Province of Kenya. This hospital services approximately seven million women.[19] The MTRH has a reproductive health wing called the Riley Mother Baby Unit, which contains both the labour ward and the New Born Unit (NBU). The NBU has three sections: the born before arrival (BBA) unit, the acute ward or critical ward, and the general ward.[20] The NBU has several incubators, newborn trolleys, and a capacity of 60 beds and is staffed with consultant paediatricians (10), registrars (6), intern doctors (one) and nurses (30) specially trained for NBU care.[20] According to the MTRH records department the total number of monthly admissions is about 120-140 newborns.[20]

Client flow in the hospital is such that pregnant/ post-partum patients are seen at a designated room (triage area) on the labour ward floor by a nurse, medical officer intern and resident doctor. Patients in active labour are usually admitted to the labour ward where they are managed by a team of obstetricians, residents, interns and midwives/nurses. Patients in latent phase of labour, or with medical conditions, are usually admitted to the ante natal ward, and other patients with medical issues after delivery are admitted to the post-natal ward. Neonates who have complications after

birth are immediately taken to the NBU which is adjacent to the labour ward. The neonatologist and paediatricians subsequently manage the neonate.[20]

A medical record review was undertaken on admissions to the newborn unit in MTRH between January 2005 and March 2011. Cases were defined as neonates who were born dead (fetal deaths) or died within seven days of birth (early neonatal deaths). Most recent cases were selected retrospectively until the desired sample size was achieved. Two controls were obtained for every case. The controls were surviving neonates born immediately preceding and following the cases within the first week of life. Exclusion criteria were late neonatal deaths (more than seven days after birth).

A structured data collection instrument was used to collect data from medical records identified from the NBU admission register. It was not possible to blind the data abstractors to case/control status as this mortality information was available in the medical records.

The primary cause of death was identified using the information from hospital medical records and post mortem reports. Where interpretation was required, the information on the cause of death was verified by the study physician. Data were coded and double entered into two separate password protected databases, which were later compared for consistency, and where there were inconsistencies, the patient's file was obtained to verify the information.

The outcome of this study was death of the neonate or foetus at birth or within seven days of birth. Explanatory variables were classified as maternal and obstetric

characteristics, maternal and obstetric complications, neonatal complications and neonatal characteristics.

Maternal and obstetric characteristics included information on women of reproductive age (15 to 49 years) such as mother's age (15-24 years, 25-34 years, or 35-45 years); gravidity categorised as primigravida (1), multigravida (2-4), or grandmultigravida (above 5); qualification of birth attendant (doctor (consultant/ registrar/ intern), or midwife); gestational age (less than 37 weeks, 37-42 weeks or above 42 weeks); mode of delivery (spontaneous vertex delivery, assisted vaginal delivery, or caesarean section); number of antenatal visits (ANC) (0-1, 2-3, or above 4); and booking status on admission (yes=attended ANC at MTRH or no=did not attend ANC at MTRH).

Maternal and obstetric complications included the presence of common causes of death, as documented in the patient records and post mortem reports; premature rupture of membranes (PROM); dystocia (prolonged or obstructed labour); pre-eclampsia; haemorrhage; and other complications (cardio respiratory diseases, previous scar, Human Immunodeficiency Virus or HIV, malaria, retained placenta, anaemia, abortion). A complication was assumed if there was an indication to this effect in the notes, otherwise it was assumed that there were no complications.

Newborn complications included the presence of causes of newborn death as documented in the records including asphyxia, congenital malformation, sepsis, Respiratory Distress Syndrome (RDS), and other complications (hypothermia, diarrhoea, jaundice, hypoglycaemia, meconium aspiration syndrome, and HIV). One single cause of death was identified or each neonate case and where there were

multiple causes the final cause of death documented in the post mortem reports was used.

Neonatal characteristics were also recorded including: sex, Apgar score at five minutes and weight in grams.

Ethical approval was provided by the University of Newcastle Human Research Ethics Committee (HREC) and the Institutional Research and Ethics Committee (IREC) in Kenya. Permission was obtained from the hospital administration to undertake the study.

6.3.1 Statistical Methods

Statistical analysis was performed using STATA version 10 (StataCorp, College Station, TX, USA). Exploratory data analysis involved checking the data for implausible relationships, outliers and errors, using frequency distributions, tables and graphs. Checks comprised visualizing the distributions by use of graphics including histograms overlaid with a normal curve, normal probability plots and box plots to identify potential errors. Bar charts were also used to compare distributions between groups.

All variables were categorical. Categories were combined where cell sizes were small. Bivariate analysis was undertaken using the Chi-squared test to compare characteristics of cases and controls. Initially, a modelling process was undertaken by including all variables with $p<0.2$ in separate models for each of the four groups of potential risk factors (maternal and obstetric characteristics, neonatal complications, maternal and obstetric complications and neonatal characteristics). Each group of

potential risk factors was analysed in separate multivariable logistic regression. A backward stepwise method was used whereby, at each step, variables with a p-value of >0.1 on the likelihood ratio test were removed. The remaining variables were combined in a final overall model. Unadjusted and adjusted odds ratios, confidence intervals and p-values are reported for all models.

For a ratio of cases to controls of 1:2, 80% power, a 5% significance level and 40% probability of exposure (i.e. risk factor prevalence) in controls, a sample of 600 neonates (200 cases and 400 controls) was required to detect an absolute difference in risk factor prevalence of at least 12%, or an odds ratio of approximately 0.6 or 1.7.

6.4 Results

A total of 600 records were reviewed (200 cases and 400 controls) from January 2005 to March 2011. As with many studies using data abstracted from medical records, data were incomplete in some areas. The proportion of missing data in variables ranged from 0.3% to 22%. Data were separately stored in the MTRH neonatal and maternal records. Missing data in individual records arose from one or both sources.

Table 6.1 shows the maternal and obstetric factors associated with fetal and early neonatal mortality at MTRH. Gestational age at admission ($p<0.001$), number of antenatal visits ($p<0.001$) and qualification of birth attendant ($p=0.01$) were all significantly associated with fetal and early neonatal mortality. The odds of gestational period below 37 weeks, relative to gestational age of 37-42 weeks were higher for cases than controls (Adjusted Odds Ratio (AOR) = 16.6; 95% CI: 8.2-33.7). The odds of having 0-1 antenatal visits relative to 2-3 visits were higher for cases than controls (AOR= 5.4;

95% CI: 2.0-14.7). Compared to controls, cases had lower odds of having four or more antenatal visits relative to 2-3 visits (AOR=0.3; 95% CI: 0.1-0.7); and having a birth attendant who was a doctor rather than a midwife (AOR= 0.4; 95% CI: 0.2-0.8).

Table 6-1: Association between maternal and obstetric factors with fetal and early neonatal death

Predictor	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value for likelihood ratio test
Age in years					0.98
15-24	97(51)	195(49)	1.0	1.0	
25-34	68(35)	172(43)	0.8(0.5-1.2)	1.1(0.5-2.3)	
35-45	27(14)	33(8)	1.6(0.9-2.9)	1.1(0.3-4.0)	
Gravidity					0.26
Multigravida	108(54)	231(58)	1.0	1.0	
Primigravida	58(29)	119(30)	1.0(0.7-1.5)	0.8(0.4(1.9)	
Grandmultigravida	34(17)	50(12)	1.5(0.9-2.4)	2.3(0.8-6.6)	
Qualification of birth attendant					0.01
Midwife	142(74)	191(50)	1.0	1.0	
Doctor	50(26)	187(49)	0.4(0.2-0.5)	0.4(0.2-0.8)	
Gestational age at admission					<0.001
<37 weeks	116(72)	74(20)	11.0(7.1-17.2)	16.6(8.2-33.7)	
37-42 weeks	39(24)	274(75)	1.0	1.0	
> 42 weeks	6(4)	15(4)	2.8(1.0-7.7)	2.4(0.4-13.4)	
Mode of delivery					0.79
Normal	146(73)	249(62)	1.0	1.0	
Assisted	9(5)	13(3)	1.2(0.5-2.8)	1.5(0.3-7.9)	
Caesarean	45(22)	138(35)	0.6(0.4-0.8)	1.3(0.5-3.1)	
Number of antenatal care visits					<0.001
0-1	31(26)	15(4)	5.9(3.0-11.6)	5.4(2.0-14.7)	
2-3	74(63)	212(59)	1.01	1.0	
Above 4	13(11)	133(36)	0.3(0.1-0.5)	0.3(0.1-0.7)	
Booking status					0.28
No	139(79)	311(80)	1.0	1.0	
Yes	38(21)	80(20)	0.9(0.6-1.5)	0.9(0.5-2.2)	

Reference category represented by 1.0

Numbers may not add to total sample size due to missing values

Maternal obstetric complications associated with fetal and early neonatal mortality at MTRH are shown in Table 6.2. PROM, haemorrhage, and dystocia were significantly associated with mortality. Compared with the controls, the cases had higher odds of

maternal PROM (AOR = 5.9; 95% CI: 3.5-9.9; p<0.001), dystocia (AOR=1.9; 95% CI: 1.2-3.1; p=0.01), and haemorrhage (AOR=2.4; 95% CI: 1.2-4.7; p=0.02). Cases had higher odds of other complications compared with controls (AOR = 2.0; 95% CI: 1.0-3.9; p=0.06) although the difference was not significant.

Table 6-2: Association between maternal obstetric complications with fetal and early neonatal mortality

Predictor	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value for likelihood ratio test
Premature rupture of membranes					<0.001
Yes	52(26)	27(7)	4.9(2.9-8.0)	5.9(3.5-9.9)	
No	148(74)	373(93)	1.0	1.0	
Dystocia					0.01
Yes	42(21)	64(16)	1.4(0.9-2.2)	1.9(1.2-3.1)	
No	158(79)	336(84)	1.0	1.0	
Pre-eclampsia					0.44
Yes	13(7)	29(7)	1.0(0.5-1.8)	1.3(0.7-2.7)	
No	187(93)	371(93)	1.0	1.0	
Haemorrhage					0.02
Yes	17(9)	21(5)	1.7(0.9-3.3)	2.4(1.2-4.7)	
No	183(91)	379(95)	1.0	1.0	
Other complications					0.06
Yes	16(8)	22(6)	1.5(0.8-2.9)	2.0(1.0-3.9)	
No	184(92)	378(94)	1.0	1.0	

Reference category for logistic regression represented by 1.0

Other complications included: cardio respiratory diseases, previous scar, HIV, malaria, retained placenta, anaemia, abortion

Numbers may not add to total sample size due to missing values

Table 6.3 shows the association between neonatal complications with fetal and early neonatal mortality at MTRH. The odds of asphyxia (AOR 2.4; 95% CI: 1.6-3.6; p<0.001), congenital malformation (AOR 2.9; 95% CI: 1.5-5.7; p=0.01) and RDS (AOR 1.6; 95% CI: 1.1-2.4; p=0.01), were higher for cases relative to controls. The odds of sepsis were

marginally non-significantly lower for cases than controls (AOR = 0.7; 95% CI: 0.4-1.0; p=0.06).

Table 6-3: Association between neonatal complications with fetal and early neonatal mortality

Predictor	Cases n(%)	Controls n(%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value for likelihood ratio test
Asphyxia					<0.001
Yes	73(37)	74(19)	2.5(1.7-3.7)	2.4(1.6-3.6)	
No	127(63)	326(81)	1.0	1.0	
Congenital malformation					0.01
Yes	21(11)	18(5)	2.5(1.3-4.8)	2.9(1.5-5.7)	
No	179(89)	182(95)	1.0	1.0	
Sepsis					0.06
Yes	37(18)	125(31)	0.5(0.3-0.8)	0.7(0.4-1.0)	
No	163(82)	275(69)	1.0	1.0	
Respiratory Distress syndrome					0.01
Yes	66(33)	94(24)	1.6(1.1-2.3)	1.6(1.1-2.4)	
No	134(67)	306(76)	1.0	1.0	
Other neonatal complications					0.50
Yes	32(16)	79(20)	0.8(0.5-1.2)	0.9(0.5-1.4)	
No	168(84)	321(80)	1.0	1.0	

Reference category for logistic regression represented by 1.0

Other complications included: hypothermia, diarrhoea, jaundice, hypoglycaemia, meconium aspiration syndrome, sero-exposed.

Numbers may not add to total sample size due to missing values

The association between neonatal characteristics and early neonatal mortality at MTRH is shown in Table 6.4. Baby's birth weight and Apgar score were significantly associated with mortality (p<0.001 for both). Relative to controls, cases had higher odds of birth weight less than 2500 grams (AOR 6.6; 95% CI: 3.8-10.2) and an Apgar score of zero to six (AOR 13.4; 95% CI 7.3-24.8) rather than seven or above at five minutes.

Table 6-4: Association between neonatal characteristics with fetal and early neonatal mortality at MTRH

Predictor	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value for likelihood ratio test
Baby's birth weight					<0.001
less than 2500gms	133(73)	116(29)	6.6(4.5-9.8)	6.6(3.8-10.2)	
Above 2500gms	49(27)	282(71)	1.0	1.0	
Baby's Apgar score					<0.001
0-6 at 5mins	78(49)	20(5)	17.2(10.0-29.8)	13.4(7.3-24.8)	
7-10 at 5mins	79(50)	349(95)	1.0	1.0	
Baby's sex					
Female	85(44)	190(48)	0.9(0.6-1.3)	1.0(0.6-1.7)	0.88
Male	105(55)	208(52)	1.0	1.0	

Reference category for logistic regression represented by 1.0
Numbers may not add to total sample size due to missing values

Table 6.5 represents the final model combining factors from the four previous models. The odds of having a birth attendant who was a doctor versus a midwife were lower for cases relative to controls (AOR=0.2; 95% CI: 0.1-0.6; p<0.01). Cases, compared to controls, had higher odds of having mothers who had 0-1 antenatal visit relative to 2-3 visits (AOR=4.5; 95% CI: 1.2-16.7; p=0.03 overall). The odds of gestational age less than 37 weeks (AOR=7.0; 95% CI 2.4-20.4) and above 42 weeks (AOR=16.2; 95% CI 2.8-92.3), rather than 37-42 weeks were higher for cases relative to controls (p<0.01). The odds of mothers with complications of PROM (AOR=4.1; 95% CI: 1.4-12.1; p=0.01), haemorrhage (AOR=4.8; 95% CI: 1.1-21.9; p=0.04) or dystocia (AOR=3.6; 95% CI: 1.2-10.9; p=0.02) were higher for cases relative to controls. Cases, compared to controls had higher odds of being born with congenital malformations (AOR=6.3; 95% CI: 1.2-31.6; p=0.04), and being born with Apgar scores of 0-6 (AOR=26.4; 95% CI: 6.1-113.8; p<0.001), rather than a score of above seven at five minutes.

Table 6-5: Determinants of fetal and early neonatal mortality

Predictor	Cases n (%)	Controls n (%)	Adjusted OR (95% CI)	LR test statistic		
				x^2	Degrees of freedom	P value
Qualification of birth attendant				10.58	1	<0.01
Midwife	142(74)	191(50)	1			
Doctor	50(26)	187(49)	0.2(0.1-0.6)			
Number of antenatal care visits				7.35	2	0.03
0-1	31(26)	15(4)	4.5(1.2-16.7)			
2-3	74(63)	212(59)	1.0			
Above 4	13(11)	133(36)	0.5(0.2-1.5)			
Gestational age at admission				19.72	2	<0.01
<37 weeks	116(72)	74(20)	7.0(2.4-20.4)			
37-42 weeks	39(24)	274(75)	1.0			
> 42 weeks	6(4)	15(4)	16.2(2.8-92.3)			
Premature rupture of membrane				6.38	1	0.01
No	148(74)	373(93)	1.0			
Yes	52(26)	27(7)	4.1(1.4-12.1)			
Haemorrhage				4.09	1	0.04
No	183(91)	371(95)	1.0			
Yes	17(9)	29(5)	4.8(1.1-21.9)			
Dystocia				5.08	1	0.02
No	158(79)	336(84)	1.0			
Yes	42(21)	64(16)	3.6(1.2-10.9)			
Other maternal complications				0.47	1	0.49
No	184(92)	378(94)	2.0(0.3-13.9)			
Yes	16(8)	22(6)	1.0			
Sepsis				0.3	1	0.58
No	163(82)	275(69)	1.0			
Yes	37(18)	125(31)	1.4(0.5-3.9)			
Asphyxia				1.65	1	0.20
No	127(63)	326(81)	1.0			
Yes	73(37)	74(19)	0.4(0.1-1.7)			
Respiratory Distress syndrome				0.05	1	0.82
No	134(67)	306(76)	1.0			
Yes	66(33)	94(24)	0.9(0.4-2.3)			
Congenital malformation				4.14	1	0.04
No	179(89)	182(95)	1.0			
Yes	21(11)	18(5)	6.3(1.2-31.6)			
Baby's birth weight				2.82	1	0.09
Above 2500gms	49(27)	282(71)	1.0			
less than 2500gms	133(73)	116(29)	2.4(0.9-6.7)			
Baby's Apgar score				26.09	1	<0.001
7-10 at 5mins	79(50)	349(95)	1.0			
0-6 at 5mins	78(49)	20(5)	26.4(6.1-113.8)			

Reference category for logistic regression represented by 1.0

Numbers may not add to total sample size due to missing values

6.5 Discussion

This study examined risk factors associated with fetal and early neonatal mortality at MTRH. Factors that were significantly associated with early neonatal mortality in adjusted analyses were: qualification of the birth attendant; gestational age; number of antenatal visits; maternal complication at birth (PROM, haemorrhage and dystocia); congenital malformations, and low Apgar scores at five minutes.

The odds of low ANC attendance (0-1 visit) were higher for cases relative to controls. This is possibly because fewer ANC visits can result in poorer supervision of the pregnancy and failure to prevent, detect, and manage maternal conditions during the pregnancy. These issues have been reported by other studies in developing countries.[19, 21] Moreover, since reasons for low ANC attendance could include lack of education, lack of female empowerment, and poverty, these factors may also explain some of the relationship between ANC attendance and fetal and early neonatal mortality.[22] Additionally, recent research has indicated that timing of visits is more important in detecting complications than the number of visits,[23] hence women who only had 0-1 visit may have been prompted by a problem with their pregnancy rather than continuous monitoring of the pregnancy. The timing of ANC was however not captured in our study.

Assistance from a doctor (consultant, registrar or medical officer intern) was protective against neonatal mortality. This finding is in agreement with other studies that have found the presence of a doctor at birth enhances appropriate management and reduces maternal and infant mortality.[1, 21, 24] Lack of emergency obstetric care increases the risk

of neonatal mortality. This is because labouring mothers cannot always access appropriate health services.

Maternal complications that were risk factors for fetal and early neonatal mortality were: PROM, dystocia, and haemorrhage. Mothers with PROM have been previously shown to be more likely to deliver preterm babies than those without this condition, with both maternal and neonatal risk of infection higher for this group.[25] This is concerning as infections are the leading cause of neonatal death in Sub Saharan Africa.[1, 10, 25] Dystocia (prolonged or obstructed labour) was also a significant risk factor for mortality and this is consistent with another study which found that dystocia may result in the foetus having asphyxia.[26] Haemorrhage can be rapidly fatal to both the mother and neonate before medical intervention can be instituted and it has been reported as one of the leading causes of neonatal mortality in developing countries.[27]

Babies born before or after 37-42 weeks carry significant risks during, and immediately after delivery and may require intervention by doctors.[4] The majority of health facilities in Sub Saharan Africa lack proper resuscitation equipment and neonatal intensive support units; and are thus unable to adequately manage neonates born prematurely.[17, 18, 28] Prematurity is among the top three major causes of neonatal death in developing countries because of slow progress in uptake of public health measures such as antenatal corticosteroids, and proper hygiene practices during child birth.[3, 5, 28]

The study found that congenital malformation was significantly associated with mortality. This is consistent with another study that reported congenital malformation as one of the causes of death in developing countries.[7] The presence of congenital

anomalies in newborns could be explained by the lack of adequate screening and detection of these conditions during the antenatal period. If this had occurred then it may have been possible to give patients and doctors opportunities to make decisions on interventions prior to birth.[28-30] Other pre-disposing factors for congenital anomalies are maternal socioeconomic and nutritional status, the presence of maternal infections, and environmental exposure to hazardous agricultural chemicals which contribute to about one-third of the disease burden in Sub Saharan Africa.[31, 32]

The majority of neonatal deaths in this study had poor Apgar scores at five minutes after birth. This is consistent with other studies that have found a high risk of asphyxia among babies born to mothers with poor nutritional status, lack of ANC, and haemorrhage.[21, 28, 33] Information on some Apgar scores was not recorded, perhaps because of lack of time between transfers from one ward to the other, especially when the neonates had to be rushed to the newborn unit for resuscitation. This is a possible reason for the high proportion of missing values, particularly for cases, and this may have contributed to the wide confidence intervals for the estimates.

The findings of this study are not only important for MTRH, which Kenya's second largest hospital, but also the Ministry of Health (MOH) in Kenya. They highlight the importance of informing stakeholders about areas where services can be improved. These include, for example, training on newborn care, the provision of adequate supplies and equipment, the development of protocols for newborn management and regular criterion based audits aimed at averting early neonatal mortality. Additionally, most recommendations from this study relate to education and advocacy, issues which are relevant to the broader community.

One major limitation of this study was that there was potential selection bias because only hospital births were included. The sample may not therefore be representative of all births in the region, because high-risk women, or women who develop complications, may be more likely to deliver in hospital. The proportion of Kenyan women who deliver in health facilities reported in the literature is 42.8%.[34] Another potential limitation is that it was not possible to blind the data abstractors to case or control status. Also MTRH did not have checklists or protocols for hospital personnel regarding medical records. Time pressures on staff were substantial and there was high patient throughput. It is therefore likely that some information may have been omitted from patient records.[35]

6.6 Conclusions

In conclusion the risk factors for fetal and early neonatal mortality included: number of antenatal visits, gestational age, qualification of the birth attendant, mother's complication at birth (PROM, haemorrhage, dystocia), low Apgar scores at five minutes and congenital malformations. Interventions that focus on educating mothers on the importance of antenatal clinic attendance, as well as ensuring screening, detection, monitoring and management of maternal conditions during the antenatal period could help reduce neonatal mortality rates.

Doctor attendance at birth and during emergencies is important and can ensure that the newborn survives beyond the first week of life. There is a need increase the availability of resuscitation equipment, train personnel on immediate newborn care and develop and implement protocols and checklists to promote efficiencies in medical record information gathering and documentation. Accurate complete maternal and

neonatal records are important for delivery of care to both the mother and baby. Combining maternal and neonatal records is one way of assisting in clinical management and also providing data for research.

This research offers some possible reasons for the high mortality among neonates in a tertiary institution in Kenya. The findings have relevance for both mothers and neonates. Further research into factors influencing the timing and uptake of antenatal care by women in the community, as well as the contribution of quality of care to neonatal mortality in health facilities, is needed.

List of Abbreviations:

MTRH: Moi Teaching and Referral Hospital; PROM: Premature Rupture of Membranes; MDGs: Millennium Development Goals; NBU: Newborn Unit; BBA: Born Before Arrival; ANC: Antenatal Care; HIV: Human Immunodeficiency Virus; RDS: Respiratory Distress Syndrome; MOH: Ministry of Health

Conflict of Interest

The authors declare no competing interests.

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Authors' contributions

FY participated in all steps of the study including; design, implementation, data collection, analysis and writing. CD contributed to the study design, questionnaire design, sample size determination, data analysis, interpreting of results, manuscript preparation, and editing. JB contributed to the study design, data interpretation, revising the manuscript for intellectual content. JSW contributed to the study design, analysis and interpretation of data and editing the manuscript. PN contributed with study design and coordination of data collection, questionnaire design and data interpretation. All authors read and approved the final manuscript.

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Chapter 7 Paper Four

Completeness of maternal and neonatal hospital records at a tertiary level hospital in Kenya

This paper describes record completeness at MTRH during the study period 2004-2011. The distributions of missing data among cases and controls are described and proportions of overall missing data are reported. The paper also discusses factors associated with missing data for selected variables.

Yego F[1], D'Este C[2], Byles J[3], Stewart Williams J [4]

This paper will be submitted to a reputable journal.

The authors' affiliations are:

[1]Moi University, P.O. Box 4606 Eldoret, Kenya 30100

[2]Chair in Biostatistics, National Centre for Epidemiology and Population Health, Research school of Population Health, the ANU College of Medicine Biology and Environment, the Australian National University, Canberra, ACT

[3]Director, Research Centre for Gender Health and Ageing, University of Newcastle, Hunter Medical Research Institute building, New Lambton Heights, NSW

[4]Research Engineer, Umeå Centre for Global Health Research, Unit of Epidemiology and Global Health, Department of Public Health and Clinical Medicine, Faculty of Medicine, Umeå University, Umeå, Sweden.

7.1 Abstract

Background: Health record data are useful for obtaining up to date and continuous information on evidence of procedures undertaken to manage patient conditions. Valid and reliable information can help monitor functioning of health facilities. The objective of this study was to assess the completeness of maternal and neonatal records at Moi Teaching and Referral Hospital in Kenya and determine factors associated with missing information.

Methods: We conducted a retrospective review of patient records for a sample of 450 maternal and 600 neonatal records for admissions from 2004-2011 for two subsequent case-control studies of maternal and neonatal mortality. We described the distributions of missing data for both samples, by case/control status, and used stepwise logistic regression to identify factors associated with missingness for variables missing 20% or more data for either cases or controls.

Results: The proportion of missing data ranged from zero to 25% for the maternal sample, and from zero to 20% for the neonatal sample, with cases having a higher proportion of missing data than controls for both samples. Data were mostly missing for maternal vital signs and neonatal characteristics. Factors such as case/control status, maternal age, vital signs on admission, labour stage, gestational age, and neonatal characteristics were associated with missing data in the maternal sample; whereas neonatal characteristics, mode of delivery, pregnancy stage, booking status and case/control status were associated with missing information in the neonatal sample.

Conclusion: Factors associated with missing data were similar for most outcomes and were mostly as a result of maternal, neonatal and health system factors. In developing countries such as Kenya for example, there is need to implement standard checklists and record keeping strategies for obtaining complete, accurate and valid medical record data to enable health facilities to have reliable information that will aid in monitoring progress for maternal and neonatal health outcomes.

7.2 Introduction

Information on morbidity and mortality are important in measuring disease impact and for public healthcare planning. By understanding the incidence of disease and patterns of morbidities in different countries, stakeholders are able to examine health differences across populations, monitor trends and develop and evaluate evidence based interventions and implementation strategies to improve health outcomes.[1] At a facility level, health information enables health planners and managers to make decisions regarding the effective functioning of health facilities, to ensure client satisfaction and set service delivery standards for the population.[2]

In developing countries, the use of hospital data may be the most feasible and efficient method of obtaining continuous, timely data on mothers and neonates to monitor progress towards the Millennium Development Goals (MDGs). Some of the indicators for progress towards MDGs include prevention and care for Human Immunodeficiency Virus (HIV) infection, utilization of family planning, skilled attendants at birth, antenatal care, post-natal care, immunization, combating sexually transmitted infections and essential newborn care.[3] Most developing countries rely on hospital data for information on the health of the population serviced by the facility

and the impact of the services offered by the facility on morbidity and mortality, risk factors for disease and actual treatment practices.[4] The availability of timely, consistent and accurate record systems is crucial for countries to be able to effectively manage their health systems, provide data for medical research, allocate resources to health facilities and ensure accountability for delivering on health commitments.[3]

In developed countries vital registration systems are the major source of maternal and neonatal mortality data, while primary sources of data in developing countries are census (sibling method), verbal autopsies, Reproductive Age Mortality Studies (RAMOS), household surveys, and health service records.[5] Each of these methods has strengths and limitations. For example, prospective population studies are time consuming, requiring large samples and potentially lengthy follow up to produce stable mortality rates; and loss to follow up is a major methodological challenge.[6] Surveys may not provide information on the relevant cause of death, may not necessarily classify maternal death within the standard definitions, and are prone to underreporting due to misclassification.[7] RAMOS are complicated, time consuming and expensive to conduct because they involve multiple sources of data, for example, interviewing family members, health records, burial records, traditional birth attendants' records and civil registers.[7] Verbal autopsies are also prone to misclassification bias, may be time consuming and sometimes inaccurate due to the quality of information obtained.[7]

Medical record reviews can provide evidence of actual practices undertaken, details on cause of death as certified by the attending physician, and can also be used to evaluate performance of health professionals and provide accountability for data recorded in

patients' charts.[8] Information obtained from health facilities can also be aggregated to the national level and plays a role in informing policy and budgetary and resource allocation for health facilities.[8] The advantage of obtaining data from hospital records is that record reviews are relatively inexpensive to conduct (compared to other methods of data collection), can be used to study rare occurrences, and can generate hypotheses for future studies.[9] The disadvantages of obtaining data from hospital records include lack of completeness, inconsistencies, inaccuracy, incomprehensiveness, conflicting entries, and poor record keeping.[8, 10, 11] Some of the reasons for these inaccuracies include complexly designed health records, uneducated staff, poor record management, work conditions and lack of a system for matching of records that relate to the same people, for example the mother and neonate.[2]

There are few studies on the quality of data collected from hospital maternal and neonatal records in the literature. However, one study on stillbirths and newborns undertaken in five hospitals in South America in 2007, revealed lack of data completeness on weight, time of death of the neonate, monitoring progress of the mother and neonate, stage of labour, and number of antenatal visits.[12] Reasons for missing information included the lack of availability of the mother's chart and mothers being admitted at the second stage of labour.[12] In another study conducted at a tertiary hospital in Malawi, records lacked accuracy for information obtained from maternity wards. There were also difficulties with record linkage given that women had up to four different health records within various maternity clinics.[2] A study of 30 health facilities in Kenya showed that entries in some records were missing, especially information on maternal and foetal outcomes and patient complications.[13] A case study

conducted in Western Kenya identified quality of data in the childbirth registers to be unsatisfactory due to organizational and technical factors that affect the healthcare providers' record-keeping behaviours.[14]

There is a need to better understand the inaccuracy and incompleteness of information to enable health institutions to design and implement efficient record systems and protocols for record keeping and the procurement of clinical and other data that are factual, accurate, clear and concise.[15] The aim of this study was to assess the completeness of maternal and neonatal data at a large tertiary hospital in Kenya and identify the factors associated with missing maternal and neonatal data at this facility.

7.3 Methods

This study involved a chart review of maternity data (maternal and neonatal records) at the Moi Teaching and Referral hospital (MTRH) in Kenya, the second largest national hospital, undertaken as part of two case-control studies to investigate risk factors for maternal and neonatal mortality.[16, 17] Data were obtained from the medical record by trained abstractors using a standard audit form. Records of women and neonates were selected from the patient registry for admissions from 2004-2011. The admission register provided information used to obtain the patient medical records. The registers contained admission and discharge summaries, medical history, progress notes, laboratory reports, partographs and any other relevant forms depending on the condition of the patient.

Cases for the maternal review were mothers aged 15-49 who were pregnant and died because of complications during pregnancy, while controls were alive women who

delivered and did not die prior to and following the death case. For the neonatal study, cases were those neonates who were born dead (fetal deaths) or died within seven days of birth at MTRH, while controls were those neonates who were still alive after seven days and born on the same day preceding and following the case. Cases for both samples were selected sequentially from the most recent record until the desired sample size was achieved.

Patients' medical records were the primary source of information for the independent variables that were based on a theoretical framework adapted from McCarthy and Maine[18] and Mosley and Chen.[19] The modified framework categorised risk factors for maternal and neonatal mortality into individual and socioeconomic factors (mother's age, education (mother/spouse), occupation (mother/spouse) and source of funding for the hospital visit; mothers' health history including drug-use, smoking, alcohol use, contraceptive use and previous abortion). Risk factors were also categorized as distal determinants including: maternal admission factors (temperature (degrees Celsius/^{o}C), pulse (beats per minute/bpm), blood pressure (millimetres of Mercury/mm Hg), respiration, haemoglobin level (grams per decilitre (g/dL)), labour stage, pregnancy stage, maternal condition), neonatal characteristics (gestational age, birth weight, Apgar score at five minutes, sex, period of neonatal death), and health system factors (number of antenatal visits, booking status, qualification of birth attendant). Discharge summaries and antenatal care (ANC) cards provided additional information where these were available.

STATA software was used to describe the variables and the amount of missing data. Tables were generated for the number and percentage of observations with missing

data for each variable for each of the two samples (maternal and neonatal). Bar charts were produced to show the distribution of observations with missing data among cases and controls for each of the study variables. In order to investigate whether there was "clustering" of missing data within observations i.e. whether there were some observations with missing data for multiple variables, a count of the total number of variables with missing data was obtained for each observation. Bar charts were then generated to show the distribution for the number of variables with missing data within observations.

Logistic regression was undertaken separately, for the maternal and neonatal samples, to examine factors associated with missingness for variables with missing data for 20% or more observations for either cases or controls. For each of these "highly missing" variables, a new "outcome" was created and coded as "one" if the value was missing or "zero" if the value was observed. Backward stepwise logistic regression was then undertaken, with all other variables included in the initial model, and variables then excluded if they had a p value of > 0.1 on the likelihood ratio test. The case/control variable was also included, irrespective of its statistical significance. In order to retain all variables in the analysis, the missing values for independent variables were recoded to a "missing" category. A 5% significance level was used.

Sample size was based on the requirements for the intended case-control studies designed to assess risk factors for maternal and neonatal mortality. For the maternal sample there were 150 cases and 300 controls, while the neonatal sample included 200 cases and 400 controls. These numbers would provide 80% power, with a 5%

significance level, to detect differences in characteristics of those with and without missing data of 17% for the maternal sample and 15% for the neonatal sample.

The University of Newcastle in Australia Human Research Ethics Committee (HREC) and the Institutional Research and Ethics Committee (IREC) at Moi University gave ethical approval for this study.

7.4 Results

In total we reviewed 1050 records (n=450 for the maternal sample and n=600 for the neonatal sample) for admissions at MTRH during the period 2004-2011.

Table 7.1 shows overall distributions of missing values for the maternal and neonatal samples. For the maternal sample, the proportion of observations with missing data ranged from zero to 25% across variables. The variables missing the most data were mother's haemoglobin (25%), baby's weight at birth (23%), mother's temperature (22%), labour stage (15%), baby's sex (14%) and baby's Apgar score at 5 minutes (13%).

The range of missing data was one percent to 20% in the neonatal sample. The variables missing the most data were the number of antenatal visits (20%), labour stage, maternal pulse, maternal respiration and gestational age - each 13%, baby's Apgar score (12%) and maternal temperature (11%).

Table 7-1 Distribution of missing data for maternal sample and neonatal sample

Observations with missing data	Maternal sample n=450		Neonatal sample n=600	
Variable	n	%	n	%
Individual and socio-economic factors				
Mother's age	0	0%	8	1%
Mother's education	24	5%	3	1%
Spouse's education	35	8%	55	9%
Mother's occupation	2	0.4%	10	2%
Spouse's occupation	7	2%	20	3%
Source of funding	1	0.2%	8	1%
Mother's health history				
Drug use	7	2%	NA	NA
Smoking	7	2%	NA	NA
Alcohol	7	2%	NA	NA
Contraceptive use	6	1%	NA	NA
Previous abortion	1	0.2%	NA	NA
Maternal admission factors				
Systolic Blood Pressure (mm Hg)	15	3%	NA	NA
Diastolic Blood Pressure (mm Hg)	16	4%	NA	NA
Temperature (ºC)	100	22%	66	11%
Pulse (bpm)	19	4%	75	13%
Respiration	30	7%	77	13%
Haemoglobin (g/dL)	114	25%	NA	NA
Pregnancy Stage	6	1%	23	4%
Labour stage	69	15%	77	13%
Maternal outcome	NA	NA	10	2%
Neonatal characteristics				
Gestational age	44	10%	76	13%
Weight	103	23%	20	3%
Apgar score at 5 minutes	58	13%	74	12%
Sex	63	14%	12	2%
Period of neonatal death	19	4%	0	0%
Health system factors				
Number of antenatal visits	13	3%	122	20%
Qualification of birth attendant	24	6%	30	5%
Booking status	0	0%	32	5%

NA: not applicable as data were not obtained for this variable

The distribution of proportion of missing values among cases and controls in the maternal sample is shown in Figure 7.1. In general, cases had more missing data than controls. In particular, over 20% of cases had missing information on mother's labour stage, gestational age, baby's weight, baby's Apgar score, and baby's sex; while among the controls, over 20% of observations had missing data for mother's temperature and mother's haemoglobin.

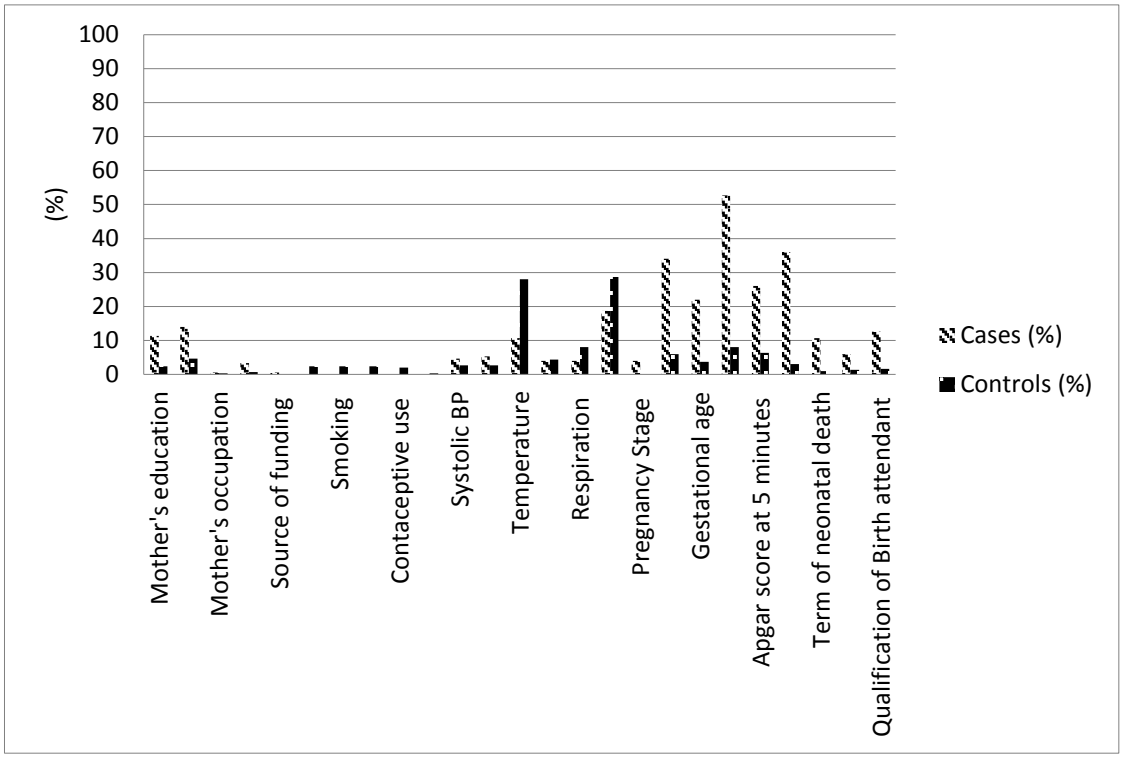

Figure 7-1 Percentage of missing values for each variable for maternal cases and control study: by case/control status

The distribution of missing values among cases and controls for the neonatal sample is shown in Figure 7.2. The variables missing data for over 20% of observations among cases were maternal vital signs (pulse, respiration and temperature), gestational age, baby's Apgar score and mother's number of antenatal visits. There were no variables that had missing data for more than 20% of observations in the control group for the neonatal sample.

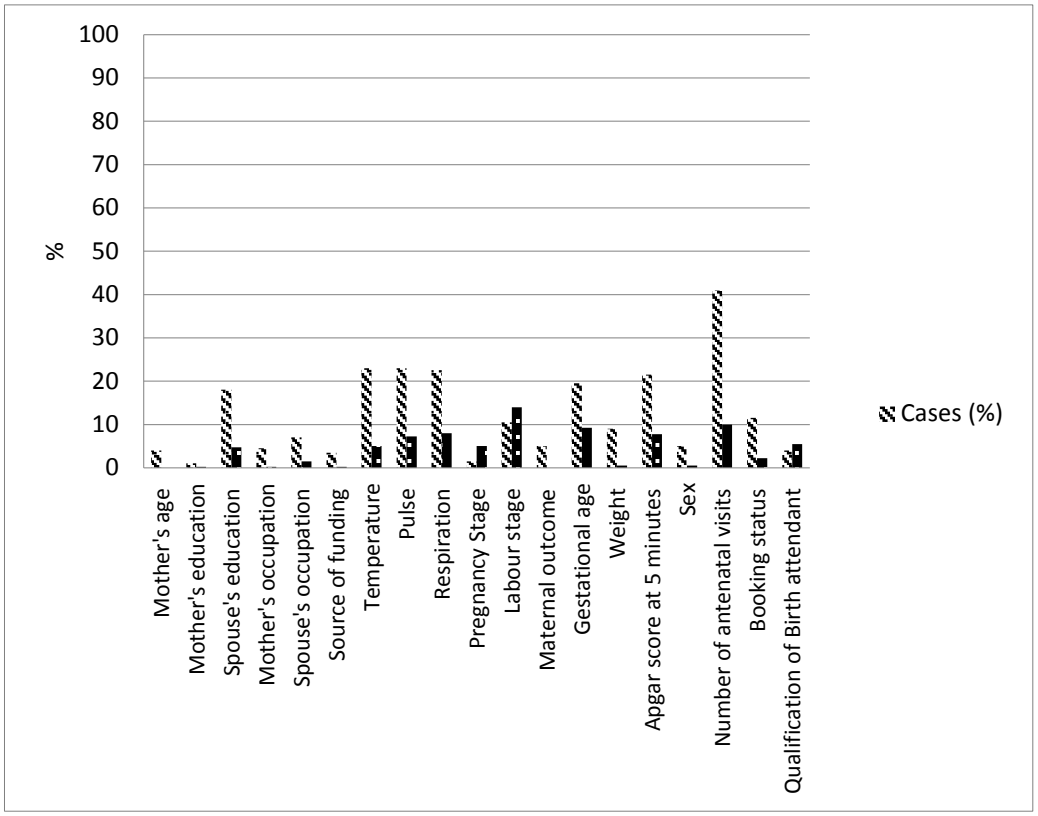

Figure 7-2 Percentage of missing values for each variable for neonatal cases and control study: by case/control status

Figure 7.3 and Figure 7.4 below show the distributions for the number of variables with missing data within observations. The distributions are skewed to the right for both samples with some extreme values. For the maternal sample, 35% of observations had no missing values and the maximum number of missing values was 12. Only 20% of maternal cases had no missing data on any variables. Maternal controls were more likely to have complete data (43%), and had a smaller total number of variables with missing data; the maximum number of variables missing for any observation for controls was nine.

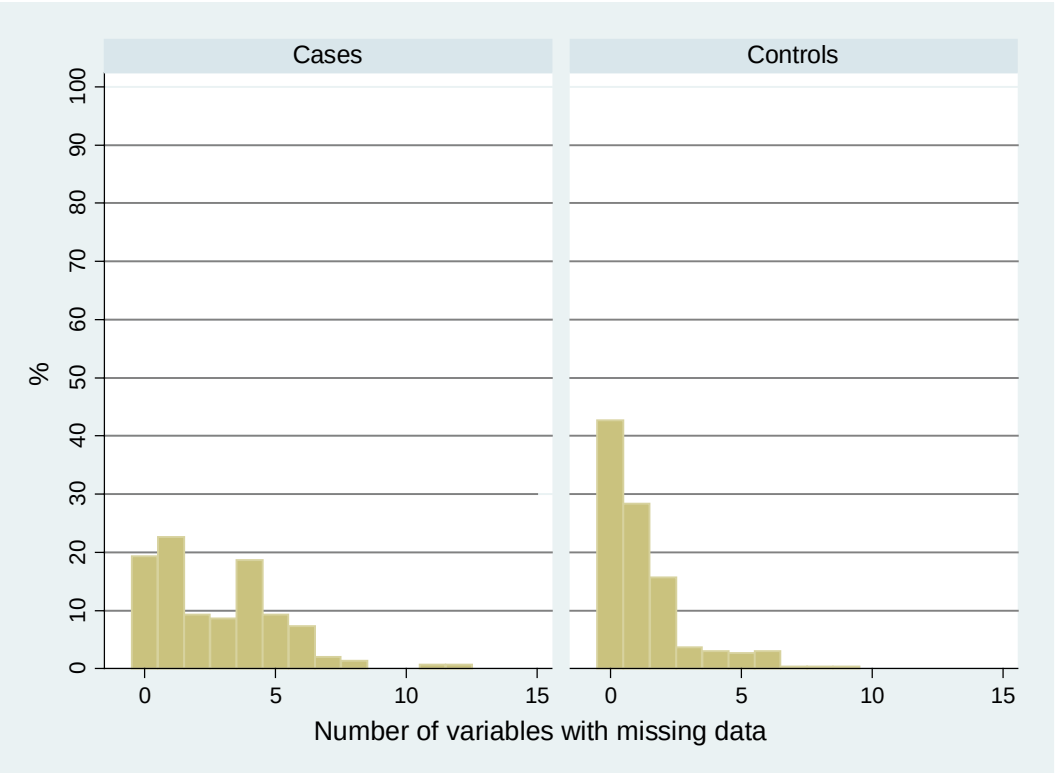

Figure 7-3 Distribution of number of variables with missing data within observations in the maternal sample

For the neonatal sample, 47% of observations had complete data and the maximum number of missing values in an observation was 11. Figure 7.4 shows that the missing data for the cases and controls for the neonatal sample have similar distribution to the maternal sample. However, only 16% of neonatal cases had no missing data on any variables, compared to 62% of controls. The control group also had a smaller total number of variables with missing data with a maximum number of eight variables missing for any observation for controls.

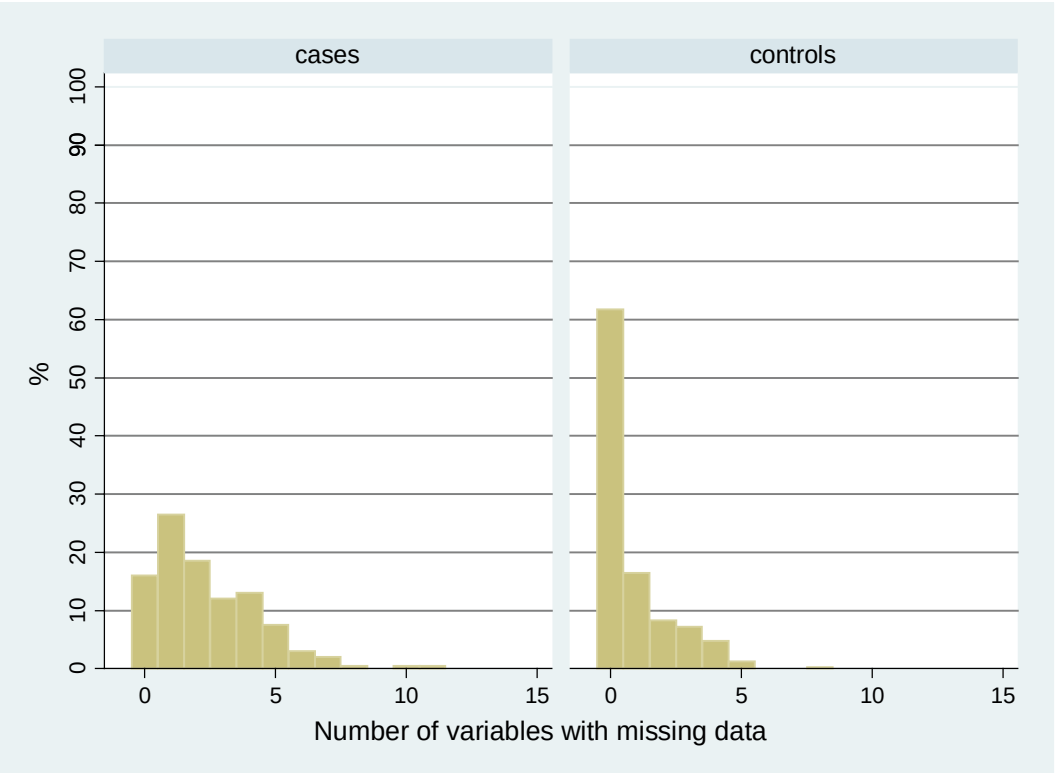

Figure 7-4 Distribution of number of variables with missing data within observations in the neonatal sample

Table 7.2 shows logistic regression results for factors associated with missing data in the maternal sample at MTRH. For example, data missing on mother's haemoglobin was higher among mothers in the control group compared to cases (OR 1.9, 95% CI 1.1-1.3, p=0.0277) and for those with missing data for mother's temperature compared to those with temperature <37.5°C (OR 2.0, 95% CI 1.2-3.3, p=0.0089). Mothers who were controls had higher odds of missing data on mother's temperature, and lower odds of missing data on baby's sex, gestational age, and labour stage. The odds of missing data on mother's temperature was lower for those aged 25-34, and higher for those aged 35-45 (compared to those aged 15-24 years), and lower for those with a higher pulse rate, compared to those with pulse <110bpm. There were lower odds of missing data on baby's weight in the maternal data set if the baby's Apgar score was above seven at five minutes, compared to those with a lower score. In turn, data on baby's Apgar

score had lower odds of being missing if mothers were admitted in the active stage of labour, compared to if they were in a latent stage. The odds of missing data on baby's sex was lower for mothers admitted in the second stage of labour, while the odds of missing data on labour stage was higher if gestational age was greater than 42 weeks, and lower if the mother had more than four ante-natal visits. Otherwise, missing data on one variable tended to be associated with missing data on another.

Table 7-2 Factors associated with missingness in the maternal records (n=450)

Variable with >= 20% of missing values for cases of controls	Independent variable	Missing value n(%)	Odds ratio (95%) CI	Likelihood ratio test (x^2), p value
Mother's haemoglobin				
	Case/control status			4.85(1), 0.03
	Case	28(19%)	1	
	Control	86(29%)	1.9(1.1-1.3)	
	Mother's temperature			9.45(2), 0.01
	<37.5ºC	71(23%)	1	
	>=37.5ºC	5(14%)	0.6 (0.2-1.6)	
	Missing	38(38%)	2.0 (1.2-3.3)	
	Number of antenatal visits			7.38(3), 0.07
	None	18(25%)	1	
	1-3	76(28%)	0.7(0.4-1.4)	
	Above 4	17(18%)	0.4(0.1-0.8)	
	Missing	3(23%)	0.7(0.2-2.8)	
Mother's temperature				
	Case/control status			14.08(1), 0.0002
	Case	16(11%)	1	
	Control	84(28%)	4.0 (1.8-8.9)	
	Maternal age			15.88(2), 0.0004
	15-24 years	45(25%)	1	
	25-34 years	37(17%)	0.5 (0.3-0.9)	
	35-45 years	18(33%)	2.6 (1.2-5.8)	
	Mother's Pulse			5.87(2), 0.053
	<110 bpm	82(21%)	1	
	>=110bpm	3(6.7%)	0.4 (0.1-0.6)	
	Missing	15(79%)	4.0 (0.8-19.1)	
	Mother's systolic blood pressure			20.16(2), <0.0001
	<140 mm HG	68(18%)	1	
	>=140 mm HG	20(37%)	4.3(2.0-9.2)	
	Missing	12(80%)	12.7(2.0-78.7)	
	Baby's sex			10.27(2), 0.006
	Male	59(30%)	1	
	Female	37(19%)	0.6 (0.4-1.0)	
	Missing	4(6.4%)	0.2 (0.0-0.7)	
	Mother's respiration			6.36(2), 0.04

Variable with >= 20% of missing values for cases of controls	Independent variable	Missing value n(%)	Odds ratio (95%) CI	Likelihood ratio test (x^2), p value
	<20	17(21%)	1	
	>20	63(19%)	0.7(0.4-1.4)	
	Missing	20(67%)	2.9(0.9-9.4)	
Baby's weight				
	Case/control status			0.61(1), 0.44
	Case	79(53%)	1	
	Control	24(8.0%)	0.7(0.3-1.7)	
	Labour stage			9.76(3), 0.02
	Latent	25(23%)	1	
	Active	20(9.2%)	1.1(0.4-2.9)	
	Second stage	9(17%)	1.1(0.4-3.5)	
	Missing	49(71%)	4.8(1.6-14.6)	
	Baby's Apgar score			52.99(2), <0.0001
	0-6 at 5 mins	48(50%)	1	
	>7 at 5 mins	7(2.4%)	0.0 (0.0-0.1)	
	Missing	48(83%)	1.5 (0.5-4.6)	
	Baby's sex			32.93(2), <0.0001
	Male	24(12%)	1	
	Female	20(10%)	0.7 (0.3-1.4)	
	Missing	59(94%)	15.6 (4.2-57.9)	
Baby's Apgar score				
	Case/control status			1.99(1), 0.16
	Case	39(26%)	1	
	Control	19(6.3%)	1.9(0.8-5.1)	
	Labour stage			18.95(3), 0.0003
	Latent	15(14%)	1	
	Active	5(2.3%)	0.2 (0.1-0.8)	
	Second Stage	4(7.4%)	0.9 (0.2-3.2)	
	Missing	34(49%)	2.5 (1.0-6.2)	
	Baby's weight			17.25(1), 0.0002
	<2500 grams	2(3.7%)	1	
	>=2500 grams	8(2.7%)	0.6(0.1-3.2)	
	Missing	48(47%)	6.2(1.2-30.9)	
	Baby's sex			9.50(2), 0.01
	Male	10(5.1%)	1	
	Female	11(5.7%)	1.1 (0.4-2.9)	
	Missing	37(59%)	4.4 (1.5-13.3)	
baby's sex				
	Case/control status			11.84(1), 0.0006
	Case	54(36%)	1	
	Control	9(3.0%)	0.2(0.1-0.5)	
	Labour stage			4.45(1), 0.03
	Latent	18(16%)	1	
	Active	9(4.2%)	0.7(0.2-2.2)	
	Second Stage	2(3.7%)	0.1(0.0-0.8)	
	Missing	34(49%)	1.1(0.4-3.2)	
	Baby's Apgar score			14.73 (2), 0.0006
	0-6 at 5 mins	12(25%)	1	
	>7 at 5 mins	2(0.7%)	0.3(0.0-1.5)	
	Missing	37(64%)	4.3(1.6-11.6)	
	Baby's weight			32.81(2), <0.0001
	<2500 grams	2(3.7%)	1	

Variable with >= 20% of missing values for cases of controls	Independent variable	Missing value n(%)	Odds ratio (95%) CI	Likelihood ratio test (x^2), p value
	>=2500 grams	2(0.7%)	0.5(0.1-4.1)	
	Missing	59(57%)	12.6(2.6-60.6)	
Gestational age				
	Case/control status			9.30(1), 0.002
	Case	33(22%)	1	
	Control	11(4.0%)	0.2(0.0-0.6)	
	Labour stage			8.87(3), 0.03
	Latent	2(1.8%)	1	
	Active	4(1.8%)	1.7(0.3-9.6)	
	Second Stage	3(5.6%)	3.1(0.5-20.2)	
	Missing	12(17%)	6.4(1.3-30.4)	
	Referral			2.71(1), 0.010
	Yes	15(9.8%)	1	
	No	6(2.0%)	0.4(0.2-1.2)	
Labour stage				
	Case/control status			11.20(1), 0.0008
	Case	51(34%)	1	
	Control	18(6.0%)	0.2(0.1-0.5)	
	Gestational age			33..38(3), <0.0001
	<36 weeks	23(18%)	1	
	37-41 weeks	10(4.2%)	0.9(0.3-2.4)	
	>42 weeks	24(39%)	11.5(3.9-33.7)	
	Missing	12(57%)	4.0(1.1-13.3)	
	Number of antenatal visits			6.76(3), 0.08
	None	32(44%)	1	
	1-3	30(11%)	0.5(0.2-1.1)	
	Above 4	3(3.2%)	0.2(0.04-0.8)	
	Missing	4(31%)	0.4(0.1-1.9)	
	Baby's weight			6.32(2), 0.04
	<2500 grams	2(3.7%)	1	
	>=2500 grams	18(6.1%)	3.7(0.6-21.8)	
	Missing	49(48%)	6.7(1.3-35.5)	
	Baby's sex			7.96(2), 0.02
	Male	12(6.2%)	1	
	Female	23(12%)	3.5(1.4-8.9)	
	Missing	34(54%)	2.8(0.9-8.6)	
	Baby's Apgar score			12.88(2), 0.002
	0-6 at 5 mins	20(21%)	1	
	>7 at 5 mins	15(5.1%)	0.8(0.2-2.8)	
	Missing	34(59%)	4.9(1.9-12.8)	

From the results in Table 7.3, case/control status was associated with lower odds of missing data on mother's temperature, baby's Apgar score, gestational age, and number of ante-natal visits. Data on mother's respiration and on mother's pulse had lower odds of being missing from the baby's data set if the baby's Apgar score was

above seven, compared to those with a poorer score. The odds of missing data on the baby's Apgar score was lower if there was a caesarean delivery (compared to spontaneous delivery), and higher if admission was during the puerperium rather than antepartum. For gestational age the odds of missing data was higher if the baby weighed >=2500 grams compared to lower birth weight, and lower if the baby was born by caesarean, or if the mother was not admitted by referral (i.e. an emergency admission). Number of ante-natal visits had lower odds of missing data for caesarean deliveries, and if the baby weighted more than 2500 grams, and higher odds of missing data if the mother was admitted in the puerperium. As for the maternal data set, missing data on one variable was often associated with missing data on another. For example, mothers with missing data on referral status had higher odds of missing data on the number of antenatal visits, compared to women who were recorded as referrals (OR 13.4, 95% CI 4.7-38.5).

Table 7-3 Factors associated with missingness in the neonatal records (n=600)

Variable with >= 20% of missing values for cases of controls	Independent variable	Missing n(%)	Odds ratio (95%) CI	Likelihood ratio test (x^2), p value
Mother's respiration				
	Case/control status			1.08(1), 0.30
	Case	45(23%)	1	
	Control	32(8.0%)	0.7(0.4-1.3)	
	Mother's age			6.71(3), 0.08
	15-24 years	36(12%)	1	
	25-34 years	23(10%)	0.8(0.5-1.5)	
	35-45 years	15(25%)	2.1(1.0-4.4)	
	Missing	3(38%)	2.7(0.6-13.3)	
	Apgar score			12.44(2), 0.002
	0-6 at 5 mins	28(29%)	1	
	>7 at 5 mins	32(7.5%)	0.3(0.2-0.6)	
	Missing	17(23%)	0.8(0.4-1.7)	
	Baby's weight			4.85(2), 0.09
	<2500 grams	40(16%)	1	
	>=2500 grams	28(8.5%)	0.7(0.4-1.3)	
	Missing	9(45%)	2.5(0.9-6.7	
Mother's temperature				

Variable with >= 20% of missing values for cases of controls	Independent variable	Missing n(%)	Odds ratio (95%) CI	Likelihood ratio test (x^2), p value
	Case/control status			9.90(1), 0.002
	Case	46(23%)	1	
	Control	40(5.0%)	0.3(0.2-0.7)	
	Baby's Apgar score			
	0-6 at 5 mins	27(28%)	1	5.56(2), 0.06
	>7 at 5 mins	28(6.5%)	0.4(0.2-0.9)	
	Missing	11(15%)	0.6(0.3-1.3)	
	Baby's weight			7.09(2), 0.03
	<2500 grams	38(15%)	1	
	>=2500 grams	19(5.7%)	0.6(0.3-1.1)	
	Missing	9(45%)	2.7(1.0-7.1)	
Mother's pulse				
	Case/control status			3.45(1), 0.06
	Case	46(23%)	1	
	Control	29(7.3%)	0.5(0.3-1.0)	
	Mother's age			7.99(3), 0.046
	15-24 years	39(13%)	1	
	25-34 years	19(7.9%)	0.6(0.3-1.1)	
	35-45 years	14(23%)	1.7(0.8-3.6)	
	Missing	3(38%)	2.2(0.5-10.5)	
	Baby's Apgar score			7.72(2), 0.02
	0-6 at 5 mins	28(29%)	1	
	>7 at 5 mins	33(7.7%)	0.4(0.2-0.8)	
	Missing	14(19%)	0.6(0.3-1.4)	
	Baby's weight			4.69(2), 0.10
	<2500 grams	39(16%)	1	
	>=2500 grams	27(8.2%)	0.4(0.2-0.8)	
	Missing	9(45%)	0.6(0.3-1.4)	
Baby's Apgar score at five minutes				
	Case/control status			23.08(1), <0.0001
	Case	43(22%)	1	
	Control	31(7.8%)	0.2(0.1-0.4)	
	Mode of delivery			18.02(2), 0.0001
	Spontaneous Vertex Delivery	65(16%)	1	
	Assisted Delivery	4(18%)	1.3(0.4-4.5)	
	Caesarean Delivery	5(2.7%)	0.2(0.1-0.5)	
	Pregnancy stage on admission			40.12(3), <0.0001
	Antepartum	13(14%)	1	
	Intrapartum	34(7.9%)	1.4(0.7-3.0)	
	Puerperium	22(42%)	10.6(4.1-27.2)	
	Missing	5(22%)	10.0(2.6-38.8)	
	Baby's sex			4.73(2), 0.10
	Male	34(11%)	1	
	Female	35(13%)	1.3(0.7-2.2)	
	Missing	5(42%)	4.4(1.2-16.5)	

Variable with >= 20% of missing values for cases of controls	Independent variable	Missing n(%)	Odds ratio (95%) CI	Likelihood ratio test (x^2), p value
Gestational age				
	Case/control status			8.91(1), 0.003
	Case	39(20%)	1	
	Control	37(9.3%)	0.4(0.2-0.7)	
	Baby's weight			10.89(2), 0.004
	<2500 grams	25(10%)	1	
	>=2500 grams	46(14%)	2.7(1.5-5.1)	
	Missing	5(25%)	2.0(0.6-6.2)	
	Baby's Apgar score at 5 mins			10.25(2), 0.006
	0-6	15(15%)	1	
	Above 7	39(9.1%)	0.8(0.4-1.8)	
	Missing	22(30%)	0.5(1.1-5.6)	
	Mode of delivery			6.67(2), 0.04
	Spontaneous Vertex Delivery	62(16%)	1	
	Assisted Delivery	1(4.6%)	0.3(0.0-2.2)	
	Caesarean Delivery	13(7.1%)	0.5(0.2-0.9)	
	Was the mother a referral			8.67(2), 0.01
	Yes	25(21%)	1	
	No	46(10%)	0.4(0.2-0.7)	
	Missing	5(16%)	0.5(0.2-1.6)	
Number of antenatal visits				
	Case/control status			39.18(1), <0.0001
	Case	82(41%)	1	
	Control	40(10%)	0.2(0.1-0.3)	
	Mode of delivery			9.08(2), 0.02
	Spontaneous Vertex Delivery	95(24%)	1	
	Assisted Delivery	6(27%)	1.2(0.4-3.6)	
	Caesarean Delivery	21(11%)	0.4(0.2-0.8)	
	Pregnancy stage on admission			12.56(3), 0.006
	Antepartum	30(32%)	1	
	Intrapartum	68(16%)	1.4(0.7-2.7)	
	Puerperium	19(37%)	4.3(1.7-10.4)	
	Missing	5(22%)	3.8(1.0-14.5)	
	Baby's weight			8.18(2), 0.02
	<2500 grams	79(32%)	1	
	>=2500 grams	37(11%)	0.5(0.3-0.9)	
	Missing	6(30%)	0.4(0.1-1.2)	
	Was the mother a referral			35.55(2), <0.0001
	Yes	22(19%)	1	
	No	75(17%)	1.0(0.6-1.9)	
	Missing	25(78%)	13.4(4.7-38.5)	

7.5 Discussion

These series of data extracted from hospital records demonstrate relatively high levels of missing data. In the maternal sample, only 35% of observations had no missing values, and some observations were missing data for 12 variables. Only 47% of observations in the neonatal sample had no missing values, and some observations were missing data for 11 variables. The most commonly missing items were mother's temperature, mother's haemoglobin and baby's birth weight for the maternal samples, and antenatal visits for the neonatal sample.

Importantly, there were differential proportions of missing data for the cases and controls. The maternal controls were more likely to be missing information on mother's labour stage, gestational age, baby's weight, sex and Apgar score (missing for over 20% of cases, and for only one to six percent of controls). These differences create potential bias between cases and controls. There were also associations between missing data on one variable and missing data on others, which may reflect when the baby's or mother's condition was severe, for example labour stage, mode of delivery, maternal vital signs (temperature, pulse and respiration) and neonatal characteristics (sex, weight and Apgar score).

Neonatal cases had over 20% data missing on maternal vital signs, gestational age and number of antenatal visits. Case/control status remained significantly associated with missingness in the multivariable models for many of these variables. This bias in ascertainment of exposure may have an effect on the estimate of association between exposure and outcome in the case/control study.[20] Such missing data was a noted limitation in our case-control studies.[16, 17]

In the maternal sample, the case status was significantly associated with lower odds of missing data for maternal vital signs, and higher odds of missing data for labour stage and gestational age. Where there were higher odds of missing for maternal cases, this effect may be because cases involved more complications or adverse outcomes than controls, and health care providers were focused more on managing the patient rather than obtaining information for the hospital record.[13, 21] For example, in this study, mothers with systolic blood pressure >140 mm Hg, or those missing this information had higher odds of missing data for mother's temperature, indicating that mothers with more critical health care needs were more likely to miss this information from their record. For other details that needed to be provided by the mother in the patient history, the maternal cases may have been less able than controls to provide information due to their illness and because they were admitted in shock or other extreme condition.[21] Additionally, mothers in critical condition may have needed attention from healthcare providers who focused more on managing the emergency condition rather than documenting the patients' charts.

An Apgar score of above seven at five minutes was associated with lower odds of having missing data on baby's birth weight for the maternal sample. An Apgar score of above seven has been reported as an indication that the infant is in good physiologic state hence the staff may have not been under pressure and had more opportunity to record the information.[22] This result was potentially because the babies born preterm and with low Apgar score likely needed resuscitation hence the urgency to save their lives may have meant that staff were not able to give priority to recording information on the baby.[12] There was a higher odds of missing data on labour stage in the maternal

sample if baby's weight and Apgar score were missing in the medical record. These findings are similar to another study where, for mothers admitted during second stage of labour, limited information was recorded about the mothers and their neonates.[12]

Missing data on booking status was significantly associated with missing information on number of antenatal visits. This result was possibly because those who were not booked were referred to MTRH and some may not have come to the hospital with all of the necessary documentation. Additionally, other studies have reported that most referrals represent emergency cases that need immediate attention, hence there may have been potential loss of information.[2, 23, 24]

In the neonatal sample, the odds of missing data on gestational age was lower for women who were not referred and also for controls, while it was higher for babies born with birth weight above 2500 grams. This finding is in agreement with another study that found recovery of data on gestational age and birth weight from medical records to be low.[25]

Mothers who gave birth by caesarean delivery had lower odds of missing data on baby's Apgar score, gestational age, and number of antenatal visits in the neonatal sample. Most caesarean deliveries are an emergency procedure conducted following complications related to pregnancy, rather than as an elective procedure.[26, 27] In this situation, information on gestational age may have been necessary to provide directions for the attending doctors to save the life of the baby. In addition, the attendance by more senior health personnel in the operating theatre may have led to more complete records as has been reported in a study of medical records in Iran.[23]

In addition to maternal and neonatal issues, health system factors may have also contributed to missing data in some of the medical records. Decentralisation of records to storage and management by individual departments creates issues of loss of information and makes record linkage difficult, which could explain why data on mothers was missing in the neonatal records and vice versa.[28]

Some information such as mothers age may have been missing on the mother and neonate potentially because of failure of health workers to recognize the importance of the information they were collecting, medical clerks lacking formal training on the collection of data, and the lack of standard checklists to ease obtaining information from patients especially when there are large patient numbers.[23] Another possible explanation for the extent of missing data would be a shortage of staff and high workload, as has been cited in other studies on health record data.[23, 29, 30]

The electronic medical record (EMR) provides better accuracy, is time saving, more economical and enables speedier and easier access to information than paper based records.[31] However, the disadvantages of EMRs are high cost, extensive training requirements, system breakdowns, software glitches, the potential for hacking, viruses, lack of funding from the government, resistance to use electronic patient registers and poor infrastructure.[15]

Our study was prone to referral filter bias since the hospital is a tertiary level facility that receives mostly difficult cases with complications that were referrals from peripheral facilities. The trained data collectors could only obtain what was available

and documented and there could have been a lack of information from the healthcare providers who completed the records. There was potential bias especially on interpretation of information that may have been subject to the documenter's decision. These limitations relate to the investigation of missing data in hospital records since they contribute substantially to the number of observations with missing data.

This study has provided important information on maternal and neonatal records at a tertiary hospital in Kenya. This study may be the first step in improving monitoring of maternal and neonatal characteristics through identifying gaps in record-keeping. The outcomes of this study could be used for education in MTRH about the type of data that is usually missing and for whom it is usually missing, and that in the future staff need to pay attention to completion of records. This information can assist in improving the quality of data recorded in hospital medical records to ensure professional and legal accountability at MTRH, and the availability of continuous, accurate and timely data to help monitor progress towards the MDGs. By identifying areas and circumstances in which there is a risk of missing data, the results could inform the development of more accurate record keeping systems.

7.6 Conclusion

This study has assessed the completeness of maternity data at MTRH. There were high proportions of missing data for some maternal vital signs and neonatal characteristics in the maternal data. The maternal controls and neonatal cases had the most missing data on maternal vital signs. The maternal cases were also missing information on labour stage, gestational age and neonatal characteristics (Apgar score, sex and weight).

Factors associated with missing data in the maternal sample included: maternal case/control status, mother's vital signs on admission (systolic blood pressure (BP), respiration and temperature), maternal age, gestational age, labour stage, and neonatal characteristics. For the neonatal sample, baby's case/control status, neonatal characteristics (Apgar score and baby's weight), mode of delivery, pregnancy stage and booking status were significantly associated with missing data.

There is a need to develop standard checklists for obtaining data from patients that is complete, accurate, timely, and consistent to enable health planners obtain sound information that will aid in monitoring progress for maternal and neonatal health outcomes. Further recommendations are that observational studies should be undertaken in hospital settings to assess procedures for, and factors associated with, documentation of patients' charts in developing countries. Implementation of EMRs should be explored in low-income settings to see whether these would improve the quality of record-keeping.

Abbreviations

MDGs: Millennium Development Goals, HIV: Human Immunodeficiency Virus, RAMOS: Reproductive Age Mortality Studies, ANC: Antenatal Care, HREC: Human Research Ethics Committee, IREC: Institute for Research and Ethics Committee, EMR: Electronic Medical Record

Conflict of interest

The authors declare no conflict of interest.

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The next chapter is a conclusion that links a summary of findings from all the four papers, a summary of this study's strengths and limitations, and provides future directions for this research.

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Chapter 8 Conclusion

The aim of this thesis was to describe the incidence of, and investigate risk factors associated with, maternal and neonatal mortality at a major tertiary hospital in Kenya. A retrospective review of maternity records (2004-2011) was conducted at the MTRH. Four main studies are presented here. They are: the incidence and determinants of maternal and neonatal mortality at MTRH (Chapter Four); a case-control study investigating risk factors associated with maternal mortality (Chapter Five); a case-control study investigating risk factors associated with fetal and early neonatal mortality at MTRH (Chapter Six), and an investigation of hospital medical record data completeness and factors associated with missing data at MTRH (Chapter Seven).

Maternal mortality remains high in Kenya and it is important that no woman or child should die during pregnancy or at birth. The purpose of this body of work was to understand the reasons for maternal and neonatal deaths, especially in health facilities, in order to improve management and prevent future mortalities. Issues about confidentiality of information, sensitivity around obtaining information related to maternal or neonatal deaths, and difficulties obtaining information about death would have made a community study difficult to conduct. A retrospective study design was used because a prospective study would have required a long recruitment period to obtain sufficient numbers deaths.

A key finding is that both maternal and neonatal mortality is high at the MTRH. Reasons for this include maternal, neonatal, socio-demographic, clinical and health system factors. In particular, findings highlight the role of maternal education in

decision-making, more frequent antenatal visits for screening and monitoring, skilled attendants present during deliveries, and quality medical record-keeping for monitoring and improving maternal and neonatal health outcomes.

This thesis has provided information that will help stakeholders evaluate the progress that Kenya's second largest hospital has made towards achieving the targets for MDGs Four and Five. These goals aim to reduce the maternal mortality ratio by three quarters and to reduce the under-five mortality rate by two thirds, between 1990 and 2015.[1] Kenyatta National Hospital is Kenya's largest hospital. Studies on maternal and neonatal mortality have been conducted at Kenyatta National Hospital and the results of these studies are included in the literature review. The main reason for choosing the MTRH, rather than Kenyatta National Hospital, was because no other study of this nature had previously been conducted at MTRH.

There was a 47% decline in maternal mortality globally from 440 maternal deaths per 100,000 live births in 1990 to 240 per 100,000 live births in 2010.[2] More specifically in Kenya, the mortality rate in 1990 was 400 per 100,000 live births compared to 360 per 100,000 live births in 2010.[3] The findings of the study on incidence of mortality presented in Chapter Four indicate an overall MMR of 426 per 100,000 live births [95% CI 260-620] for the MTRH for the period 2004-2011.[4] This mortality rate is higher than the rate for all of Kenya in 1990, and substantially higher than the 2010 rate. One major reason for the higher mortality rate in this study could be that high-risk pregnancies are referred and admitted to the MTRH, because of its role as a referral hospital. The mortality rate is therefore expected to be higher for MTRH admissions than among women who give birth in their homes and in peripheral hospitals.

There have been some success stories on the progress towards achieving MDGs Four and Five in African countries, for instance in Malawi, Niger, Liberia and Sierra Leone. Reports indicate that these countries have had a decrease in maternal and early neonatal mortality rates. Reasons that have been cited for the progress include the fact that these countries have tailored programs for their maternal health services.[2] Kenya was listed as one of the countries which had made insufficient progress towards achieving the targets for MDGs Four and Five.[2]

Reasons for the high maternal mortality rates in MTRH could be attributed to the risk factors identified from the case-control study presented in Chapter Five. One risk factor identified in the maternal case-control study was birth attendance. Cases had higher odds of doctors versus nurse/midwife attending at birth (OR 4.6, 95% CI 2.1-10.1, p=0.0001), primarily because doctors attended more high-risk patients who were mostly referrals. In the maternal case-control study, the majority (>50%) of referral were among cases relative to controls, possibly because referring hospitals are less equipped to handle complications.[4]

There was low ANC attendance by women in MTRH. Despite a high antenatal care coverage of 92% according to the 2008/09 Kenya demographic and health survey, women still do not attend the recommended four visits, potentially because of ignorance, poverty, and poor decision-making.[5] In the maternal mortality case-control study, the odds of no antenatal visits among cases was four times that of controls (OR 4.1; 95% CI 1.6-10.4). This makes it difficult for mothers and their babies to be screened for conditions that need to be monitored and managed prior to delivery, as reported in the maternal and neonatal case-control studies in Chapters Five and Six.[6, 7] Appropriate

attendance for antenatal care is particularly important given the observed relationship between maternal mortality and underlying medical conditions (OR 3.9; 95% CI 1.7-9.2), co-morbidities (OR 9.0; 95% CI 4.2-19.3), eclampsia (OR 10.9; 95% CI 3.7-31.9), and tachycardia (OR 10.7; 95% CI 2.7-43.4).[6]

A major contributor to maternal and child mortality is poverty that makes it difficult for the mother to have adequate nutrition during pregnancy. Even though nutrition was not considered as a risk factor for mortality in this study, it was identified as risk factor for stillbirths in Chapter Six. The lack of adequate nutrition makes the mother prone to infections that may put her and her baby at risk of prematurity. Congenital malformations that mostly result from malnutrition contribute to neonatal mortality. See Chapter Six.[7] Poverty is heightened by lack of education which was identified as a significant risk factor for maternal mortality. As shown in Chapter Five, cases had three times the odds of having no education versus secondary education compared with controls(OR 3.3; 95% CI 1.1-10.4).[4] Education plays an important role in informed decision-making, pregnancy management and identifying danger signs early in order to seek care at hospitals during delivery. The majority of women are not empowered. Their lack of knowledge about management of pregnancy, and what to do when complications arise, puts them at risk of losing their lives and that of their neonates.

Half of the women in this study were under the age of 24 years, and even though age was not a significant risk factor for maternal and early neonatal mortality, early childbearing is still an issue that contributes to health risks among mothers and their newborns.[4] Having too many pregnancies has been cited as one of the reasons for slow progress in meeting the MDG target; of notable importance was the fact that about 50%

of mothers in this study were multigravida, with the highest number of deliveries by a single mother being 13.[2, 4]

There has been a global reduction in under five mortality from 12 million deaths in 1990 to about eight million in 2010, representing about a 35% decrease.[2] However, this decrease represents under-five mortality rate rather than fetal or early neonatal death rate (less than seven days after birth). Reports indicate that despite a two percent decline in neonatal mortality rate (death within the first 28 days) the proportion of these deaths among the under-five year age group rose from 37% to about 40% between 1990-2010.[2]

The overall early neonatal mortality rate at MTRH between 2004-2011 was 68 per 1000 live births [95% CI 59-72] compared with the overall mortality rate in Kenya which was 27 per 1000 live births in 2011 according to the World Bank.[4, 8] The reason for the improved under five mortality rates in Africa could be due to the huge focus on integrated interventions that improve survival of the child beyond the neonatal period such as immunization, nutrition.[2] One reason for the high neonatal mortality rate at MTRH may be because it is a tertiary hospital and therefore admits high-risk cases.

Some of the reasons for lack of progress in neonatal mortality in MTRH could be due to potential risk factors identified in the neonatal case-control study in Chapter Six. They include: low antenatal attendance by the mother (OR: 4.5; 95% CI: 1.2-16.7) relative to more than four visits, and the presence of maternal complications including PROM (OR 4.1; 95% CI 1.4-12.1), haemorrhage (OR 4.8; 95% CI 1.1-29.1) and dystocia (OR 3.6; 95% 1.2-10.9). Neonatal characteristics that resulted in higher odds of death included

neonates born with congenital anomalies (OR 6.3; 95% CI 1.2-31.6), low gestational age below 37 weeks (OR 7.0; 95% CI 2.4-20.4) or gestational age above 42 weeks (OR 16.2; 95% CI 2.8-92.3) and low Apgar score of below six at five minutes (OR 26.4; 95% CI 6.1-113.8). Contrary to the maternal case-control study, doctor attendance at birth was protective for neonates in the neonatal study (OR 0.2; 95% CI 0.1-0.6).

It is important to note that education for the mother on issues such as adequate nutrition and appropriate antenatal care, are important for ensuring that she can make the right decisions that impact on her and her baby during pregnancy. There are also opportunities for screening during the antenatal period to ensure that the mother and baby are at less risk of complications during pregnancy.

Due to the high mortality rates and lack of progress to MDGs Four and Five, the Kenyan government recently offered free maternity services to women in government hospitals (including MTRH).[9] The findings from this research contributed to deliberations undertaken during the development of the policy on free maternity services in Kenya. See Appendix Four. The program began in June 2013 with the aim of helping women access maternal care and reduce maternal deaths; however the effects of this initiative are yet to be seen.[9]

There are two key factors which may impact on the potential of free maternity to reduce maternal and early neonatal mortality. The first issue is low doctor to patient ratio (1:5000), which affects the performance of health personnel in providing quality care especially to high-risk cases. Additionally, this doctor to patient ratio may lead to issues of poor documentation because health providers have a lot of patients to

manage and may not have enough time to devote to appropriate record-keeping as noted in Chapter Eight.[10] Over the past few years, there has been an increase in annual number of deliveries from about 4000 in 2004 to 8000 in 2011 as presented in Chapter Four.[4] The second factor, which might reduce the effect of free maternity services, is the lack of sufficient funding to fully equip hospitals to manage the high patient load. Recent reports show that only 6.5% of the Kenyan government budget is allocated to health, which is less than the recommended 15% minimum.[11]

The role of record-keeping in ensuring availability of information that is sound, reliable and accurate was also a major finding in this retrospective study. Some of the most commonly missing items were: mother's temperature (22%), mother's haemoglobin (25%) and baby's birth weight (23%) for the maternal samples, and antenatal visits (20%) for the neonatal sample.[10] Factors such as case/control status, maternal age, vital signs on admission, labour stage, gestational age, and neonatal characteristics were associated with missing data in the maternal sample. In the neonatal sample, neonatal characteristics, mode of delivery, pregnancy stage, booking status and case/control status were associated with missing information.[10] There is a need to educate hospital workers about the importance of information that they record. It is also important to implement checklists and structured forms to ensure that all necessary and relevant information on patients is captured during their hospital stay.

This thesis has provided information that will assist in designing prospective and intervention studies that are time consuming and costly to conduct. The maternal and neonatal mortality studies have also highlighted areas that need to be focused on in order to avert maternal and neonatal mortality. They include the need for skilled

attendants at birth, maternal education, and antenatal and post-natal care. Some of the main priorities outlined in MDGs Four and Five are to reduce the maternal mortality ratio, reduce the proportion of neonatal deaths during the first month, increase access to ANC, and increase proportion of births by skilled personnel.[1] There are some aspects of care that need particular attention in order to improve the provision of best care to mothers and babies during childbirth. These aspects include the areas stimulated by the MDG targets as well as accurate documentation and record-keeping to assist in monitoring outcomes.

This research has been published in international journals and feedback has been provided to the hospital. These findings have provided information that will potentially help design programs and protocols that will contribute to a reduction number of maternal and child deaths especially in these major hospitals in Kenya. More specifically, the study contributed to the development of protocols covering the management of major causes of maternal mortality, training of health personnel on emergency obstetric and neonatal care, regular purchase of basic equipment for newborn management, and supportive supervision and feedback to referring hospitals. The results of these studies have informed deliberations towards the development and implementation of the Free Maternity Program in Kenya (see Appendix Four).

The studies presented in this thesis each have methodological limitations that have been discussed in previous chapters. They include difficulty in estimating the MMR and NMR due to small numbers in the denominators, and the reliance on data from hospital records which may have led to potential selection bias. For example, only cases and controls that came to the hospital for care were included in the studies. There

was also missing information in the charts due to poor documentation, especially among cases. This limits statistical power and can introduce bias.[10]

Potential initiatives for reducing maternal and neonatal mortality in MTRH include the provision of more education to women on the importance of antenatal care attendance during pregnancy, and creating empowerment programs to provide women with the knowledge and power to make informed decisions, especially during their pregnancy. There is a need to formulate polices and strategies that promote facility-based deliveries as well as increasing access to these facilities by providing incentives, education and information campaigns for mothers and health workers.

Future research into the reception and adoption of maternal and child health programs and initiatives are needed, especially in community settings. This can improve understanding of how to tailor these programs and initiatives to make them more relevant for women and their families. In addition, future research into attendance of ANC and reasons for non-attendance should be explored. There is also a need to understand the role of nutrition and education interventions in determining birth outcomes. Qualitative studies could also help improve our understanding of mortality patterns and risk factors for maternal and neonatal mortality.

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Appendices

Appendix 1: Publications

A1.1 Published paper 1

A1.2 Published paper 2

A 1.3 Published paper 3

A1.4 Statements of contribution from each author

Appendix 2: Study Approvals

A2.1 Ethics approval

A2.2 Letter of approval for the study

A2.3 Advisor approvals

Appendix 3: Study Questionnaire

A3.1 Study questionnaire

Appendix 4: Letter from MTRH

Appendix 1: Publications

A1.1 Published paper 1

REPRODUCTIVE HEALTH

A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya

Faith Yego[1*], Jennifer Stewart Williams[2], Julie Byles[2], Paul Nyongesa[3], Wilson Aruasa[4] and Catherine D'Este[5]

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Background

In developing countries, more than nine million infants die every year before birth and in the first week of life as a result of complications occurring during pregnancy. Many of these deaths are preventable [1]. In 2000 the United Nations (UN) made a declaration to include maternal and child mortality reduction as a target in its Millennium Development Goals (MDGs) [2]. Maternal mortality is high throughout Africa, yet the ratios are particularly high in Kenya, where a woman's lifetime risk of dying is one in 38 compared to one in 2000 in the developed world [1]. The World Health Organization (WHO) reported that Kenya's progress towards improving maternal and neonatal health is presently "insufficient" with little or no progress having been made over the past decade [3].

Of the more than 500,000 women who die each year as a result of complications arising during pregnancy, half live in Sub-Saharan Africa [4]. Yet death is not the only outcome resulting from pregnancy complications. For every woman who dies, at least 30 others are injured and disabled. Globally seven million women are affected

* Correspondence: yegofaith@gmail.com
[1]Department of Health Policy and Management, Moi University, Nandi Road, Eldoret 30100, Kenya
Full list of author information is available at the end of the article

by health problems related to childbearing [5]. Despite the inauguration of the Safe Motherhood Initiative (SMI) in Nairobi in 1987, Kenya has made limited progress towards improving maternal mortality.

Between 1980 and 2010, the national maternal mortality ratio (MMR) was 400–560 per 100,000 live births [1,6,7]. The ratios are higher for the major teaching and referral hospitals where obstetrics complications are concentrated. For example, the MMR in Kenya's largest referral hospital, Kenyatta National Hospital (KNH), was 922 per 100,000 live births in 2004 [8]. In Kilifi District Hospital in Kenya, the MMR was 250 per 100,000 live births between 2008 and 2010 [9]. In nearby Sub-Saharan African countries, MMRs in teaching hospitals are also high. For instance, in Adeoyo Hospital in Nigeria, the MMR was 963 per 100,000 live births between January 2003 and December 2004 [10]. The Neonatal Mortality Rate (NMR) in KNH from January to December of 2000 was 215 per 1000 live births [11]. The NMRs are high in other African countries such as Nigeria, (53 per 1000 live births) and Ethiopia (51 per 1000 live births) [12].

Newborn deaths represent 38% of all deaths among children under five years of age [13]. One in five women in Africa risks losing a newborn baby during her lifetime [14]. Pre-term birth accounts for 29% of neonatal deaths globally and approximately 14% of babies are born with low birth weight [13]. Early neonatal outcomes can be affected by nutrition, lifestyle and socio-economic status of mothers. "The best care in the world cannot save a woman's life if she cannot reach it, cannot afford it, does not know it is there when to seek it, or is not permitted to use it" [15].

The Delay Model by Thaddeus and Maine [16,17] provides a suitable conceptual framework for understanding risk factors associated with maternal mortality at a tertiary referral hospital. The Model identifies three types of delays. They are: delay in the decision to seek care, delay in arrival at a health facility and delay in the provision of adequate care [16]. Some risk factors that have been linked to the delay model are: lack of funding, inaccessibility, poor infrastructure, inadequate staffing, inadequate equipment and supplies, lack of information, cultural issues, social vulnerability, and low socio-economic status [17].

Ensuring the continuum of care throughout pregnancy is an important requirement for the reduction of maternal and early neonatal deaths. There is evidence that a significant number of stillbirths and neonatal deaths could be prevented if all women were adequately nourished and received good quality care during pregnancy, delivery, and the postpartum period [14,18]. The antenatal period helps the health care provider to assess risks and treat conditions that could affect both the mother and baby [19]. It is essential that during delivery, obstetric emergencies are effectively managed to prevent complications which account for up to 58% of stillbirths and early neonatal deaths [20]. Countries such as Thailand, Sierra Leonne, Libera, Pakistan, Sudan, Bosnia, Uganda, Tanzania, and Northern Kenya, have established intervention projects to improve the availability of emergency obstetric care (EmOC) [21]. These projects include the use of signal funtions to assess whether their health facilties adhere to international standard operating procedures for the management of emergencies during pregnancy.

In the post-partum period, the provision of family planning advice after delivery is of vital importance, especially in settings where the birth rate is high and multiparous women are at repeated risk of pregnancy complications and adverse birth outcomes [19].

Health care infrastructure in Kenya includes two national tertiary teaching and referral hospitals as well as provincial hospitals, district and sub-district hospitals, health centres and dispensaries, or chemists. The private sector provides about one third of outpatient care and 14% of inpatient care. High-risk patients are managed in the tertiary hospitals where clinical resources are more specialized. A number of measures have been introduced to help meet the MDGs in Kenya. For example, Kenya's second largest referral hospital, the Moi Teaching and Referral Hospital (MTRH) has initiated 24 hour maternal and perinatal death reviews and monthly maternal mortality reviews for all maternal deaths. Over the past two years the MTRH has also established standard operating procedures for managing both direct and indirect maternal complications in pregnancy. However more work is needed to achieve progress in this area.

While there have been many maternal health studies in Kenya, little has been published specifically on maternal and early neonatal mortality [8,11,22-26]. The aim of this study is to measure the incidence of maternal and neonatal mortality in women who gave birth at MTRH and describe clinical characteristics and circumstances associated with maternal and early neonatal deaths following deliveries at MTRH. As one of only two teaching and referral hospitals in Kenya, the MTRH serves an important role in the country's health system. MTRH is also the largest hospital in the rural western region of Kenya. High maternal and early neonatal mortality at MTRH has local and national implications and therefore requires investigation.

Methods

A retrospective audit of maternal and neonatal records at MTRH between January 2004 and March 2011 was conducted. Detailed information was independently extracted by trained abstractors. The sample included the most recently hospitalized 150 women, aged 15–

49 years, who were classified as maternal deaths, and the most recently hospitalized 200 neonates, who died after delivery or within seven days of delivery. Record numbers were based on the sample size needed for a subsequent case control study of maternal and early neonatal deaths at MTRH. This was obtained by assuming the probability of exposure was 40% and the ratio of deaths to survivors was 1:2. A sample of approximately 450 women (150 cases and 300 controls) was sufficient to detect an absolute difference in risk factor prevalence of at least 15% (80% power, 95% significance). These calculations were made using PS power software. Standard definitions of maternal mortality, early neonatal mortality, neonatal mortality, and direct causes of death were used [27,28]. Non-pregnancy related deaths were not included.

Data source and setting

The MTRH is located in Kenya's Rift Valley province [29] providing a range of curative, preventive and rehabilitative services. The catchment covers a population of over seven million inhabitants [6] and the MTRH also accepts referrals from Kenya's 13 million indigent population in the north and west [29]. The reproductive health department at MTRH has 17 obstetrician-gynaecologists, five medical officers, two clinical officers, 100 nurses who are either trained midwives or have basic training in midwifery [29]. The reproductive department at MTRH has four medical wards, and an obstetric mother/baby unit with a capacity of 150 beds [29].

Patients at MTRH are referred either from other hospitals or the community, usually following evidence of complications [29]. Deliveries at MTRH occur in the labour wards where women are delivered in maternity couches and mostly attended by midwives, but in cases of complications, attended by doctors [29]. The Hospital provides gloves and linen necessary for deliveries [29].

Descriptive variables

Information extracted from mothers' hospital records included: age, parity, gestational age, maternal complication on admission, pregnancy stage, stage of labour, birth attendant at delivery, and booking status. Patients who were referred i.e. from lower level clinical facilities or self referred from home or by a traditional birth attendant, were classified here as "unbooked". All other patients who attended antenatal clinics at MTRH and had been scheduled to deliver at MTRH were classified as "booked".

Information extracted from neonates' hospital records included: outcome at birth, apgar score, birth weight, gender, complication at birth, and mothers' and neonates' condition at discharge. All definitions of causes of death were based on the WHO International Classification of Diseases Version 10 (ICD-10). Where multiple causes of death were recorded, the primary cause was identified using available documentation and post mortem reports.

Statistical analyses

The retrospective audit at MTRH, which covered the period January 2004 to March 2011, provided descriptive information on mothers and babies. This was determined by data available at the time the study was undertaken. The annual incidence estimates were augmented by data provided by the records department at the MTRH, giving total numbers of live births and maternal and early neonatal deaths per year between 1st January 2004 and 31st December 2011. These data were used to calculate the annual maternal mortality ratios and early neonatal mortality rates. STATA version 11 was used for all statistical analyses. The study was approved by the Human Resource and Ethics Committee at University of Newcastle, Australia, and the Institute of Research and Ethics Committee at Moi University and MTRH.

Results

Figures 1 and 2 show annual changes in the MMRs and NMRs with 95% confidence intervals. The overall MMR was 426 per 100,000 live births and the overall NMR was 68 per 1,000 live births. There were wide variations between 2004 and 2011. For example in 2010, the MMR was the lowest and the NMR was second highest for the period. Despite different point estimates, year-to-year differences in maternal mortality were not statistically significant as seen by the overlapping 95% confidence intervals. However neonatal mortality was significantly different between 2005 and 2006, 2009 and 2010, and 2010 and 2011.

Table 1 shows the maternal and obstetric characteristics for the 150 maternal deaths and the 200 early neonatal deaths. Half (51%) of the early neonatal mortalities were for young mothers (15–24 years), and 64% of maternal deaths occurred in women aged between 25 and 45 years. For both the maternal and early neonatal deaths, high proportions (49% and 54% respectively) of mothers were multigravid. The majority of birth attendants were midwives for both maternal and early neonatal deaths (53% and 71% respectively). The majority of mothers with early neonatal deaths (56%) were admitted at the intrapartum stage of pregnancy (which is the period from start of labour to delivery). A high proportion of mothers who died (42%) were also admitted at the intrapartum stage. The labour stage at admission was mostly active (87%) for the neonatal deaths. The labour stage for the maternal deaths was mostly latent (42%). This is the early or slow phase of labour. The gestational age was commonly less than 36 weeks. A high proportion of these deliveries were vaginal (43% for the maternal deaths and 73% for the neonatal deaths). Most mothers (58%) were not pre-booked at the MTRH but

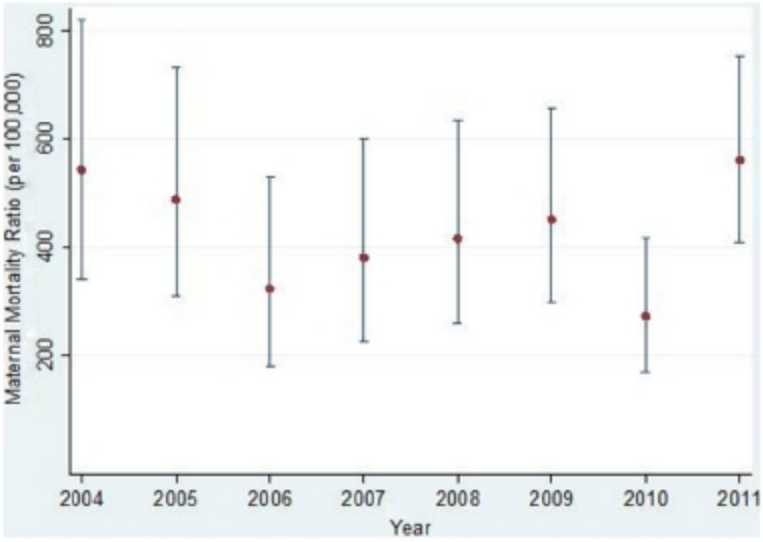

Figure 1 Annual maternal mortality ratios with 95% confidence intervals at MTRH from January 2004 to December 2011. Source: MTRH records department.

referred from home and other facilities, and most neonates (79%) were referrals.

Pregnancy complications associated with maternal and early neonatal deaths at MTRH are shown in Table 2. Eclampsia (22%) was the leading direct complication for maternal death, followed by dystocia (14%), and hemorrhage (13%). For neonatal deaths the leading maternal complication was premature rupture of the membrane (PROM) (26%) followed by dystocia (22%). Table 3 shows that the leading neonatal complications among the maternal and early neonatal deaths were asphyxia (17% of maternal deaths and 25% of early neonatal deaths) and pre-term birth (13% of maternal deaths and 38% of early neonatal deaths).

Neonatal outcomes for both maternal and early neonatal deaths at MTRH are given in Table 4. Among the neonatal deaths, majority of the neonates (86%) were alive at birth. Among the maternal deaths, 45% of the neonates were alive at birth but only 25% were discharged alive. There was a high proportion of missing information for the neonates born to mothers who died (e.g. weight 55%, gender 38%, and apgar score 39%). Amongst neonates, the apgar score had the highest proportion of missing information (21%).

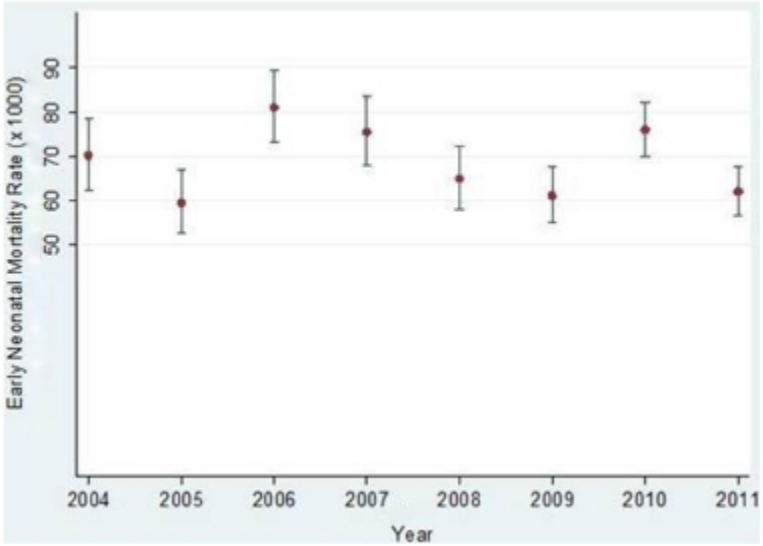

Figure 2 Annual neonatal mortality rates with 95% confidence intervals at MTRH from January 2004 - to December 2011.

Table 1 Maternal and obstetric characteristics of maternal and early neonatal deaths at MTRH from January 2004 to March 2011

Characteristic n = 150	Maternal deaths		Neonatal deaths n = 200	
n		%	n	%
Age (years)				
15-24	54	36	97	51
25-34	66	44	68	35
35-45	30	20	27	14
Gravida				
Primigravida (1)	34	23	58	29
Multigravida (2–4)	73	49	108	54
Grandmultigravida (5–7)	32	21	26	13
Grandgrandmultigravida (>8)	11	7	8	4
Birth attendant at delivery				
Doctor	61	47	50	26
Midwife	70	53	136	71
Pregnancy stage on admission				
Antepartum	53	37	73	37
Intrapartum	61	42	110	56
Puerperium	30	21	14	7
Labour stage on admission				
Latent	42	42	16	9
Active	37	37	156	87
Second stage	20	20	7	4
Gestational age				
<36 weeks	78	59	116	58
37-41 weeks	37	28	39	19
<42 weeks	3	2	5	2
Post partum	14	11	40	20
Mode of delivery				
Vaginal	64	43	146	73
Operation	51	34	45	22
Assisted delivery	27	18	9	5
Other	8	5	0	0
Booking status				
Booked	63	42	38	21
Unbooked (referral)	87	58	139	79

Denominators vary for each item depending on missing data.
The highest number of deliveries by a single mother at the MTRH was 13.

Table 2 Pregnancy complications for maternal and early neonatal deaths at MTRH from January 2004 to March 2011

Pregnancy complication	Maternal deaths n = 150		Neonatal deaths n = 200	
n % n		%		
Eclampsia	33	22	13	7
Dystocia	21	14	44	22
Hemorrhage	20	13	17	8
Sepsis	10	7	0	0
Post abortal	10	7	5	3
Premature rupture of membrane (PROM)	2	1	52	26
Post datism	1	1	3	1
Other (indirect)†	53	35	66	33

Denominators vary for each item depending on missing data.
†Indirect causes include: HIV, malaria and cardiovascular diseases.

Discussion

This study provides important information about maternal and early neonatal mortality in Kenya's second largest tertiary hospital. The MTRH draws referrals from a large catchment area and a high proportion of admissions are for women with obstetric complications. By conducting a secondary analysis of records in this large tertiary referral Hospital with high-risk obstetrics admissions, we were able to measure annual ratios for maternal mortality and early neonatal mortality rates in women who gave birth at MTRH, and describe clinical and other characteristics and circumstances surrounding maternal and early neonatal deaths following deliveries at MTRH. It is intended that this information will be used to change policies and practices that will lead to improvements in maternal and early neonatal mortality.

The findings are in agreement with other studies in developing countries in which, like Kenya, progress in reducing maternal and early neonatal mortality has been slow [30,31]. The MMR and NMR are best estimates based on available data from a major referral hospital. The peaks in maternal and early neonatal mortality at MTRH in 2011 and 2010 may be explained in part by industrial strikes at the Hospital during this time. The strikes reduced staffing levels placing pressure on Hospital resources at a time when birth numbers were fairly high. Birth rates have increased in Kenya over the past decade leading to a tripling in the population [6]. These trends may also have contributed to the higher mortality ratios seen here.

The study found that half (51%) of the early neonatal mortalities were for younger mothers (15–24 years) and 64% of maternal deaths were in women aged between 25 and 45 years. Evidence from other studies in developing countries also shows that high proportions of early neonatal deaths occur among teenage mothers and that maternal deaths occur among women who are multigravid [32-35]. In this study most maternal and early neonatal deaths occurred for multiparous women and in unbooked women whose gestational age was under 37 weeks. Mortality occurred among women who were admitted in the latent stage of labour (42%). This could be due to, for

Table 3 Neonatal complications for maternal and early neonatal deaths at MTRH from January 2004 to March 2011

Neonatal complication n = 150	Maternal deaths		Neonatal deaths n = 200	
n		%	n	%
None	84	56	0	0
Pre-term birth	16	13	75	38
Asphyxia	20	17	51	25
Sepsis	1	1	29	14
Congenital malformation	2	2	21	11
Other	12	10	24	10

Denominators vary for each item depending on missing data.

Table 4 Early neonatal and maternal outcomes at MTRH from January 2004 to March 2011

Outcome	Maternal deaths n = 150		Neonatal deaths n = 200	
	n	%	n	%
Baby's outcome at birth				
Alive	66	45	172	86
Stillbirth	61	41	28	14
Early neonatal death	20	14	0	0
Missing	4	2	0	0
Baby's weight at birth				
500-2499gms	31	20	133	67
2500-4499gms	36	24	49	25
Missing	82	55	18	9
Apgar score at 5 mins				
0-6	61	41	78	39
7-10	31	20	79	40
Missing	58	39	43	21
Baby's gender at birth				
Male	41	27	105	52
Female	52	35	85	43
Missing	57	38	10	5
Baby's condition on discharge				
Alive	38	25	0	0
Neonatal death	96	64	200	100
Missing	15	10	0	0
Mothers condition on discharge				
Alive	0	0	186	98
Death	150	100	4	2
Missing	0	0	0	0

Denominators vary for each item depending on missing data.

example, delayed labour ward admission, and lack of strict criteria for admission into labour wards [36].

Indirect obstetric complications accounted for about one third of the maternal and early neonatal deaths, with direct complications accounting for two thirds, possibly reflecting poor diagnosis and treatment of diseases that developed during pregnancy. However, other studies have shown that direct pregnancy complications contribute to a higher proportion of maternal deaths than indirect complications [3,37,38]. In this study the majority of maternal and early neonatal deaths were among women whose babies were at lower gestational age. Lower gestational age increases risk of death [33,34] and other studies have reported similar findings. Babies born under 37 weeks gestation are at higher risk of pre-mature birth and hence adverse birth outcomes [3,12,32].

Compared with assisted or caesarean delivery, the majority of the maternal and early neonatal deaths followed vaginal deliveries. Studies show that maternal and early neonatal deaths are associated with the mode of delivery and also medical practices. For example, some doctors may be unwilling to intervene aggressively on behalf of the fetus [33]. Access to skilled birth attendants (including doctors and midwives) is essential for the prevention of maternal and early neonatal deaths and this is still an issue in Sub-Saharan Africa. In Kenya, the majority of deliveries are managed by traditional birth attendants in the communities. Many such attendants lack appropriate skills which can contribute to maternal and early neonatal morbidities and mortalities.

Of the maternal and early neonatal deaths at MTRH, more than half were referred admissions. Studies in Africa have shown that of the women who are referred to hospitals for deliveries, many have severe or life threatening complications [10]. There is evidence that newborn deaths are higher in cases where best practice for newborn care is limited [12,35].

While there are a number of areas that could be followed up, some key points are noted here. There is a need to improve hospital referral policies, and also review clinical guidelines and management protocols for at-risk mothers. There is also need for attendance at antenatal clinics in order to screen for underlying illnesses and ensure proper management of complications that can occur in pregnancy.

This work has strengths and limitations. This is the first study of its kind to be conducted at a major tertiary teaching and referral hospital in Kenya. The MTRH allowed access to individual patient records. This provided a means of describing the characteristics and circumstances surrounding maternal and early neonatal deaths associated with deliveries at MTRH. Importantly this study provides a platform for identifying a range of issues that can be addressed in future efforts to reduce maternal and early neonatal deaths in other similar hospitals. The fact that detailed hospital level data were analysed also makes it possible to suggest changes in hospital policies, practices and procedures that may

ultimately reduce maternal and early neonatal mortality. Although undertaken from a hospital perspective, the work contributes more generally to understanding some of the reasons for Kenya's lack of progress towards achieving MDGs 4 and 5 by 2015.

A possible limitation is that the work is not generalizable at a national level. The data comprise only hospital births. Both nationally and in the MTRH catchment, approximately 40-43% of births are in hospitals. The proportion is similar in the MTRH catchment area [6]. A second limitation was the difficulty in estimating the MMR and NMR due to small numbers in the denominators, as evident from the overlapping confidence intervals. A further limitation is that a high proportion of the medical records collected for the study were incomplete or had missing data. It was impossible to say how much data were missing, and it is not known to what extent the missing data may have biased results. The huge proportion of missing data in neonatal variables highlights the need to link maternal and neonatal records so that information can be easily retrieved for both mothers and their babies, especially when there are adverse outcomes.

Conclusion

Maternal and early neonatal mortality remains high in Kenya despite the efforts to achieve MDGs four and five. Using data collected in a large tertiary referral hospital, this descriptive study identified a range of socio demographic, clinical and health system factors as possible contributors to Kenya's poor progress towards reducing maternal and early neonatal mortality. Further research is needed in order to understand other possible contributors, such as those found in the community, and factors associated with quality of care.

Consent

Written and informed consent was obtained for publication of this report and any accompanying images.

Abbreviations

MTRH: Moi Teaching and Referral Hospital; UN: United Nations; WHO: World Health Organization; MDGs: Millennium Development Goals; SMI: Safe Motherhood Inititative; ICD: International Classification of Diseases; NMR: Neonatal Mortality Rate; MMR: Maternal Mortality Ratio; PROM: Premature rupture of membranes; EmOC: Emergency Obstetric Care.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FY participated in all stages of the study including design, implementation, data collection, analysis and writing. JSW contributed input to the study design, analysis and interpretation, and assisted in drafting and editing the manuscript. JB contributed to the study design and provided intellectual input at all stages of the research. PN assisted with the design of the study, data collection, interpretation and manuscript preparation. WA provided input regarding study design and data interpretation. CD advised on all statistical issues and also provided intellectual input at all stages of the study. All authors read and approved the final manuscript.

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Author details

[1]Department of Health Policy and Management, Moi University, Nandi Road, Eldoret 30100, Kenya. [2]Research Centre for Gender, Health and Ageing, HMRI Building, University of Newcastle, University Drive, Callaghan, NSW 2308, Australia. [3]Reproductive Health Department, Moi University, Nandi Road, Eldoret, Kenya 30100, Australia. [4]Clinical Services, Moi Teaching and Referral Hospital, Nandi Road, Eldoret 30100, Kenya. [5]Centre for Clinical Epidemiology and Biostatistics, HMRI Building, University of Newcastle, University Drive, Callaghan, NSW 2308, Australia.

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A1.2 Published paper 2

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Risk factors for maternal mortality in a Tertiary Hospital in Kenya: a case control study

Faith Yego[1,2*], Catherine D'Este[2,3,6], Julie Byles[2,4], Jennifer Stewart Williams[2,4,7] and Paul Nyongesa[5]

Background

The maternal mortality ratio (MMR) is defined as "the ratio of the number of maternal deaths during a given period per 100,000 live births during the same time-period". The global MMR is 210 per 100,000 live births [1]. Despite worldwide declines since 1990, the MMR is 15 times higher in developing than developed regions [1]. Sub-Saharan Africa has the highest MMR at 500 per 100,000 live births. In developed regions the MMR is 16 per 100,000 live births [1]. The target for Millennium Development Goal (MDG) Five is to reduce the global MMR by three quarters and to achieve universal access to reproductive health by 2015 [2]. In Kenya, the MMR has remained at 400-600 per 100,000 live births over the past decade - resulting in little or no progress being made towards achieving MDG Five [1,3].

The main direct causes of maternal death in developing countries include haemorrhage, sepsis, obstructed labour and hypertensive disorders [4]. The risk of death from haemorrhage is one in 1,000 deliveries in developing countries, compared with one in 100,000 in developed countries, and accounts for one third of the maternal deaths in Africa [5]. A study in Canada found increased risk of eclampsia among women with existing heart disease and anaemia [6]. A retrospective study undertaken at a tertiary hospital in Nigeria in 2007 found

* Correspondence: yegofaith@gmail.com
[1]Department of Health Policy and Management, Moi University, P. O Box 4606, Eldoret 30100, Kenya
[2]University of Newcastle, HMRI Building, Callaghan, NSW 2308, Australia
Full list of author information is available at the end of the article

that the most common risk factors for maternal mortality were primaparity, haemorrhage, anaemia, eclampsia and malaria [7]. Risk factors for complications arising from infections include birthing under unhygienic conditions, poor nutrition, anaemia, caesarean section, membrane rupture, prolonged labour, retained products and haemorrhage [8].

In developing countries, indirect causes of maternal death include both previously existing diseases and diseases that develop during pregnancy. These include HIV, malaria, tuberculosis, diabetes, and cardiovascular disease, all of which and have an enormous impact on maternal and fetal outcomes during pregnancy [4].

Many individual and socioeconomic factors have been associated with high maternal mortality. These include lack of education, parity, previous obstetric history, employment, socioeconomic status, and types of care seeking behaviours during pregnancy. There is also evidence of increased risk of death among women who are less than 24 and older than 35 years [9]. A study in Tanzania found that low level of spouse education was a risk factor for maternal mortality [10]. Lack of knowledge regarding the need for skilled attendants is a barrier to women seeking care, especially during birth emergencies. A survey conducted in Kenya in 2006 showed that 15% of pregnant women were not informed of the importance of hospital deliveries [11]. In Nigeria, a cross-sectional survey revealed that the most common risk factors for maternal death were primigravidity (19%), and unbooked status (19%) [12]. Poverty has also been associated with adverse maternal outcomes, not directly, but as a contributor to maternal ability to access and utilise care where complications occur [13,14]. There is also evidence that contraceptive use is efficient for the primary prevention of maternal mortality in developing countries by about 44% [15].

Antenatal care (ANC) is very important during pregnancy. International organizations recommend a minimum of four visits, the administration of two doses of tetanus toxoid and folic acid supplementation during ANC attendance [16]. When women receive good care during the pre-partum period, they have been shown to be at less risk of maternal morbidity and mortality, since they had a higher likelihood of using a professional health facility during birth [10,17].

In the Kenya Demographic and Health Survey (2008-2009), it was reported that 92% of women received ANC from a skilled provider (doctor, nurse, or midwife), especially those who were more educated and resided in urban areas [3]. The report further showed that 83% of women who visited public hospitals were required to pay for antenatal services, which may explain why only 47% of antenatal women attended the recommended four visits [3]. Women had also been required to pay for delivery services until June 2013, when the Kenyan government rolled out a program where pregnant women can receive free maternity services in public hospitals.

Health systems functioning with adequate equipment, resources and trained personnel to handle maternal complications can reduce the risks of mortality. In Africa maternal deaths are associated with delayed referrals for women from lower level facilities, and where referral systems are not well equipped to handle emergency obstetric care [18]. The presence of skilled attendants during birth is also important in managing life threatening complications. In Kenya, the use of skilled attendants at delivery is currently 50% [19].

The Delay Model by McCarthy and Maine is a conceptual framework that has been used to assess factors contributing to maternal mortality in developing countries [20]. This framework attributes mortality to certain determinants that contribute to the delay in deciding to seek care, the delay in reaching a health facility, and the delay in receiving quality care upon reaching a health facility. In Kenya there has been insufficient progress made towards achieving MDG Five. The aim of this study is to identify risk factors associated with maternal mortality in a tertiary level hospital in Kenya. Using a framework adapted from the Delay Model, this study analyses four sets of determinants: individual and socio-demographic, maternal history, reproductive or obstetric, and hospital admission/health system.

Methods

An unmatched case control study of women who delivered between January 2004 and March 2011 was conducted at Moi Teaching and Referral Hospital (MTRH) located in the Western region of the Rift Valley Province, Kenya [21]. As the second largest national hospital in Kenya with over 800 beds, MTRH provides a range of curative, preventive and rehabilitative health services to a population of about 400,000 inhabitants, and an indigent referral population of 16 million from Northern and Western Kenya [21]. The Mother and Baby Unit at MTRH at has an antenatal ward, post natal ward, labour ward, Newborn Unit (NBU) and two theatres dedicated for obstetrics. The bed capacity is approximately 20 for the antenatal and labour wards, and 50 for the post natal wards [21].

Cases (n = 150) were maternal deaths identified from a manual review of hospital records. Two controls (n = 300) were selected per case. Controls were surviving women who were admitted immediately preceding and following cases. Cases were selected retrospectively and sequentially from the most recent delivery until the required sample size was achieved. Trained staff collected information using a standard audit form. Abortion related deaths were excluded from the study.

Maternal hospital death was the outcome. This was a clearly defined adverse event certified by medical personnel. The data collection form included: mother's age, mother's marital status, mother's education, spouse's education, mother's occupation, spouse's occupation, and the source of funding for the delivery. Information relating to the mother's medical history included: smoking, alcohol use, contraceptive use, previous abortion, previous twins, gravida, and pre-existing medical conditions. Obstetric or reproductive factors were pregnancy stage, labour stage, number of ANC visits, and place of ANC care. Health system factors included mode of delivery, qualification of birth attendant, and referral from another facility (yes/no). Information on the mother's admission factors comprised: clinical cause of death or diagnosis on admission (e.g. eclampsia, dystocia haemorrhage, or comorbid causes), diastolic blood pressure (millimetres of mercury/mm Hg), systolic blood pressure (mm HG), haemoglobin level (grams per decilitre g/dL), pulse rate (beats per minute/bpm), and temperature (degrees Celsius/°C). The primary obstetric cause of death was that documented in the patient hospital and post mortem records.

Statistical analyses

Analyses were performed using Stata version 10.0 (StataCorp, College Station, TX, USA). Following initial data checking and exploratory analysis, univariable logistic regression analysis was conducted for each potential risk factor. The multivariable models initially included all variables with $p < 0.2$ in the univariable models. Backward stepwise multiple logistic regression was undertaken separately for the four groups of risk factors in the framework adapted from the Delay Model, (individual and socio-demographic; maternal history; reproductive or obstetric; and admission). Variables were removed from the models where p-values > = 0.1 on the Likelihood Ratio Test. The variables in each of the final models were then included in a combined model and removed where p-values > = 0.1 in order to derive a final parsimonious model. Odds ratios (ORs), 95% confidence intervals and p-values are reported for all models. The reference group was the category with the lowest expected risk of death, or if there were few cases in this category, the group with the majority of respondents.

Assuming the probability of exposure in controls was 40% and the ratio of cases to controls was 1:2, with 80% power and a 5% level of significance, a sample of approximately 450 women (150 cases and 300 controls) was needed to detect an odds ratio of approximately 0.5 or 1.8.

Ethical approval was sought from the Human Research Ethics Committee (HREC) at the University of Newcastle and The Institute for Research and Ethics Committee (IREC) in Kenya.

Results

Table 1 shows the demographic factors associated with maternal mortality. In this model, mother's age and mother's education were significantly associated with mortality. Relative to controls, cases had three times the odds of being aged 35-45 years rather than 15-24 years (OR 3.1, 95% CI 1.5- 6.2; $p < 0.0001$). Cases had eight times the odds of having no education versus secondary education compared with controls (OR 8.0, 95% CI 4.0-16.3; $p < 0.0001$).

Table 2 shows the association between maternal history of prevailing conditions and obstetric and reproductive factors with maternal mortality. After adjusting for all other factors in the model, cases had higher odds than controls of having a history of maternal alcohol use (OR 2.5, 95% CI 1.2-5.3; $p = 0.018$), more than five previous pregnancies (OR 2.6, 95% CI 1.4-4.8; $p = 0.0049$), and a history of pre-existing illnesses (OR 3.0, 95% CI 1.7-5.3; $p < 0.0001$). Contraceptive use was protective (OR 0.3 95% CI 0.1-0.6; $p = 0.0007$). Table 2 also shows obstetric and reproductive characteristics associated maternal mortality. Compared to controls, cases had higher odds of assisted or caesarean deliveries (OR 3.0 95% CI 1.5-5.6; $p < 0.0006$). Cases had higher odds than controls of having a doctor, rather than a nurse or midwife attend the birth (OR 4.1 95% CI 2.2-7.6; $p < 0.0001$). Relative to controls, cases had almost nine times the odds of arriving at hospital at the puerperium stage (OR 8.9, 95% CI 3.5, 22.7; $p < 0.0001$), and almost six times the odds of lack of antenatal care (OR 5.7, 95% CI 2.6-12.4; $p < 0.0001$).

Table 3 shows maternal admission factors associated with mortality. Admission from comorbid complications (OR 6.7, 95% CI 3.8-11.8; $p < 0.0001$), eclampsia (OR 4.7, 95% CI 1.6, 13.7; $p = 0.0038$), non-normal blood pressure (OR 7.5, 95% CI 1.5-37.7; $p = 0.0039$), tachycardia (OR 16.5, 95% CI 4.8-57.3; $p < 0.0001$), and being referred to MTRH (OR 3.3, 95% CI 1.9-5.7; $p < 0.0001$) were all statistically significant risk factors for maternal mortality.

Table 4 shows the multivariable analysis combining all factors from the previous models. Statistically significant risk factors for maternal mortality included: no education, relative to secondary education (OR 3.3, 95% CI 1.1-10.4, $p = 0.0284$), history of pre-existing medical conditions (OR 3.9, 95% CI 1.7-9.2, $p = 0.0016$), doctor attendance at birth (OR 4.6, 95% CI 2.1-10.1, $p = 0.0001$), having no antenatal visits (OR 4.1, 95% CI 1.6-10.4, $p = 0.0007$), being admitted with eclampsia (OR 10.9 95% CI 3.7-31.9, $p < 0.0001$), having comorbid complications on admission (OR 9.0, 95% CI 4.2-19.3, $p < 0.0001$), having elevated pulse (OR 10.7, 95% CI 2.7-43.4, $p = 0.0002$), and being referred to MTRH (OR 2.1, 95% CI 1.0-4.3, $p = 0.0459$).

Discussion

In the multivariable analysis of each of the four groups of risk factors (socio-demographic, maternal history,

Table 1 Individual and Socio-demographic risk factors for maternal mortality in a tertiary hospital in Kenya from January 2004 to March 2011

Individual and socio-demographic characteristics					
Risk factor	Cases n = 150 n (%)	Controls n = 300n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	P-value[†]
Age					<0.0001
15–24 years	66(44)	147(49)	1	1	
25–34 years	54(36)	129(43)	1.1(0.7–1.6)	1.4(0.9–2.4)	
35–45 years	30(20)	24(8)	3.0(1.6–5.6)	3.1(1.5–6.2)	
Marital status					
Married	111(74)	240(80)	1		
Single	39(26)	60(20)	1.4(0.9–2.2)		
Mother's education					<0.0001
None	31(23)	17(6)	8.5(4.3–17.0)	8.0(4.0–16.3)	
Primary	66(50)	108(37)	2.9(1.8–4.6)	2.9(1.8–4.7)	
Secondary	36(27)	168(57)	1	1	
Spouse's education*					
None	20(22)	14(6)	5.9(2.8–12.7)		
Primary	30(33)	46(20)	2.7(1.5–4.8)		
Secondary	40(44)	166(74)	1		
Occupation of mother					
Unemployed	106(71)	176(59)	1		
Formal employment	28(19)	88(29)	0.5(0.3–0.9)		
Informal employment	15(10)	35(12)	0.7(0.4–1.4)		
Occupation of spouse					
Informal employment	59(41)	124(42)	1		
Formal employment	47(32)	114(38)	0.9 (0.5–1.3)		
NA	39(27)	60(20)	1.4(0.8–2.3)		
Funding for delivery					
Self	105(70)	210(70)	1		
Insurance	16(11)	47(16)	0.7(0.4–1.3)		
Waiver	28(19)	43(14)	1.3(0.8–2.2)		

*Spouse's education was not included in the multiple regression model due to high cases of missing data and correlation with mothers education.
[a]Adjusted for variables included in the final demographic model.
[†]P- value for Likelihood Ratio Test in the adjusted model.
Reference category for logistic regression represented by 1.
Numbers may not add to total sample due to missing values.

reproductive/ obstetric and admission factors) variables significantly associated with maternal mortality included: age, education, alcohol use, contraceptive use, gravida, pre-existing medical conditions, mode of delivery, type of birth attendant, pregnancy stage, number of ANC visits, having comorbid complications on admission, eclampsia, diastolic blood pressure, elevated pulse, and referral status. However, in the final model combining only significant factors from the four separate sets of analyses into a parsimonious model, only education, underlying medical conditions, birth attendant, number of ANC visits, having comorbid complications, eclampsia, having an elevated pulse on admission, and referral status were significant risk factors for maternal mortality.

Cases had three times the odds of having no education versus secondary education compared with controls. This is in agreement with another study that also reported a higher risk of mortality among illiterate women [22]. This finding is important since it emphasizes the role of education for both the mother and her spouse in obtaining and understanding the benefits of good health and being able to make appropriate decisions during pregnancy. It is important to note that despite the woman's

Table 2 Mother's history of prevailing conditions and obstetric characteristics associated with maternal mortality in a tertiary hospital in Kenya from January 2004 to March 2011

History of prevailing medical conditions					
Risk factor	Cases n = 150 n (%)	Controls n = 300 n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	P-value[†]
Smoking					
Yes	2(1)	7(2)	0.6(0.1–2.7)		
No	148(99)	286(98)	1		
Alcohol					0.018
Yes	16(11)	20(7)	1.6(0.8–3.2)	2.5(1.2–5.3)	
No	134(89)	273(93)	1		
Contraceptives					0.0007
Yes	17(11)	74(25)	0.4(0.2–0.7)	0.3(0.1–0.6)	
No	133(89)	220(75)	1		
Abortion					
Yes	11(7)	20(7)	1.1(0.5–2.4)		
No	139(93)	279(93)	1		
Twins					
Yes	10(7)	17(6)	1.2(0.5–2.7)		
No	140(93)	283(94)	1		
Gravida					0.0049
Primigravida	34(23)	104(35)	1		
Multigravida	73(49)	153(51)	1.5(0.9–2.4)	1.5(0.9–2.5)	
Grandmultigravida	43(29)	43(14)	3.1(1.7–5.4)	2.6(1.4–4.8)	
Underlying medical conditions*					
Yes	41(27)	29(10)	3.5(2.1–5.9)	3.0(1.7–5.3)	
No	109(73)	271(90)	1		
Obstetric and reproductive characteristics					
Mode of delivery					0.0006
Normal	64(43)	230(77)	1		
Assisted	27(18)	13(4)	7.5(3.6–15.3)	4.4(1.7–11.2)	
Caesarean	51(34)	57(19)	3.2(2.0–5.1)	3.0(1.5–5.6)	
Did not deliver	8(5)	0	omitted	omitted	
Birth attendant					<0.0001
Nurse/midwife	70(53)	264(89)	1	1	
Doctor	61(47)	31(11)	7.4(4.5–12.3)	4.1(2.2–7.6)	
Pregnancy stage					<0.0001
Intrapartum	61(42)	259(86)	1	1	
Antepartum	53(37)	29(10)	7.8(4.6–13.2)	3.0(1.5–6.2)	
Puerperium	30(21)	12(4)	10.6(5.1–21.9)	8.9(3.5–22.7)	
Labour stage					
Latent	42(42)	68(24)	1		
Active	37(37)	180(63)	0.3(0.2–0.6)		
Second stage	20(20)	34(12)	1.0(0.5–1.9)		

Table 2 Mother's history of prevailing conditions and obstetric characteristics associated with maternal mortality in a tertiary hospital in Kenya from January 2004 to March 2011 (Continued)

Number of ANC visits					<0.0001
1 to 3	71(50)	199(67)	1	1	
None	59(42)	14(5)	11.8(6.2–22.5)	5.7(2.6–12.4)	
Above 4	11(8)	83(28)	0.4(0.2–0.7)	0.6(0.3–1.2)	
Place of ANC attendance††					
Health centre	41(28)	122(41)	1		
Hospital	26(18)	60(20)	1.3(0.7–2.3)		
MTRH	19(13)	100(34)	0.6(0.3–1.0)		
None	59(41)	14(5)	12.5(6.3–24.8)		

*These include: HIV, malaria, rheumatic heart disease, cardiovascular disease, and diabetes.
†P- value for Likelihood Ratio Test in the adjusted model.
[a]Adjusted for variables included in the final demographic model.
Reference category for logistic regression represented by 1.
††Did not include ANC place because of high correlation with number of ANC visits.
Numbers may not add to total sample due to missing values.

weaker role in decision-making in African settings, education has a strong influence on mortality. In this study, we used mother's education as a proxy for the husband's education. Although there was considerable missing data for spouse's education, there was correlation between these two education variables.

Having no antenatal care during pregnancy was associated with mortality in this study, a finding which corresponds with those of other studies [22,23]. Antenatal care is important in screening for pre-existing illnesses and complications in the early stages of pregnancy that could impact adversely during pregnancy and childbirth [24]. Since ANC coverage is high in Kenya, there is a need to scale up interventions that empower women to make at least four visits during pregnancy as recommended by international organizations [16,19].

The findings here were that comorbid conditions including HIV, malaria, rheumatic heart disease, cardiovascular disease, and diabetes contributed to maternal deaths. This is contrary to other research showing that direct pregnancy complications are the leading causes of maternal deaths [4]. However, other research shows that the significant increase in MMRs in Sub-Saharan Africa are predominantly due to increasing HIV prevalence in that region [25]. The finding that the odds of comorbid conditions were higher in cases than controls also demonstrates the importance of ANC for screening, detection and management of underlying illnesses that could potentially pose a threat to the mother during pregnancy and childbirth.

Contraceptive use was protective for maternal mortality, which coincides with findings from another study that found that maternal mortality would be 77% higher globally in the absence of family planning programs and contraceptive use [15]. The role of contraceptives in tackling maternal mortality has been through reducing exposure to incidence of pregnancy, lowering hazards of fragility from high parity pregnancies, reducing vulnerability to abortion risks, and postponing pregnancies, especially in countries with high fertility rates [15].

In this study, hypertensive disorders during pregnancy were higher among cases than controls. Our study demonstrated increased odds of eclampsia in cases, which is in agreement with another study that found that the delay in diagnosis, triage, transport and treatment of eclampsia increases the risk of maternal death [26]. There is evidence that screening for hypertensive conditions during the antenatal period plays a significant role in reducing the risk of death to the mother [13]. This study also found higher odds of elevated pulse amongst cases, which could explain the increased risk of death due to eclampsia. After adjusting for other factors, haemorrhage was not significantly associated with mortality possibly as a result of hospital protocols for management of haemorrhage.

This study found health care system related factors that identified cases as being at risk including doctor attendance at birth and referrals. Cases had higher odds than controls of a doctor attending their delivery, potentially because they were diagnosed with the most difficult complications. This has been previously reported, especially in low resource settings where uptake of professional birth attendants is low hence women only seek help when the condition is critical or too late for the doctor to save their lives [4]. Cases had twice the odds of referral relative to controls, potentially because the number of referrals represented over half of the cases who were referred following complications of birth.

This study provides information that is important for the identification of risk factors that contribute to

Table 3 Maternal admission factors associated with maternal mortality in a tertiary hospital in Kenya from January 2004 to March 2011

Admission factors					
Risk factor	Cases n = 150 n (%)	Controls n = 300 n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	P-value††
Comorbid complications					<0.0001
Yes	93(62)	63(21)	0.2(0.1–0.3)	6.7(3.8–11.8)	
No	57(38)	237(79)	1	1	
Eclampsia					0.0038
Yes	33(22)	16(5)	5.0(2.7–9.4)	4.7(1.6–13.7)	
No	117(78)	284(95)	1	1	
Dystocia					
Yes	21(14)	51(17)	0.8(0.5–1.4)		
No	129(86)	249(83)	1		
Haemorrhage					
Yes	20(13)	15(5)	2.9(1.5–5.9)		
No	120(87)	285(95)	1		
Diastolic blood pressure (mm HG)**					0.0039
Normal	102(72)	280(96)	1	1	
Low	16(11)	2(1)	22.0(5.0–97.2)	7.5(1.5–37.7)	
High	24(17)	10(3)	6.6(3.0–14.3)	3.2(0.9–10.6)	
Systolic blood pressure (mm HG)**					
Normal	93(65)	271(93)	1		
Low	33(23)	6(2)	16.0(6.5–39.5)		
High	17(12)	15(5)	3.3(1.6–6.9)		
Haemoglobin†					
<10 g/dL	63(52)	43(20)	4.2(2.6–6.9)		
> = 10 g/dL	59(48)	171(80)	1		
Pulse					<0.0001
<110 bpm	103(71)	283(99)	1	1	
> = 110 bpm	41(28)	4(1)	28.2(9.8–80.6)	16.5(4.8–57.3)	
Temperature†					
<37.5°C	110(82)	205(95)	1		
> = 37.5°C	24(18)	11(5)	4.1(1.9–8.6)		
Referral					<0.0001
No	63(42)	234(78)	1	1	
Yes	87(58)	66(22)	4.9(3.2–7.5)	3.3(1.9–5.7)	

**Diastolic blood pressure was used as a proxy for systolic because of high correlation.
†Temp and haemoglobin were omitted in the adjusted model because of too many missing values.
††P- value for Likelihood Ratio Test in the adjusted model.
[a]Adjusted for variables included in the final demographic model.
Reference category for logistic regression represented by 1.
Numbers may not add to total sample due to missing values.

maternal mortality in the second largest referral hospital in Kenya. It also provides information that will aid in identifying areas of improving health facilities locally and nationally in terms of referrals, antenatal care, and the availability of skilled birth attendants who are able to manage pregnancy related complications. This study is timely given the free maternity program roll out in Kenya since June 2013. Importantly, these findings will inform policy makers about ways of strengthening the health system and promoting more hospital births.

This study has some limitations. Firstly, it only includes deaths that occurred during the hospital admission and

Table 4 Multivariable model showing risk factors for maternal mortality in a tertiary hospital in Kenya from January 2004 to March 2011

Final multivariable model				
Risk factor	Cases n = 150 n (%)	Controls n = 300 n (%)	OR (95% CI)	Likelihood ratio test X^2 (df), p-value
Mothers education				
Secondary	36(27)	168(57)	1	
None	31(23)	17(6)	3.3(1.1–10.4)	
Primary	66(50)	108(37)	2.4(1.1–5.3)	7.13(2), 0.0284
Underlying medical conditions				
No	109(73)	271(90)	1	
Yes	41(27)	29(10)	3.9(1.7–9.2)	9.95(1), 0.0016
Birth attendant				
Nurse/midwife	70(53)	264(89)	1	
Doctor	61(47)	31(11)	4.6(2.1–10.1)	14.41(1), 0.0001
Number of ANC visits				
1 to 3	71(50)	199(67)	1	
None	59(42)	14(5)	4.1(1.6–10.4)	
Above 4	11(8)	83(28)	0.5(0.2–1.2)	14.56(2), 0.0007
Comorbid complications†				
No	57(38)	237(79)	1	
Yes	93(62)	63(21)	9.0(4.2–19.3)	36.33(1), <0.0001
Eclampsia				
No	117(78)	284(95)	1	
Yes	33(22)	16(5)	10.9(3.7–31.9)	21.29(1), <0.0001
Pulse				
<110 bpm	103(71)	283(99)	1	
> = 110 bpm	41(28)	4(1)	10.7(2.7–43.4)	13.58(1), 0.0002
Referral				
No	63(42)	234(78)	1	
Yes	87(58)	66(22)	2.1(1.0–4.3)	3.98(1), 0.0459

Final model included all variables with P-value of 0.1 or less on the likelihood ratio test.
Reference category for logistic regression represented by 1.
†These include: HIV, malaria, rheumatic heart disease, cardiovascular disease, and diabetes.
Numbers may not add to total sample due to missing values; the final model included 367 observations.

therefore the risk factors identified here were specifically associated with in-hospital mortality. Pregnancy related mortality that occurs outside hospital may have other risk factors that were not identified here. Secondly, bias may have resulted from the misclassification of causes of death data and missing information in some fields.

Conclusions

This study highlights risk factors for mortality at a tertiary hospital in Kenya showing the importance of antenatal care and maternal education in preventing maternal mortality. The findings are timely given Kenya's limited progress towards achieving MDG Five by 2015. Antenatal visits provide opportunities for the detection of risk factors for eclampsia and other underlying illnesses that may put a mother at risk during birth. There is need to focus on integrated care throughout the pregnancy by improving women's knowledge and empowering them to take an active role in their own health as well as gaining access to skilled care at birth and during pregnancy.

Abbreviations

MDG: Millennium development goal; MMR: Maternal mortality ratio; ANC: Antenatal care; MTRH: Moi teaching and referral hospital; NBU: Newborn unit; WHO: World Health Organization; HIV: Human immunodeficiency virus.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FY conceived the study. FY, CD, JB, JSW, and PN all contributed to the protocol design, questionnaire design and ethics application process. FY contributed in data collection and extraction. PN contributed in providing consultation and advice during data extraction. FY, CD, PN and JB contributed to data analysis and writing of the paper. CD, JB, FY and JSW contributed to the drafting and editing the paper. All authors contributed to reviewing the paper and approved the final version for publication.

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Author details

[1]Department of Health Policy and Management, Moi University, P. O Box 4606, Eldoret 30100, Kenya. [2]University of Newcastle, HMRI Building, Callaghan, NSW 2308, Australia. [3]Centre for Clinical Epidemiology and Biostatistics, Callaghan, NSW 2308, Australia. [4]Research Centre for Gender, Health and Ageing, Callaghan, NSW 2308, Australia. [5]Department of Reproductive Health, Moi University, P.O. Box 4606, Eldoret 30100, Kenya. [6]National Centre for Epidemiology and Population Health, ANU College of Medicine, Biology and Environment, The Australian National University, Canberra, ACT, Australia. [7]Department of Public Health and Clinical Medicine Epidemiology and Global Health, Umeå University, Umeå, Sweden.

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A case-control study of risk factors for fetal and early neonatal deaths in a tertiary hospital in Kenya

Faith Yego[1*], Catherine D'Este[2†], Julie Byles[3†], Paul Nyongesa[4†] and Jennifer Stewart Williams[5,6†]

Background

Neonatal death is defined as newborn death occurring within the first four weeks after birth [1]. Neonatal deaths represent 40% of under-five deaths worldwide [2,3]. Despite the reduction in overall under five mortality in developing regions, from 97 deaths per 1000 live births in 1990 to 63 per 1000 live births in 2010, there has been little change in neonatal deaths as a proportion of under five deaths [2,3]. In Sub-Saharan Africa, for example, the proportion of neonatal deaths among under five deaths increased from 37% in 1990 to 40% in 2010 [2,3]. Neonatal mortality rates in the developing world are generally high, for example, there were 32 deaths per 1000 live births in Central Africa in 2009 [4], and in Somalia the estimated neonatal mortality rate was 52 per 1000 live births in 2012 [5]. In comparison, the neonatal mortality rate in Kenya is currently 28 per 1000 live births and there has been little progress towards achieving the Millennium Development Goal (MDG) Four for child survival [2,6]. The main direct causes of neonatal deaths globally are preterm births (27%), severe infections (26%), asphyxia (23%), and neonatal tetanus (7%) [3,7,8].

Early neonatal death is defined as all deaths of live-born infants occurring on or before the first seven days of life

* Correspondence: yegofaith@gmail.com
†Equal contributors
[1]Department of Health Policy and Management, Moi University, College of Health Sciences, Eldoret 30100, Kenya
Full list of author information is available at the end of the article

[9]. There is evidence that there has been no measurable reduction in early neonatal mortality over the past decade [2]. Most programs addressing childhood mortality focus on pneumonia, malaria, diarrhoea and vaccine preventable conditions, which are geared towards improving child survival after the first four weeks of life [5,6]. There is evidence that the highest numbers of early neonatal deaths in Sub-Saharan Africa are due to infections [10,11].

Fetal death is defined as any fetus born without a heartbeat, respiratory effort or movement, or any other sign of life [9]. It is estimated that globally 2.9 million babies experience fetal death or die within the first week of life, with 99% of these deaths occurring in developing countries [12]. Studies have shown that 50% of maternal deaths occur within the first day after childbirth and approximately 30% of stillbirths occur during labour [5].

The health and survival of newborns has been shown to be closely linked to that of their mothers, since inadequate maternal care during the pregnancy and postpartum period can also affect the neonate [13]. It has been suggested that access to antenatal care and emergency obstetric care could reduce neonatal mortality by 10-15% [5,14]. There is evidence that 10% of intrapartum-related and preterm deaths can be reduced by immediate assessment and stimulation of newborns [15]. Treatment with antenatal corticosteroids has been associated with a decrease in overall neonatal deaths, especially for women with premature rupture of membranes (PROM) [16].

Health system factors have been associated with newborn deaths, especially in low resource settings where quality of care is generally poor and inadequate [17]. An assessment of six African countries showed that less than 12% of personnel working in health facilities were trained to conduct neonatal resuscitation and no more than 22% of the facilities had sufficient equipment for neonatal resuscitation [18].

Due to these high mortality rates it is important to understand the risk factors for fetal and neonatal mortality which are major contributors to high under five deaths globally. Fetal and neonatal mortality is also a sensitive indicator of maternal health in society because healthy mothers give birth to healthy babies. This study was undertaken to assess maternal and neonatal risk factors associated with fetal and early neonatal deaths in the second largest tertiary hospital in Kenya in order to provide insights into the circumstances surrounding fetal and early neonatal deaths.

Methods

This retrospective case-control study was conducted in Moi Teaching Referral Hospital (MTRH) in Kenya. The study was undertaken in Uasin Gishu County which is in the Rift Valley Province of Kenya. This hospital services approximately seven million women [19]. The MTRH has a reproductive health wing called the Riley Mother Baby Unit, which contains both the labour ward and the New Born Unit (NBU). The NBU has three sections: the born before arrival (BBA) unit, the acute ward or critical ward and the general ward [20]. The NBU has several incubators, newborn trolleys, a capacity of 60 beds, and is staffed with consultant paediatricians (10), registrars (6), intern doctors (one) and nurses (30) specially trained for NBU care [20]. According to the MTRH records department the total number of monthly admissions during the study period was about 120-140 newborns [20].

Client flow in the hospital is such that pregnant/postpartum patients are seen in a designated room (triage area) on the labour ward floor by a nurse, medical officer intern and resident doctor. Patients in active labour are usually admitted to the labour ward where they are managed by a team of obstetricians, residents, interns and midwives/nurses. Patients in a latent phase of labour, or with medical conditions, are usually admitted to the antenatal ward, and other patients with medical issues after delivery are admitted to the post natal ward. Patients without complications are discharged. Neonates who have complications after birth are immediately taken to the NBU which is adjacent to the labour ward. The neonatologist and paediatricians subsequently manage the neonate [20].

A medical record review was undertaken on admissions to the newborn unit in MTRH between January 2005 and March 2011. Cases were defined as neonates who were born dead (fetal deaths) or died within seven days of birth (early neonatal deaths). Most recent cases were selected retrospectively until the desired sample size was achieved. Two controls were obtained for every case. The controls were surviving neonates born immediately preceding and following the cases within the first week of life. Exclusion criteria were late neonatal deaths (more than seven days after birth).

A structured data collection instrument was used to collect data from medical records identified from the NBU admission register. It was not possible to blind the data abstractors to case/control status because mortality information was in the medical records.

The primary cause of death was identified using the information from hospital medical records and post mortem reports. Where interpretation was required, the information on the cause of death was verified by the study physician. Data were coded and double entered into two separate password protected databases, which were later compared for consistency. Where there were inconsistencies, the patient's file was obtained to verify the information.

The outcome of this study was death of the neonate or fetus at birth or within seven days of birth. Explanatory variables were classified as maternal and obstetric characteristics, maternal and obstetric complications, neonatal complications and neonatal characteristics.

Maternal and obstetric characteristics included information on women of reproductive age (15 to 49 years) such as: mother's age (15-24 years, 25-34 years, or 35-45 years); gravidity categorised as primigravida (1), multigravida (2-4), or grandmultigravida (above 5); qualification of birth attendant (doctor (consultant/registrar/intern), or midwife); gestational age (less than 37 weeks, 37-42 weeks or above 42 weeks); mode of delivery (spontaneous vertex delivery, assisted vaginal delivery, or caesarean section); number of antenatal visits (ANC) (0-1, 2-3, or above 4), and booking status on admission (yes = attended ANC at MTRH or no = did not attend ANC at MTRH).

Maternal and obstetric complications included the presence of common causes of death, as documented in the patient records and post mortem reports; premature rupture of membranes (PROM); dystocia (prolonged or obstructed labour); pre-eclampsia; haemorrhage; and other complications (cardio respiratory diseases, previous scar, Human Immunodeficiency Virus or HIV, malaria, retained placenta, anaemia, abortion). A complication was assumed there was an indication to this effect in the notes, otherwise it was assumed that there were no complications.

Newborn complications included the presence of causes of newborn death as documented in the records including asphyxia, congenital malformation, sepsis, Respiratory Distress Syndrome (RDS), and other complications (hypothermia, diarrhoea, jaundice, hypoglycaemia, meconium aspiration syndrome, and HIV). One single cause of death was identified for each neonate case and where there were multiple causes the final cause of death documented in the post mortem reports was used.

Neonatal characteristics including sex, Apgar score at five minutes and weight in grams were also recorded.

Ethical approval was provided by the University of Newcastle Human Research Ethics Committee (HREC) and the Institutional Research and Ethics Committee (IREC) in Kenya. Permission was obtained from the MTRH administration to undertake the study.

Statistical methods

Statistical analysis was performed using STATA version 10 (StataCorp, College Station, TX, USA). Exploratory data analysis involved checking the data for implausible relationships, outliers and errors using frequency distributions, tables and graphs. Checks comprised visualizing the distributions by use of graphics including histograms overlaid with a normal curve, normal probability plots and box plots to identify potential errors. Bar charts were also used to compare distributions between groups.

All variables were categorical. Categories were combined where cell sizes were small. Bivariate analysis was undertaken using the Chi-squared test to compare characteristics of cases and controls. Initially, a modelling process was undertaken by including all variables with $p < 0.2$ in separate models for each of the four groups of potential risk factors (maternal and obstetric characteristics, neonatal complications, maternal and obstetric complications and neonatal characteristics). Each group of potential risk factors was analysed in separate multivariable logistic regression. A backward stepwise method was used whereby, at each step, variables with a p-value of >0.1 on the likelihood ratio test were removed. The remaining variables were combined in a final model. Unadjusted and adjusted odds ratios, confidence intervals and p-values are reported for all models.

For a ratio of cases to controls of 1:2, 80% power, a 5% significance level and 40% probability of exposure (i.e. risk factor prevalence) in controls, a sample of 600 neonates (200 cases and 400 controls) was required to detect an absolute difference in risk factor prevalence of at least 12%, or an odds ratio of approximately 0.6 or 1.7.

Results

A total of 600 records were reviewed (200 cases and 400 controls) from January 2005 to March 2011. As with many studies using data abstracted from medical records, data were incomplete in some areas. The proportion of missing data in variables ranged from 0.3% to 22%. Data were separately stored in the MTRH neonatal and maternal records. Missing data in individual records arose from one or both sources.

Table 1 shows the maternal and obstetric factors associated with fetal and early neonatal mortality at MTRH. Gestational age at admission ($p < 0.001$), number of antenatal visits ($p < 0.001$) and qualification of birth attendant ($p = 0.01$) were all significantly associated with fetal and early neonatal mortality. The odds of gestational period below 37 weeks, relative to gestational age of 37-42 weeks were higher for cases than controls (Adjusted Odds Ratio (AOR) = 16.6; 95% CI: 8.2-33.7). The odds of having 0-1 antenatal visits relative to 2-3 visits were higher for cases than controls (AOR = 5.4; 95% CI: 2.0-14.7). Compared to controls, cases had lower odds of having four or more antenatal visits relative to 2-3 visits (AOR = 0.3; 95% CI: 0.1-0.7); and having a birth attendant who was a doctor rather than a midwife (AOR = 0.4; 95% CI: 0.2-0.8).

Maternal obstetric complications associated with fetal and early neonatal mortality at MTRH are shown in Table 2. PROM, haemorrhage, and dystocia were significantly associated with mortality. Compared with the controls, the cases had higher odds of maternal PROM (AOR = 5.9; 95% CI: 3.5-9.9; $p < 0.001$), dystocia (AOR = 1.9; 95% CI: 1.2-3.1; $p = 0.01$), and haemorrhage (AOR = 2.4; 95% CI: 1.2-4.7; $p = 0.02$). Cases had higher odds of other complications compared with controls (AOR =2.0; 95% CI: 1.0-3.9; $p = 0.06$) although the difference was not significant.

Table 3 shows the association between neonatal complications with fetal and early neonatal mortality at MTRH.

Table 1 Association between maternal and obstetric factors with fetal and early neonatal death at MTRH from Jan 2005-Mar 2011

Predictor (95% CI)	Cases n (%)	Controls n (%)	Unadjusted OR	Adjusted OR (95% CI)	p-value for likelihood ratio test
Age in years					0.98
15-24	97 (51)	195 (49)	1.0	1.0	
25-34	68 (35)	172 (43)	0.8 (0.5-1.2)	1.1 (0.5-2.3)	
35-45	27 (14)	33 (8)	1.6 (0.9-2.9)	1.1 (0.3-4.0)	
Gravidity					0.26
Multigravida	108 (54)	231 (58)	1.0	1.0	
Primigravida	58 (29)	119 (30)	1.0 (0.7-1.5)	0.8 (0.4-1.9)	
Grandmultigravida	34 (17)	50 (12)	1.5 (0.9-2.4)	2.3 (0.8-6.6)	
Qualification of birth attendant					0.01
Midwife	142 (74)	191 (50)	1.0	1.0	
Doctor	50 (26)	187 (49)	0.4 (0.2-0.5)	0.4 (0.2-0.8)	
Gestational age at admission					<0.001
<37 weeks	116 (72)	74 (20)	11.0 (7.1-17.2)	16.6 (8.2-33.7)	
37-42 weeks	39 (24)	274 (75)	1.0	1.0	
> 42 weeks	6 (4)	15 (4)	2.8 (1.0-7.7)	2.4 (0.4-13.4)	
Mode of delivery					0.79
Normal	146 (73)	249 (62)	1.0	1.0	
Assisted	9 (5)	13 (3)	1.2 (0.5-2.8)	1.5 (0.3-7.9)	
45 (22)		138 (35)	0.6 (0.4-0.8)	1.3 (0.5-3.1)	
Number of antenatal care visits					<0.001
0-1	31 (26)	15 (4)	5.9 (3.0-11.6)	5.4 (2.0-14.7)	
2-3	74 (63)	212 (59)	1.01	1.0	
Above 4	13 (11)	133 (36)	0.3 (0.1-0.5)	0.3 (0.1-0.7)	
Booking status					0.28
No	139 (79)	311 (80)	1.0	1.0	
Yes	38 (21)	80 (20)	0.9 (0.6-1.5)	0.9 (0.5-2.2)	

Reference category represented by 1.0.
Numbers may not add to total sample size due to missing values.

The odds of asphyxia (AOR 2.4; 95% CI: 1.6-3.6; p < 0.001), congenital malformation (AOR 2.9; 95% CI: 1.5-5.7; p = 0.01) and RDS (AOR 1.6; 95% CI: 1.1-2.4; p = 0.01), were higher for cases relative to controls. The odds of sepsis were marginally non-significantly lower for cases than controls (AOR = 0.7; 95% CI: 0.4-1.0; p = 0.06).

The association between neonatal characteristics and early neonatal mortality at MTRH is shown in Table 4. Baby's birth weight and Apgar score were significantly associated with mortality (p < 0.001 for both). Relative to controls, cases had higher odds of birth weight less than 2500 grams (AOR 6.6; 95% CI: 3.8-10.2) and an Apgar score of zero to six (AOR 13.4; 95% CI 7.3-24.8) rather than seven or above at five minutes.

Table 5 represents the final model combining factors from the four previous models. The odds of having a birth attendant who was a doctor versus a midwife were lower for cases relative to controls (AOR = 0.2; 95% CI: 0.1-0.6; p < 0.01). Cases, compared to controls, had higher odds of having mothers who had 0-1 antenatal visit relative to 2-3 visits (AOR = 4.5; 95% CI: 1.2-16.7; p = 0.03 overall). The odds of gestational age less than 37 weeks (AOR = 7.0; 95% CI 2.4-20.4) and above 42 weeks (AOR = 16.2; 95% CI 2.8-92.3), rather than 37-42 weeks were higher for cases relative to controls (p < 0.01). The odds of mothers with complications of PROM (AOR = 4.1; 95% CI: 1.4-12.1; p = 0.01), haemorrhage (AOR = 4.8; 95% CI: 1.1-21.9; p = 0.04) or dystocia (AOR = 3.6; 95% CI: 1.2-10.9; p = 0.02) were higher for cases relative to controls. Cases, compared to controls had higher odds of being born with congenital malformations (AOR = 6.3; 95% CI: 1.2-31.6; p = 0.04), and being born with Apgar scores of 0-6 (AOR = 26.4; 95% CI: 6.1-113.8; p < 0.001), rather than a score of above seven at five minutes.

Table 2 Association between maternal obstetric complications with fetal and early neonatal mortality at MTRH from Jan 2005-Mar 2011

Predictor	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value for likelihood ratio test
Premature rupture of membranes					<0.001
Yes	52 (26)	27 (7)	4.9 (2.9-8.0)	5.9 (3.5-9.9)	
No	148 (74)	373 (93)	1.0	1.0	
Dystocia					0.01
Yes	42 (21)	64 (16)	1.4 (0.9-2.2)	1.9 (1.2-3.1)	
No	158 (79)	336 (84)	1.0	1.0	
Pre-eclamspia					0.44
Yes	13 (7)	29 (7)	1.0 (0.5-1.8)	1.3 (0.7-2.7)	
No	187 (93)	371 (93)	1.0	1.0	
Haemorrhage					0.02
Yes	17 (9)	21 (5)	1.7 (0.9-3.3)	2.4 (1.2-4.7)	
No	183 (91)	379 (95)	1.0	1.0	
Other complications					0.06
Yes	16 (8)	22 (6)	1.5 (0.8-2.9)	2.0 (1.0-3.9)	
No	184 (92)	378 (94)	1.0	1.0	

Reference category for logistic regression represented by 1.0.
Other complications included: cardio respiratory diseases, previous scar, HIV, malaria, retained placenta, anaemia, abortion.
Numbers may not add to total sample size due to missing values.

Discussion

This study examined risk factors associated with fetal and early neonatal mortality at MTRH. Factors that were significantly associated with early neonatal mortality in adjusted analyses were: qualification of the birth attendant; gestational age; number of antenatal visits; maternal complication at birth (PROM, haemorrhage and dystocia); congenital malformations, and low Apgar scores at five minutes.

The odds of low ANC attendance (0-1 visit) were higher for cases relative to controls. This is possibly because fewer

Table 3 Association between neonatal complications with fetal and early neonatal mortality at MTRH from Jan 2005-Mar 2011

Predictor (95% CI)	Cases n (%)	Controls n (%)	Unadjusted OR	Adjusted OR (95% CI)	p-value for likelihood ratio test
Asphyxia					<0.001
Yes	73 (37)	74 (19)	2.5 (1.7-3.7)	2.4 (1.6-3.6)	
No	127 (63)	326 (81)	1.0	1.0	
Congenital malformation					0.01
Yes	21 (11)	18 (5)	2.5 (1.3-4.8)	2.9 (1.5-5.7)	
No	179 (89)	182 (95)	1.0	1.0	
Sepsis					0.06
Yes	37 (18)	125 (31)	0.5 (0.3-0.8)	0.7 (0.4-1.0)	
No	163 (82)	275 (69)	1.0	1.0	
Respiratory Distress syndrome					0.01
Yes	66 (33)	94 (24)	1.6 (1.1-2.3)	1.6 (1.1-2.4)	
No	134 (67)	306 (76)	1.0	1.0	
Other neonatal complications					0.50
Yes	32 (16)	79 (20)	0.8 (0.5-1.2)	0.9 (0.5-1.4)	
No	168 (84)	321 (80)	1.0	1.0	

Reference category for logistic regression represented by 1.0.
Other complications included: hypothermia, diarrhoea, jaundice, hypoglycaemia, meconium aspiration syndrome, sero-exposed.
Numbers may not add to total sample size due to missing values.

Table 4 Association between neonatal characteristics with fetal and early neonatal mortality at MTRH from Jan 2005-Mar 2011

Predictor	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value for likelihood ratio test
Baby's birth weight					<0.001
less than 2500 gms	133 (73)	116 (29)	6.6 (4.5-9.8)	6.6 (3.8-10.2)	
Above 2500 gms	49 (27)	282 (71)	1.0	1.0	
Baby's Apgar score					<0.001
0-6 at 5 mins	78 (49)	20 (5)	17.2 (10.0-29.8)	13.4 (7.3-24.8)	
7-10 at 5 mins	79 (50)	349 (95)	1.0	1.0	
Baby's sex					
Female	85 (44)	190 (48)	0.9 (0.6-1.3)	1.0 (0.6-1.7)	0.88
Male	105 (55)	208 (52)	1.0	1.0	

Reference category for logistic regression represented by 1.0.
Numbers may not add to total sample size due to missing values.

ANC visits can result in poorer supervision of the pregnancy and failure to prevent, detect, and manage maternal conditions during the pregnancy. These issues have been reported by other studies in developing countries [19,21]. Moreover, since reasons for low ANC attendance could include lack of education, lack of female empowerment, and poverty, these factors may also explain some of the relationship between ANC attendance and fetal and early neonatal mortality [22]. Additionally, recent research has indicated that timing of visits is more important in detecting complications than the number of visits [23], hence women who only had 0-1 visit may have been prompted by a problem with their pregnancy rather than continuous monitoring of the pregnancy. The timing of ANC was however not captured in our study.

Assistance from a doctor (consultant, registrar or medical officer intern) was protective against neonatal mortality. This finding is in agreement with other studies that have found the presence of a doctor at birth enhances appropriate management and reduces maternal and infant mortality [1,21,24]. Lack of emergency obstetric care increases the risk of neonatal mortality. This is because labouring mothers cannot always access appropriate health services.

Maternal complications that were risk factors for fetal and early neonatal mortality were: PROM, dystocia, and haemorrhage. Mothers with PROM have been previously shown to be more likely to deliver preterm babies than those without this condition, with both maternal and neonatal risk of infection higher for this group [25]. This is concerning as infections are the leading cause of neonatal death in Sub-Saharan Africa [1,10,25]. Dystocia (prolonged or obstructed labour) was also a significant risk factor for mortality and this is consistent with another study which found that dystocia may result in the fetus having asphyxia [26]. Haemorrhage can be rapidly fatal to both the mother and neonate before medical intervention can be instituted and it has been reported as one of the leading causes of neonatal mortality in developing countries [27].

Babies born before or after 37-42 weeks carry significant risks during, and immediately after delivery and may require intervention by doctors [4]. The majority of health facilities in Sub-Saharan Africa lack proper resuscitation equipment and neonatal intensive support units, and are thus unable to adequately manage neonates born prematurely [17,18,28]. Prematurity is among the top three major causes of neonatal death in developing countries because of slow progress in uptake of public health measures such as antenatal corticosteroids, and proper hygiene practices during child birth [3,5,28].

The study found that congenital malformation was significantly associated with mortality. This is consistent with another study that reported congenital malformation as one of the causes of death in developing countries [7]. The presence of congenital anomalies in newborns could be in part explained by the lack of adequate screening and detection of these conditions during the antenatal period. If this had occurred then it may have been possible to give patients and doctors opportunities to make decisions on interventions prior to birth [28-30]. Other pre-disposing factors for congenital anomalies are maternal socio-economic and nutritional status, the presence of maternal infections, and environmental exposure to hazardous agricultural chemicals which contribute to about one-third of the disease burden in Sub-Saharan Africa [31,32].

The majority of neonatal deaths in this study had poor Apgar scores at five minutes after birth. This is consistent with other studies that have found a high risk of asphyxia among babies born to mothers with poor nutritional status, lack of ANC, and haemorrhage [21,28,33]. Information on some Apgar scores was not recorded, perhaps because of lack of time between transfers from one ward to the other, especially when the neonates had to be rushed to the newborn unit for resuscitation. This is a possible

Table 5 Determinants of fetal and early neonatal mortality at MTRH from Jan 2005-Mar 2011

Predictor	Cases n (%)	Controls n (%)	Adjusted OR (95% CI)	LR test statistic x^2	Degrees of freedom	P value
Qualification of birth attendant				10.58	1	<0.01
Midwife	142 (74)	191 (50)	1			
Doctor	50 (26)	187 (49)	0.2 (0.1-0.6)			
Number of antenatal care visits				7.35	2	0.03
0-1	31 (26)	15 (4)	4.5 (1.2-16.7)			
2-3	74 (63)	212 (59)	1.0			
Above 4	13 (11)	133 (36)	0.5 (0.2-1.5)			
Gestational age at admission				19.72	2	<0.01
<37 weeks	116 (72)	74 (20)	7.0 (2.4-20.4)			
37-42 weeks	39 (24)	274 (75)	1.0			
> 42 weeks	6 (4)	15 (4)	16.2 (2.8-92.3)			
Premature rupture of membrane				6.38	1	0.01
No	148 (74)	373 (93)	1.0			
Yes	52 (26)	27 (7)	4.1 (1.4-12.1)			
Haemorrhage				4.09	1	0.04
No	183 (91)	371 (95)	1.0			
Yes	17 (9)	29 (5)	4.8 (1.1-21.9)			
Dystocia				5.08	1	0.02
No	158 (79)	336 (84)	1.0			
Yes	42 (21)	64 (16)	3.6 (1.2-10.9)			
Other maternal complications				0.47	1	0.49
No	184 (92)	378 (94)	2.0 (0.3-13.9)			
Yes	16 (8)	22 (6)	1.0			
Sepsis				0.3	1	0.58
No	163 (82)	275 (69)	1.0			
Yes	37 (18)	125 (31)	1.4 (0.5-3.9)			
Asphyxia				1.65	1	0.20
No	127 (63)	326 (81)	1.0			
Yes	73 (37)	74 (19)	0.4 (0.1-1.7)			
Respiratory Distress syndrome				0.05	1	0.82
No	134 (67)	306 (76)	1.0			
Yes	66 (33)	94 (24)	0.9 (0.4-2.3)			
Congenital malformation				4.14	1	0.04
No	179 (89)	182 (95)	1.0			
Yes	21 (11)	18 (5)	6.3 (1.2-31.6)			
Baby's birth weight				2.82	1	0.09
Above 2500 gms	49 (27)	282 (71)	1.0			
less than 2500 gms	133 (73)	116 (29)	2.4 (0.9-6.7)			
Baby's Apgar score				26.09	1	<0.001
7-10 at 5 mins	79 (50)	349 (95)	1.0			
0-6 at 5 mins	78 (49)	20 (5)	26.4 (6.1-113.8)			

Reference category for logistic regression represented by 1.0.
Numbers may not add to total sample size due to missing values.

reason for the high proportion of missing values, particularly for the cases, and this may have contributed to the wide confidence intervals for the estimates.

The findings of this study are not only important for MTRH, which is Kenya's second largest hospital, but also for the Ministry of Health (MOH) in Kenya. They highlight the importance of informing stakeholders about areas where services can be improved. These include, for example, training for newborn care, the provision of adequate supplies and equipment, the development of protocols for newborn management and regular criterion-based audits aimed at averting early neonatal mortality. Additionally, most recommendations from this study relate to education and advocacy, issues which are relevant to the broader community.

One major limitation of this study was that there was potential selection bias because only hospital births were included. The sample may not therefore be representative of all births in the region, because high risk women, or women who develop complications, may be more likely to deliver in hospitals. The proportion of Kenyan women who deliver in community health facilities reported in the literature is 42.8% [34]. Another potential limitation is that it was not possible to blind the data abstractors to case or control status. Also MTRH did not have checklists or protocols for hospital personnel regarding medical records. Time pressures on staff were substantial and there was high patient throughput. The doctor to patient ratio was approximately 1:5000. It is therefore likely that some information may have been omitted from patient records [35].

Conclusions

In conclusion, the risk factors for fetal and early neonatal mortality included: number of antenatal visits, gestational age, qualification of the birth attendant, mother's complication at birth (PROM, haemorrhage, dystocia), low Apgar scores at five minutes and congenital malformations. Interventions that focus on educating mothers on the importance of antenatal clinic attendance, as well as ensuring screening, detection, monitoring and management of maternal conditions during the antenatal period, could help reduce neonatal mortality rates.

Doctor attendance at birth and during emergencies is important and can help to ensure that the newborn survives beyond the first week of their life. There is a need to increase the availability of resuscitation equipment, train personnel in newborn care and develop and implement protocols and checklists to promote efficiencies in medical record information gathering and documentation. Accurate complete maternal and neonatal records are important for the delivery of care to both the mother and baby. Combining maternal and neonatal records is one way of assisting clinical management and also providing data for research.

This research offers some possible reasons for the high mortality among neonates in a tertiary institution in Kenya. The findings have relevance for both mothers and neonates. Further research into factors influencing the timing and uptake of antenatal care by women in the community, as well as the contribution of quality of care to neonatal mortality in health facilities, is needed.

Abbreviations

MTRH: Moi Teaching and Referral Hospital; PROM: Premature rupture of membranes; MDG: Millennium development goals; NBU: Newborn unit; BBA: Born before arrival; ANC: Antenatal care; HIV: Human immunodeficiency virus; RDS: Respiratory distress syndrome; MOH: Ministry of Health.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FY participated in all steps of the study including; design, implementation, data collection, analysis and writing. CD contributed to the study design, questionnaire design, sample size determination, data analysis, interpreting of results, manuscript preparation, and editing. JB contributed to the study design, data interpretation, revising the manuscript for intellectual content. JSW contributed to the study design, analysis and interpretation of data and editing the manuscript. PN contributed with study design and coordination of data collection, questionnaire design and data interpretation. All authors read and approved the final manuscript.

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Author details

[1]Department of Health Policy and Management, Moi University, College of Health Sciences, Eldoret 30100, Kenya. [2]Chair in Biostatistics, National Centre for Epidemiology and Population Health, Research School of Population Health, The ANU College of Medicine Biology and Environment, the Australian National University, Canberra, ACT, Australia. [3]Research Centre for Gender, Health and Ageing, University of Newcastle, Hunter Medical Research Institute, New Lambton Heights, NSW, Australia. [4]Department of Reproductive Health, Moi University, College of Health Sciences, Eldoret 30100, Kenya. [5]Conjoint Academic, Research Centre for Gender, Health and Ageing, University of Newcastle, Newcastle, Australia. [6]Research Engineer, Umeå Centre for Global Health Research, Unit of Epidemiology and Global Health, Department of Public Health and Clinical Medicine, Faculty of Medicine, Umeå University, Umeå, Sweden.

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A1.4 Statements of contribution from each author

Statement of contribution

I, Julie Byles, attest that Research Higher Degree candidate Faith Yego contributed to the listed papers/publications by conducting and writing- up the literature review, contributing to the collection of data, undertaking the statistical analysis, description and interpretation of results and writing discussion and conclusions to the following publications:

List of publications included as part of the thesis

Yego, F., Stewart Williams, J., Byles, J., Nyongesa, P., Aruasa, W., DEste, C. (2013). "A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya." Reprod Health **10** (13).

Yego, F., DEste, C., Byles, J., StewartWilliams, J., Nyongesa, P. (2013). Risk factors associated with maternal mortality in a tertiary hospital in Kenya. Awaiting acceptance of revised manuscript for publication in BMC Pregnancy and Childbirth

Prof. Julie Byles (Co-author) Date: 5/12/13

Faith Yego (Candidate) Date: 5/12/13

Prof. Robert Callister
(Asst. Dean Research and Training) Date: 10.12.2013

Statement of contribution of others

I, Wilson Aruasa, attest that Research Higher Degree candidate Faith Yego contributed to the listed papers/publications by conducting and writing- up the literature review, contributing to the collection of data, undertaking the statistical analysis, description and interpretation of results and writing discussion and conclusions to the following publications:

List of publications included as part of the thesis

Yego, F., Stewart Williams, J., Byles, J., Nyongesa, P., Aruasa, W., DEste, C. (2013). "A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya." Reprod Health **10** (13).

Dr. Wilson Aruasa (Co-author) Date: 28/11/2013

Faith Yego (Candidate) Date: 2/12/2013

Prof. Robert Callister (Asst. Dean Research and Training) Date: 10·12·2013

Statement of contribution of others

I, Paul Nyongesa, attest that Research Higher Degree candidate Faith Yego contributed to the listed papers/publications by conducting and writing- up the literature review, contributing to the collection of data, undertaking the statistical analysis, description and interpretation of results and writing discussion and conclusions to the following publications:

List of publications included as part of the thesis

Yego, F., Stewart Williams, J., Byles, J., Nyongesa, P., Aruasa, W., DEste, C. (2013). "A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya." Reprod Health **10** (13).

Yego, F., DEste, C., Byles, J., StewartWilliams, J., Nyongesa, P. (2013). Risk factors associated with maternal mortality in a tertiary hospital in Kenya. Accepted for publication in BMC Pregnancy and Childbirth

Dr. Paul Nyongesa (Co-author) Date: 28/11/2013.

Faith Yego (Candidate) Date: 2/12/2013

Prof. Robert Callister (Asst. Dean Research and Training) Date: 10.12.2013

Statement of contribution

I, Catherine D'Este, attest that Research Higher Degree candidate Faith Yego contributed to the listed papers/publications by conducting and writing- up the literature review, contributing to the collection of data, undertaking the statistical analysis, description and interpretation of results and writing discussion and conclusions to the following publications:

List of publications included as part of the thesis

Yego, F., Stewart Williams, J., Byles, J., Nyongesa, P., Aruasa, W., D'Este, C. (2013). "A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya." Reprod Health **10** (13).

Yego, F., D'Este, C., Byles, J., StewartWilliams, J., Nyongesa, P. (2013). Risk factors associated with maternal mortality in a tertiary hospital in Kenya. Awaiting acceptance of revised manuscript for publication in BMC Pregnancy and Childbirth

Prof. Catherine D'Este (Co-author) Date: 5/12/2013

Faith Yego (Candidate) Date: 5/12/2013

Prof. Robert Callister
(Asst. Dean Research and Training) Date: 10.12.2013

Statement of contribution of others

I, Jennifer Stewart Williams, attest that Research Higher Degree candidate Faith Yego contributed to the listed papers/publications by conducting and writing- up the literature review, contributing to the collection of data, undertaking the statistical analysis, description and interpretation of results and writing discussion and conclusions to the following publications:

List of publications included as part of the thesis

Yego, F., Stewart Williams, J., Byles, J., Nyongesa, P., Aruasa, W., DEste, C. (2013). "A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya." Reprod Health **10** (13).

Yego, F., DEste, C., Byles, J., Stewart Williams, J., Nyongesa, P. (2013). Risk factors associated with maternal mortality in a tertiary hospital in Kenya. Accepted for publication in BMC Pregnancy and Childbirth

Dr. Jennifer Stewart Williams (Co-author) Date: 25/11/13

Faith Yego (Candidate) Date: 14/12/2013

Prof. Robert Callister (Asst. Dean Research and Training) Date: 10.12.13

Appendix 2: Study Approvals

A2.1 Ethics approval

HUMAN RESEARCH ETHICS COMMITTEE

Notification of Expedited Approval

To Chief Investigator or Project Supervisor:	**Professor Catherine d'Este**
Cc Co-investigators / Research Students:	**Professor Julie Byles** **Doctor Jennifer Stewart Williams** **Ms Faith Yego**
Re Protocol:	**Maternal and neonatal morbidity and mortality in Moi Teaching and Referral Hospital, Kenya: assessing the role of referrals in averting Maternal Morbidity and Mortality**
Date:	**17-Dec-2010**
Reference No:	**H-2010-1251**
Date of Initial Approval:	**16-Dec-2010**

Thank you for your **Response to Conditional Approval** submission to the Human Research Ethics Committee (HREC) seeking approval in relation to the above protocol.

Your submission was considered under **Expedited** review by the Chair/Deputy Chair.

I am pleased to advise that the decision on your submission is **Approved** effective **16-Dec-2010**.

In approving this protocol, the Human Research Ethics Committee (HREC) is of the opinion that the project complies with the provisions contained in the National Statement on Ethical Conduct in Human Research, 2007, and the requirements within this University relating to human research.

Approval will remain valid subject to the submission, and satisfactory assessment, of annual progress reports. *If the approval of an External HREC has been "noted" the approval period is as determined by that HREC.*

The full Committee will be asked to ratify this decision at its next scheduled meeting. A formal *Certificate of Approval* will be available upon request. Your approval number is **H-2010-1251**.

If the research requires the use of an Information Statement, ensure this number is inserted at the relevant point in the Complaints paragraph prior to distribution to potential participants You may then proceed with the research.

Conditions of Approval

This approval has been granted subject to you complying with the requirements for *Monitoring of Progress*, *Reporting of Adverse Events*, and *Variations to the Approved Protocol* as detailed below.

PLEASE NOTE:
In the case where the HREC has "noted" the approval of an External HREC, progress reports and reports of adverse events are to be submitted to the External HREC only. In the case of Variations to the approved protocol, or a Renewal of approval, you will apply to the External HREC for approval in the first instance and then Register that approval with the University's HREC.

- ***Monitoring of Progress***

Other than above, the University is obliged to monitor the progress of research projects involving human participants to ensure that they are conducted according to the protocol as approved by the HREC. A progress report is required on an annual basis. Continuation of your HREC approval for

this project is conditional upon receipt, and satisfactory assessment, of annual progress reports. You will be advised when a report is due.

- ***Reporting of Adverse Events***

1. It is the responsibility of the person **first named on this Approval Advice** to report adverse events.
2. Adverse events, however minor, must be recorded by the investigator as observed by the investigator or as volunteered by a participant in the research. Full details are to be documented, whether or not the investigator, or his/her deputies, consider the event to be related to the research substance or procedure.
3. Serious or unforeseen adverse events that occur during the research or within six (6) months of completion of the research, must be reported by the person first named on the Approval Advice to the (HREC) by way of the Adverse Event Report form within 72 hours of the occurrence of the event or the investigator receiving advice of the event.
4. Serious adverse events are defined as:
    - Causing death, life threatening or serious disability.
    - Causing or prolonging hospitalisation.
    - Overdoses, cancers, congenital abnormalities, tissue damage, whether or not they are judged to be caused by the investigational agent or procedure.
    - Causing psycho-social and/or financial harm. This covers everything from perceived invasion of privacy, breach of confidentiality, or the diminution of social reputation, to the creation of psychological fears and trauma.
    - Any other event which might affect the continued ethical acceptability of the project.

5. Reports of adverse events must include:
    - Participant's study identification number;
    - date of birth;
    - date of entry into the study;
    - treatment arm (if applicable);
    - date of event;
    - details of event;
    - the investigator's opinion as to whether the event is related to the research procedures; and
    - action taken in response to the event.

6. Adverse events which do not fall within the definition of serious or unexpected, including those reported from other sites involved in the research, are to be reported in detail at the time of the annual progress report to the HREC.

- ***Variations to approved protocol***

If you wish to change, or deviate from, the approved protocol, you will need to submit an *Application for Variation to Approved Human Research*. Variations may include, but are not limited to, changes or additions to investigators, study design, study population, number of participants, methods of recruitment, or participant information/consent documentation. **Variations must be approved by the (HREC) before they are implemented** except when Registering an approval of a variation from an external HREC which has been designated the lead HREC, in which case you may proceed as soon as you receive an acknowledgement of your Registration.

Linkage of ethics approval to a new Grant

HREC approvals cannot be assigned to a new grant or award (ie those that were not identified on the application for ethics approval) without confirmation of the approval from the Human Research Ethics Officer on behalf of the HREC.

Best wishes for a successful project.

Professor Alison Ferguson

Chair, Human Research Ethics Committee

For communications and enquiries:

Human Research Ethics Administration

Research Services
Research Office
The University of Newcastle
Callaghan NSW 2308
T +61 2 492 18999
F +61 2 492 17164
Human-Ethics@newcastle.edu.au

Linked University of Newcastle administered funding:

Funding body	Funding project title	First named investigator	Grant Ref

A2.2 Letter of approval for the study

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke

P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2007

4th August, 2009

Ms. Faith Yego & Team,
Moi University,
School of Public Health,
P.O. Box 4606-30100,
ELDORET.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:

"An Assessment of the Appropriateness of Promptness of Referrals from Peripheral Hospitals to Moi Teaching and Referral Hospital in Averting Maternal Morbidity and Mortality".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

PROF. H.N.K. Arap MENGECH
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
APPROVED
04 AUG 2009
P.O. Box 4606, ELDORET

CC - Deputy Director (CS)
- Chief Nurse
- HOD, HRISM

A2.3 Advisor approvals

SCHOOL OF MEDICINE & PUBLIC HEALTH
CENTRE FOR CLINICAL EPIDEMIOLOGY & BIOSTATISTICS

JOHN HALL

Associate Professor

Level 3, David Maddison Clinical Sciences Building
University of Newcastle, University Drive, CALLAGHAN 2308

Telephone: +61 (0)2 49138811
Facsimile: +61 (0)2 49138148

e-mail: John.Hall@newcastle.edu.au

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

22 February 2011

To whom it may concern

This is to certify that Faith Yego is a Research Higher Degree Student with the University of Newcastle, Australia and as part of her PhD she is conducting research at hospitals throughout Kenya .

Dr. Paul Nyongesa is a Clinical advisor for this research from the Department of Reproductive Health at Moi University. His role will be to advise on the clinical issues related to maternal and neonatal mortality and also to assist with reviewing records of participants especially on the obstetric issues.

John Hall
Associate Professor
Acting Deputy Head of School (Public Health)

SCHOOL OF MEDICINE & PUBLIC HEALTH
CENTRE FOR CLINICAL EPIDEMIOLOGY & BIOSTATISTICS

JOHN HALL

Associate Professor

Level 3, David Maddison Clinical Sciences Building
University of Newcastle, University Drive, CALLAGHAN 2308

Telephone: +61 (0)2 49138811
Facsimile: +61 (0)2 49138148

e-mail: John.Hall@newcastle.edu.au

THE UNIVERSITY OF
NEWCASTLE
AUSTRALIA

22 February 2011

To whom it may concern

This is to certify that Faith Yego is a Research Higher Degree Student with the University of Newcastle, Australia and as part of her PhD she is conducting research at hospitals throughout Kenya .

Dr. Wilson Aruasa is a Clinical advisor for this research from the Moi Teaching and Referral Hospital head of clinical Services.. His role will be to advise on the clinical issues related to maternal and neonatal mortality and to oversee the research process at the hospital.

John Hall
Associate Professor
Acting Deputy Head of School (Public Health)

Appendix 3: Study Questionnaire

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

Questionnaire for maternal and early neonatal mortality study at MTRH

Study ID _____

PT#_____

Individual Characteristics	
1.Age _____years / DOB ☐☐ DD ☐☐ MM ☐☐☐☐ YR	11. Source of funding for treatment ☐ Self ☐ Insurance ☐ other_____
2. Parity _____	12. Gestation _____weeks
3. Gravida _____	13. Gestation _____ days since delivery or abortion
4. Marital status ☐ Single ☐ married ☐ separated ☐ divorced	14. History of drug use ☐ Yes ☐ No
5. Residence _____	15. History of smoking ☐ Yes ☐ No
6. Level of education (mother) ☐ none ☐ primary ☐ secondary ☐ tertiary	16. History of alcohol use ☐ Yes ☐ No
7. Level of education (spouse) ☐ none ☐ primary ☐ secondary ☐ tertiary	17. History of contraceptive use ☐ Yes ☐ No
8. Occupation (mother) ☐ unemployed ☐ housewife ☐ trader ☐ public servant ☐ farmer ☐ other _____	18. Previous twins ☐ Yes ☐ No
9. Occupation (spouse) ☐ unemployed ☐ trader ☐ public servant ☐ farmer ☐ other _____	19. Previous abortion ☐ Yes ☐ No
10. Religious affiliation ☐ Christian ☐ Traditional ☐ Muslim ☐ other_____	20. History of underlying disease (tick all that apply) ☐ Infections _____ ☐ None ☐ cardiovascular disease ☐ tuberculosis ☐ psychiatric illness_____ ☐ epilepsy ☐ diabetes ☐ other_____

Questionnaire for maternal and early neonatal mortality study at MTRH

Study ID _____

Obstetric characteristics	
21. Date of last delivery ☐☐ DD ☐☐ MM ☐☐☐☐ YR	35. Maternal complication on admission (tick all that apply) ☐ antepartum haemorrhage ☐ ruptured uterus ☐ postpartum haemorrhage ☐ sepsis _____ ☐ pre-eclampsia ☐ obstructed labour ☐ post-abortal complication ☐ other_____ ☐ none
22. Arrival time ☐☐☐☐ am/pm	
23. Date of admission ☐☐ DD ☐☐ MM ☐☐☐☐ YR	36. Mode of delivery ☐ spontaneous vertex delivery ☐ assisted delivery ☐ operative delivery
24. Time of initial review ☐☐☐☐ am/pm	37. Gestational age on admission _____ weeks
25.Date of delivery ☐☐ DD ☐☐ MM ☐☐☐☐ YR	38. Pregnancy stage on admission ☐ antepartum ☐ intrapartum ☐ puerperium ☐ ectopic pregnancy ☐ abortion
26. Time of delivery ☐☐☐☐ am /pm	
27. LMP ☐☐ DD ☐☐ MM ☐☐☐☐ YR 28. EDD ☐☐ DD ☐☐ MM ☐☐☐☐ YR	39. Labour stage ☐ latent ☐ active (established) ☐ second stage
29. Vital signs on admission 30. Blood pressure _____mm/HG 31. Temperature_____◦C 32. Pulse _____beats/min 33. Respiration_____/min 34. HB _____gm/dl	40. Complication during or post admission (tick all that apply) ☐ none ☐ haemorrhage ☐ anaesthesia ☐ sepsis/infections ☐ embolism ☐ obstructed labour ☐ ectopic pregnancy ☐ hypertensive diseases ☐ other _____

Questionnaire for maternal and early neonatal mortality study at MTRH

Study ID _____

Obstetric characteristics

41. Procedures done for treatment of haemorrhage complications
☐Yes ☐No (tick all that apply below)
- ☐ Blood transfusion
- ☐ Surgery
- ☐ Administration of parenteral oxytoxic drugs
- ☐ Removal of retained products
- ☐ Manual removal of placenta

42. Procedures done for prevention of haemorrhage complications (Active management of Third Stage Labour/AMTSL)
☐ Yes ☐ No

43. Procedures done for pre-eclampsia/eclampsia
☐ Yes ☐ No (tick all that apply below)
- ☐ Administration of parenteral anticonvulsants
- ☐ Surgery/caesarean section
- ☐ Induction of labour

44. Procedures done for ectopic pregnancy
☐ Yes ☐ No (tick all that apply below)
- ☐ Surgery (laparatomy/laparoscopic)
- ☐ Blood transfusion
- ☐ Conservative management

45. Other procedures performed other than above
- ☐none
- ☐other_____

46. Outcome of baby at birth
- ☐ Alive ☐ baby not born
- ☐ fresh stillbirth ☐ fetal heart rate present
- ☐ macerated stillbirth
- ☐ neonatal death

47. Baby's birth weight _____ grams/ _____ kgs

48. Apgar score at 5 minutes ____/10

49. Date of neonatal death
☐☐ DD ☐☐ MM ☐☐☐☐ YR

50. Time of neonatal death ☐☐☐☐ am /pm

51. Baby's gender at birth ☐ Male ☐ Female

52. Outcome of mother
☐Alive ☐dead

53. Date of maternal death
☐☐ DD ☐☐ MM ☐☐☐☐ YR

54. Time of maternal death ☐☐☐☐ am /pm

55. Term of neonatal death
- ☐ Fresh stillborn (intrapartum)
- ☐ Macerated stillborn (ante partum)
- ☐ Neonatal death (post partum)

56. Babies complication (tick all that apply)
- ☐ Asphyxia ☐ Hypothermia
- ☐ Pre-term baby ☐ Diarrhoea
- ☐ Pneumonia ☐ Low birth weight
- ☐ Neonatal tetanus
- ☐ Congenital (birth defect)
- ☐ Sepsis (specify)_____
- ☐ Other (specify)_____

57. Discharge date
☐☐ DD ☐☐ MM ☐☐☐☐ YR

58. Baby's condition on discharge
- ☐ Alive
- ☐ Dead within 24 hours
- ☐ unknown

Questionnaire for maternal and early neonatal mortality study at MTRH

Study ID _____

Antenatal Care and Referral characteristics

59. Place of ANC booking
- ☐ home
- ☐ clinic
- ☐ health centre
- ☐ district hospital
- ☐ provincial hospital
- ☐ MTRH
- ☐ Faith Based Hospital
- ☐ private hospital
- ☐ other_____

63. Referral ☐Yes ☐No

64. Referral note present ☐Yes ☐No

60. Number of previous antenatal visits
- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4
- ☐ >4
- ☐ None

65. Referred by
- ☐ doctor (specialist)
- ☐ medical officer
- ☐ medical officer (intern)
- ☐ clinical officer (clerk)
- ☐ nurse
- ☐ midwife
- ☐ TBA
- ☐ other_____

61. Qualification of ANC attendant
- ☐ doctor (specialist)
- ☐ medical officer
- ☐ medical officer (intern)
- ☐ clinical officer (clerk)
- ☐ nurse
- ☐ midwife
- ☐ TBA
- ☐ other_____

66. Type of facility referred from
- ☐ self/home
- ☐ clinic
- ☐ health centre
- ☐ district hospital
- ☐ provincial hospital
- ☐ Faith Based Hospital
- ☐ private hospital

Name of hospital _____

62. Qualification of birth attendant (tick all that apply)
- ☐ doctor (specialist)
- ☐ medical officer
- ☐ medical officer (intern)
- ☐ clinical officer (clerk)
- ☐ nurse
- ☐ midwife
- ☐ TBA
- ☐ other_____

Appendix 4: Letter from MTRH

An ISO 9001:2008 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: (+254)053-2033471/2/3/4
Fax: 2061749
Email: director@mtrh.or.ke

NANDI ROAD
P.O Box 3 - 30100
ELDORET, KENYA

Ref:.....ELD/MTRH/D.T2/VOL.II/2012

14th January, 2014

Dr. Faith Yego & Research Team
Moi University, School of Public Health
P.O. Box 4606
ELDORET
Tel: 0701-079203

Dear Dr Yego,

QUALITY CARE CONTRIBUTION OF THE STUDY "A RETROSPECTIVE ANALYSIS OF MATERNAL AND NEONATAL MORTALITY AT A TEACHING AND REFERRAL HOSPITAL IN KENYA" AT MOI TEACHING AND REFERRAL HOSPITAL

The above study covered the period January 2004 to December 2011.

Its objective was to measure the incidence of maternal and early neonatal mortality on women who gave birth at Moi Teaching and Referral Hospital (MTRH) in Kenya and describe clinical and other characteristics and circumstances associated with maternal and neonatal deaths following deliveries at MTRH.

The overall maternal mortality ratio in this study was 426 per 100,000 live births and the early neonatal mortality rate (<7 days) was 68 per 1000 live births. Half (51%) of neonatal mortalities were for young mothers (15-24 years) and 64% of maternal deaths were in women between 24 and 45 years. Most maternal and early neonatal deaths occurred in multiparous women, in referred admissions, when the gestational age was under 37 weeks and in latent stage of labour. Indirect complications accounted for the majority of deaths. Where there were direct obstetric complications associated with the delivery, the leading cause of maternal

death was eclampsia and the leading cause of early neonatal death was premature rupture of membranes. Preterm birth and asphyxia were the leading causes of early neonatal deaths. Majority of the deliveries were vaginal and performed by midwives.

This study, covering an 8-year period, was the first comprehensive audit of maternal and neonatal deaths at MTRH.

The study has contributed a lot in terms of Practice and Policy Formulation, both within MTRH and outside, including at the national level.

Some of the key contributions include:

<u>In MTRH</u>

(1) Introduction of Criterion-Based Clinical Audits to gauge the actual practice by midwives and obstetricians with regards to specific causes of maternal mortality such as Pre-eclampsia/eclampsia, ante- and post-partum haemorrhage.

(2) Development of over 30 Clinical Protocols, covering all the major causes of maternal morbidity and mortality.

(3) Strengthening of maternal and perinatal mortality reviews by forming strong Maternal Mortality Committee and Perinatal Mortality Committee.

(4) Training of all midwives, registrars and obstetricians on Emergency Obstetric and Neonatal Care through the Advances in Labour and Risk Management (ALARM) courses.

(5) Opening up of 2 theatres dedicated for caesarean sections.

(6) Regular purchase of basic equipment such as laboratory equipment (uristicks), sphygmomanometers, thermometers, etc.

<u>Nationality</u>

(1) Training of midwives in the Western half of Kenya (MTRH's catchment area) on ALARM causes. Over 1000 have been trained to-date.

(2) Written feedback to all referring hospitals regarding maternal/neonatal outcomes of patients referred to MTRH.

(3) On-the site supportive supervision of referring hospitals- inspection of their structures, processes and outcomes with adequate corrective measures.

(4) This paper formed part of the Kenya National Government's deliberations towards implementation of Government - Sponsored Free Maternity Services. These services aim at offering delivery services and neonatal care services at the Government cost. Implemented since 1st June, 2013, the services has seen the number of deliveries at MTRH more than double since then.

We would like to sincerely thank you and your team for choosing MTRH as your study site and we would ask that we continue partnering for the purpose of improving services to our clients.

Yours

DR. WILSON K. ARUASA
DEPUTY DIRECTOR, CLINICAL SERVICES