Pregnancy and perinatal health outcomes in Northern Tanzania: a registry based study

Neonatal care admissions and recorded causes of neonatal and perinatal deaths

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Contributors

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List of Abbreviations

ANC	Antenatal care
BMI	Body mass index
DHS	Demographic and Health Survey
END	Early neonatal death
HIC	High income countries
KCMC	Kilimanjaro Christian Medical Centre
LBW	Low Birth weight
IMCI	Integrated Management of childhood illness
LMIC	Low and Middle Income Countries
MBR	Medical Birth Registry
MDG	Millennium Developmental Goals
NCU	Neonatal Care Unit
NICE	Neonatal and Intrauterine deaths Classification according to Etiology
NMR	Neonatal mortality rate
PMR	Perinatal mortality rate
SB	Stillbirth
SBR	Stillbirth rate
PROM	Prolonged rupture of membrane
UNICEF	United Nations Children's Fund
WHO	World Health Organization

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Abstract

Introduction: Globally, more than 3 million neonatal deaths occur each year of which 75% during first week of life (early neonatal deaths). In addition there are 3.2 million stillbirths of which 1 million are intrapartum related stillbirths. Global trends show a decline in under-five deaths, whereas, neonatal mortality and in particular mortality during the first week, remain unchanged. Hence, the share of under-five deaths that occur during the neonatal period has increased. It is unlikely to achieve the Millennium development goal on child survival without a substantial reduction in neonatal mortality.

Aims: This thesis aimed at identifying risk factors for neonatal morbidity and causes of neonatal and perinatal deaths in a high risk setting.

Methods: A total of 21206 singleton live births registered at the Kilimanjaro Christian Medical Centre Medical Birth Registry (KCMC-MBR) from July 2000 to August 2008 were studied (paper **I**). Multivariable analysis with generalized linear models was carried out in 3 steps to study the relationship of transfer to neonatal care unit by 1) pre-pregnancy conditions, 2) pregnancy, labour and delivery complications, and 3) neonatal conditions. The recorded causes of neonatal deaths (paper **II)** and causes of perinatal deaths (paper **III**) were studied using KCMC-MBR and a neonatal registry data from July 2000 to October 2010. A total of 5033 neonates were admitted to the neonatal care unit. Clinical diagnosis, gestational age, birth weight, Apgar score and date of admission and discharge were registered. Recorded causes of neonatal deaths were classified by the Wigglesworth classification. Recorded causes of perinatal deaths were classified according to the Neonatal and Intrauterine death Classification according to Etiology (NICE), aimed at identifying underlying cause of death. SPSS 15.0 (paper **I**), 18.0 (paper **II)** and 19.0 (paper **III**) were used for analysis.

Results: The incidence of newborn transfer to neonatal care unit was 15% (3190) (paper **I**). Socio demographic factors were weakly associated with transfer to neonatal care unit, with relative risks below 1.5. Among maternal health conditions, pre

pregnancy diabetes and eclampsia were strongly associated with transfer (RRs 4.7), followed by gestational diabetes (RR 3.1). Among pregnancy and labour complications, abruption placenta (RR 4.4) and PROM (RR 3.9) were the strongest risk factors of transfer. Neonatal transfer was strongly associated with conditions of the baby such as birth weight above 4000 g, birth weight below 1500 g or 1500-2500g (RR=7.2, 9.8 and 4.3, respectively), 5-minutes Apgar score less than 7 (RR=6.9) and gestational age <34 weeks or 34-36 weeks (RR=5.6 and 2.2, respectively). Associations with most pre pregnancy and pregnancy related factors disappeared after accounting for neonatal factors in a multivariable model, whereas the effects of neonatal factors remained strong in the multivariable analysis.

Leading causes of admission to the neonatal care unit were birth asphyxia (26.8%), prematurity (18.4%), risk of infection (16.9%), neonatal infection (15.4%), and birth weight above 4000 g (10.7%), (paper **II**). Overall neonatal mortality was 10.7% (536 deaths). The leading single causes of neonatal death were birth asphyxia 245 (45.7%), prematurity 188 (35.1%), congenital malformations 49 (9.1%), and infections 46 (8.6%). Babies with birth weight below 2500 g constituted 29% of all admissions and 52.1% of all deaths. Except for congenital malformations, case fatality declined with increasing birth weight. Birth asphyxia was the most frequent cause of death in normal birth weight babies (n=179/246, 73.1%) and prematurity in low birth weight babies (n=178/188, 94.7%). The majority of deaths; 304 (56.7%) occurred within 24 hours, and 490 (91.4%) within the first week.

Overall perinatal mortality was 57.7/1000 births (paper **III**). Major recorded causes of perinatal mortality were *unexplained asphyxia* (12.5/1000), *obstetric complications* (8.9/1000), *maternal disease* (8.5/1000), *unexplained antepartum stillbirths* after 37 weeks of gestation (6.5/1000), and *unexplained antepartum stillbirths* before 37 weeks of gestation (5.4/1000). Among *obstetric complications*, obstructed/prolonged labour was the leading condition (82.8%). Among deaths caused by *maternal disease*, preeclampsia/eclampsia was the leading condition (88.2%). After excluding women who were referred for delivery at KCMC due to medical reasons, overall perinatal

mortality was reduced to 45.6/1000 births. This reduction was mainly due to fewer deaths from *obstetric complications* (from 8.9 to 2.1/1000) and *maternal disease* (from 8.5 to 5.5/1000).

Conclusion: We found that neonatal factors were strongly associated with transfer to neonatal care unit. Also some pre-pregnancy and pregnancy-related factors were predictors of neonatal transfer, but these factors were only weakly associated with neonatal transfer when the condition of the baby was accounted for (paper **I**). Birth asphyxia and prematurity were the leading recorded causes of early neonatal deaths in a neonatal care unit. Birth asphyxia in normal birth weight and prematurity in low birth weight babies each accounted for one third of all deaths (paper **II**). Perinatal mortality was high in this setting with the leading recorded causes of death being *unexplained asphyxia*, *obstetric complications*, *maternal disease*, and *unexplained stillbirths* (paper **III**). Obstructed/prolonged labour and preeclampsia/eclampsia were the major conditions among the *obstetric complications* and *maternal disease*, respectively, with the highest risks for babies of medically referred mothers. Although this systematic use of registry data may not uncover all the underlying causes of the perinatal deaths, we suggest that the findings indicate potential areas for targeting interventions to reduce perinatal deaths. Possible areas of prevention may include strengthening antenatal care screening for pregnancy related risks, reorganization of referral system to allow timely access to obstetric care, monitoring of labour, and neonatal care.

List of original papers

I. Mmbaga BT, Lie RT, Kibiki GS, Olomi R, Kvåle G, Daltveit AK: **Transfer of newborns to neonatal care unit: a registry based study in Northern Tanzania**. *BMC Pregnancy and Childbirth* 2011, **11**:68

II. Mmbaga BT, Lie RT, Olomi R, Mahande MJ, Kvåle G, Daltveit AK: **Cause-specific neonatal mortality in a neonatal care unit in Northern Tanzania: a registry based cohort study**. *BMC Pediatrics* 2012, **12**:116

III. Mmbaga BT, Lie RT, Kibiki GS, Olomi R, Olola O, Daltveit AK: **Causes of perinatal deaths at a tertiary care hospital in Northern Tanzania 2000-2010: a registry based study**. *BMC Pregnancy and Childbirth* 2012, **12**:139

In this thesis each paper will be referred by a roman number as paper **I**, **II** and **III**.

1 Introduction

1.1 Background

The target for the fourth Millennium development goal (MDG4) was to reduce under five mortality rate (U5MR) by two thirds from 1990 by the end of 2015 [1-4]. This is equivalent to an annual reduction of 4.4% [5]. Globally, there has been a decline in under-five deaths but with no or low reduction of neonatal deaths, and the share of under-five deaths that occur during the neonatal period increased from 37% in 2000 [6] to more than 40% during the last decade [7-9]. Globally, about 3.3 million neonatal death occurred in 2009 [8] declining to 3.1 million in 2010 [9, 10]. Close to 50% of the neonatal deaths occur within the first 24 hours of life and three quarter within the first week [1, 11]. A further 3 million babies are stillborn [12], of which at least 1 million die during labour [13]. In most countries where the under-five mortality has declined, the reduction has mainly been in children after first month of life, whereas neonatal mortality and in particular first week mortality remain unchanged, **Figure 1** [3, 14, 15]. The slow decline in neonatal mortality has increased attention to the contribution of neonatal deaths in achieving the MDG4 [5].

Globally, less than 5% of neonatal deaths [1] and only 2% of stillbirths [12] are estimated to occur in high income countries, where vital registration has been implemented for registration of all births and deaths. Since the vast majority of deaths occur in developing countries, where vital registration is limited [1], the global burden of neonatal deaths is mainly based on statistical modelling from public health surveillance such as Demographic and Health Surveys (DHS) reports [1, 8, 16].

This study was designed to describe risk factors for neonatal morbidity and causes of perinatal and neonatal deaths at a tertiary care hospital in Northern Tanzania, by using data from the Kilimanjaro Christian Medical Centre Medical Birth Registry (KCMC-MBR) and neonatal registry. The study was structured to answer three key questions:-

1. What are the socio-demographic, maternal and newborn factors associated with newborn transfer to neonatal care unit in a high risk setting? (**Paper I**)
2. What are the causes of admission and cause-specific neonatal mortality in this setting? (**Paper II**)
3. What are the causes of perinatal mortality in this setting? (**Paper III**)

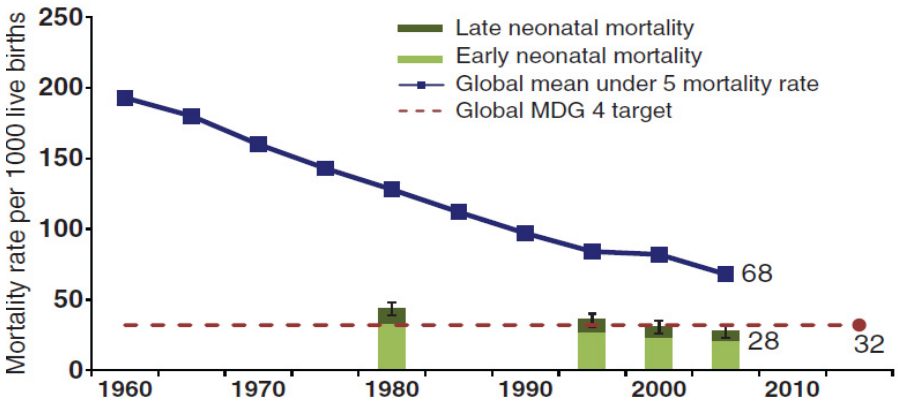

Figure 1: Progress towards MDG4 for child survival 1960-2010

Source: Lawn et al 2009 [15].

1.1.1 Epidemiology of under-five deaths

Globally, it is estimated that 7.6 million children under the age of five died in 2010 [9, 10, 16, 17] declining to 7.2 million in 2011 [18]. More than 98% are from developing countries [8], and the majority of deaths are from preventable and easily treatable disease conditions [19]. Worldwide, major causes of under-five deaths are pneumonia (18%), preterm birth complications (14%), diarrhoea (11%), intrapartum related complications (9%) and malaria (7%) [10, 20] (**Figure 2**). Globally, the under-five

mortality rate declined by 35 per cent from 88 per 1000 live births in 1990 to 57 in 2010 [9, 17], whereas the global share of under-five deaths that occur during the neonatal period increased, from 36% in 1990 to about 43% in 2011 [20].

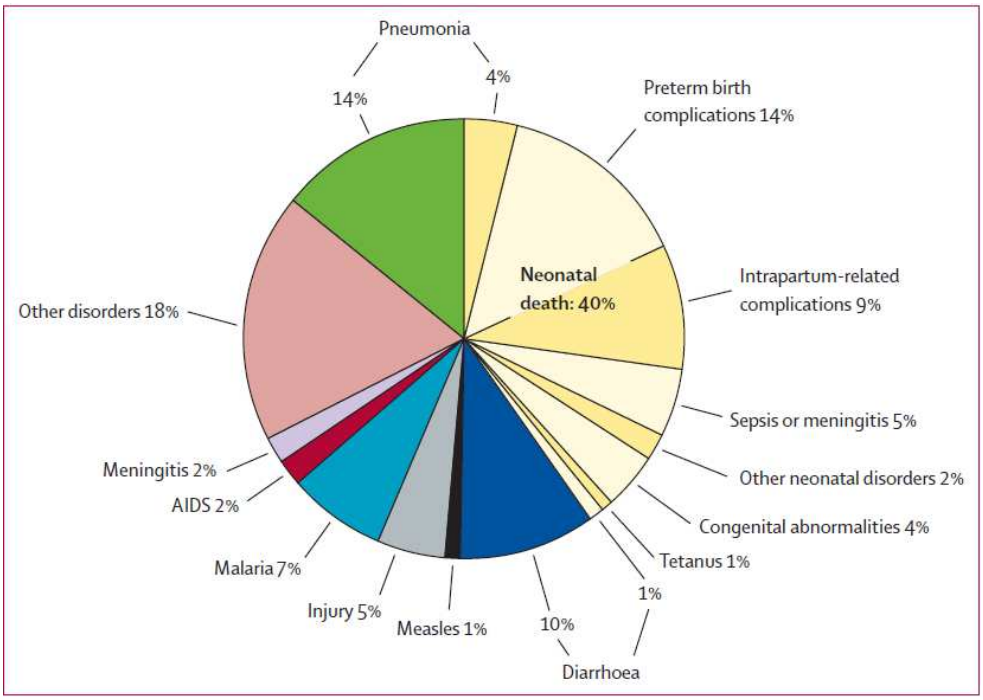

Figure 2: Global causes of under-five deaths in 2010

Source: Liu et al 2012 [10].

In Sub-Saharan Africa, 4.4 million children under five years of age die each year, which is equivalent to 50% of the world's under-five deaths [21, 22]. Since 2000 there has been a reduction in under-five mortality in some African countries, however slow for early neonatal deaths [15]. By 2010, Sub Saharan Africa has achieved a 30 per cent under-five mortality reduction which is less than half of what is required to reach the MDG 4 [9, 17]. The fraction of global under five deaths from sub Saharan Africa increased from 33% in 1990 to 49% in 2010 [17, 18]. In Africa it is estimated that more than 73% of the under-five deaths are caused by infections [10].

Tanzania is among the countries with the highest under five mortality rate, currently estimated to 81/1000 births [23]. A 24% reduction in under-five deaths was observed since the year 2000; from 147 /1000 live births in 2000 to 112 in 2004 [24, 25], and a further 28% reduction to 81 in 2010 [23]. Simultaneously, the proportion of under-five deaths that occurred during the neonatal period increased from 27% in 2000 to 33% in 2010 (**Figure 3**). The remarkable decline in post-neonatal deaths may be attributed to improvements in Tanzania's health system, including doubled public expenditure on health, decentralisation and sector-wide basket funding, increased coverage of key child-survival interventions, such as IMCI, insecticide-treated nets, vitamin A supplementation, immunisation, and exclusive breastfeeding [25, 26].

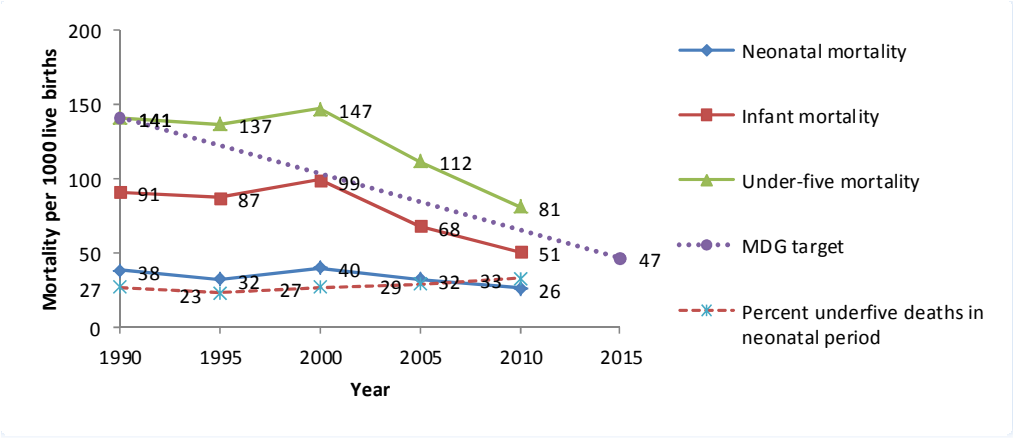

Figure 3: Trend in child mortality in Tanzania 1990 to 2010

Data source: TDHS 1992, TDHS 1996, TRCH 1999, TDHS 2004-5 and TDHS 2010 [23, 24, 27-29].

1.1.2 Epidemiology of perinatal deaths

The WHO-ICD 10 defines perinatal death as a stillbirth (SB) from 22 completed weeks of gestational age (birth weight equivalent to 500 g) or death of a live born

infant during the first week of life (early neonatal death, END) [30]. For international comparisons the WHO recommends birth weight ≥ 1000 g or gestational age ≥28 weeks as cut off point for foetal death [12, 30]. Globally, approximately 5.9 million perinatal deaths occur each year, of which 3.2 million stillbirths and 2.7 million early neonatal deaths [31]. The highest burden of perinatal deaths is in developing countries which account for about 98% of world's perinatal deaths [12, 31, 32]. Worldwide, perinatal mortality is about 47/1000 births, ranging from 10 in most developed countries to more than 60 in least developed countries [32]. Africa has the highest estimated perinatal rate of 62/1000 births, despite a high number of unregistered stillbirths and early neonatal deaths [2].

Several definitions of perinatal mortality exist within countries and regions based on birth weight, gestational age and birth length [12, 33]. Birth weight is considered more reliable and is prioritized over gestational age. Estimated perinatal mortality in sub Saharan African countries will depend on cut-off point used for definition, study type and study area [34-52] (**Table 1)**.

Table 1: Summary of selected studies on perinatal mortality in Africa

Author (year)	Country	Number deliveries	Study area (period and duration)	Study tittle	Definition	PMR (per 1000 births)
Fawole et al (2011) [34]	Nigeria	9208	Cross sectional survey 21 health facilities (Oct 2004-Feb 2005)	Determinant of perinatal mortality in Nigeria	≥500 g or GA ≥22 weeks	78.6
Tachiweyika et al (2011) [35]	Zimbabwe	5485 (3242 + 2243)	Marondera district (Aug 2008 to July 2009)	Determinant of perinatal mortality in Marondera district, Mashonaland East Province Zimbabwe, 2009: a case control study	> 22 weeks	61.1 (58.6-64.6)
Ekure et al (2011) [36]	Nigeria	603	Lagos University teaching hospital (June 2002-Nov 2002)	Prospective audit of perinatal mortality among stillborn babies in a tertiary health center in Lagos, Nigeria	≥500 g	84.6
Ibekwe et al (2011) [37]	Nigeria	7678	Ebony state university hospital	Perinatal mortality in Southern Nigeria. Less than half a	≥28 weeks	62.7

			(Jan 2004-Dec 2005)	decade to the Millennium developmental goals		
Nankabirwa et al (2011) [38]	Uganda	835	Mbale district, community study (Jan 2006-Sept 2007)	Perinatal mortality in Eastern Uganda: A community based prospective cohort study	≥28 weeks	40.7
Mbaruku et al (2009) [39]	Tanzania	10200	Regional hospital in western Tanzania (July 2002-July 2004)	Perinatal Audit using the 3 delays in Western Tanzania	>2000 g	38
Metaferia et al (2009) [40]	Malawi	10,700	Queen Elizabeth Central Hospital, Blantyre-Malawi (Feb 2004-Oct 2005)	Stillbirths and hospital early neonatal deaths at Queen Elizabeth Central Hospital, Blantyre-Malawi	≥ 20 weeks or 500 g	78.9
Habib et al (2008) [41]	Tanzania	14934 singletons	Kilimanjaro Christian medical Centre (Feb 1999-May 2006)	Social demographic characteristics and perinatal mortality among singletons in North East Tanzania. a registry-based study	≥500 g	41.1
Feresu et al (2005) [42]	Zimbabwe	17072	Harare Maternity Hospital (Oct 1997- Sept 1998)	Incidence of stillbirth and perinatal mortality and their associated factors among women delivering at Harare Maternity Hospital, Zimbabwe: a cross-sectional retrospective analysis	≥500 g	56
Kuti et al (2003) [43]	Nigeria	5050	Wesley Gild Teaching Hospital, Nigeria (Jan 1996-Dec 2000)	Analysis of perinatal Mortality in a Nigerian Teaching hospital	Not given	77.03
Weiner et al (2003) [44]	Kenya	910	Kilifi district hospital (Jan 1996-Jul 1997)	Labour complications remain risk factors for perinatal deaths	Not given	118
Hinderaker et al (2003) [45]	Tanzania	3512	Haydom Lutheran Hospital (Jan 1995-March 1996)	Perinatal mortality in Northern rural Tanzania	≥28 weeks	27
Iriya et (2002) [46]	Tanzania	2088	Hai district-Kilimanjaro (July 1996-June 1997)	Verbal autopsy in establishing cause of perinatal deaths	Not given	58
Elamin et al (2002) [47]	Sudan	2260	Omdurman maternity hospital	Classification of perinatal death in a developing country	≥1000 g or	73.5

			(May –Aug 2000)		≥28weeks	
Naidu et al 2001 [48]	South Africa	7789	King Edward VIII hospital (6 months)	Clinico-pathological study of causes of perinatal mortality in a developing country	500 g	59
Aisien et al (2000) [49]	Nigeria	4135	Jos University teaching hospital (Jan 1992 –Dec 1993)	Two years prospective study of perinatal mortality in Jos, Nigeria	Not given	89
Kidanto et al (1999) [50]	Tanzania	77815	Muhimbili National Hospital (1999-2003)	Analysis of perinatal mortality at a teaching hospital in Dar-es-salaam, Tanzania, 1999-2003	≥500 g	124
Walvaren et al (1995) [51]	Tanzania	447	Kwimba district-community (1990)	Perinatal mortality in home births in rural Tanzania	≥1000 g, ≥28 wks	68

1.1.3 Epidemiology of stillbirths

Globally, more than 3.2 million stillbirths occur each year [12, 31, 33]. Higher rates (98%) are estimated to come from low and middle income countries (LMIC) where coverage of vital registration is low [33, 53]. Only about 2% of all stillbirths are counted from countries with vital registration systems [12, 53]. The stillbirth rate is up to 32/1000 births in LMIC whereas, in high income countries (HIC) is less than five per 1000 births [54]. Sub Saharan Africa has the highest stillbirth rate (32/1000 births) [12, 54]. In HIC, improved intrapartum care and adequate interventions during labour have led to a marked reduction in labour related stillbirths [54, 55]. Worldwide, more than two third of all stillbirths occur in rural families without skilled birth attendant and without access to adequate delivery care such as caesarean section [56]. Stillbirths are not included in the MDG goals, in WHO routine mortality data, in most population-based surveys, or in most vital registration systems [12, 56].

Stillbirths are classified into 2 types i) antepartum (macerated) stillbirths where death occurs before the onset of labour or more than 12 hours prior to delivery, accounting for nearly two third of all stillbirths, and ii) intrapartum (fresh) stillbirths where death occurs after the onset of labour and less than 12 hours before birth, accounting for about one third of all stillbirths [13, 33, 57]. The risk of intrapartum stillbirth is about 24 times higher for an African woman (living in a low income country) as compared

to a woman living in a high income country [56]. Macerated stillbirths can be identified from foetal appearance after birth where signs of disintegration such as soft skull, darkly stained amniotic fluids and peeling off or discoloured can be observed, whereas fresh stillbirths show intact skin and no signs of maceration or disintegration [13].

1.1.4 Causes of stillbirths

The most important causes of stillbirths in LMIC include obstructed or prolonged labour, hypertensive disease of pregnancy, syphilis, gram-negative infection, malaria in endemic areas, and maternal undernutrition [54]. Most intrapartum stillbirths are associated with obstetric complications and are closely linked to place of delivery and care during delivery [56, 58], whereas antepartum stillbirths are associated with maternal infection and foetal growth restriction [56]. In HIC, foetal and maternal infection contribute to about 10-25% of all stillbirths; this proportion is expected to be higher in LMIC [59, 60]. Other important causes of stillbirth include congenital malformations, abruption placenta, asphyxia, and cord accidents [59, 60].

1.1.5 Epidemiology of neonatal deaths

The neonatal period is defined as the interval from birth to 28 completed days of life. Globally, about 3.3 million neonatal death occurred in 2009 [8] declining to 3.1 million in 2010 [9, 10]. Three quarters of all neonatal deaths occur during the first week of life and up to 50% within the first 24 hours [1, 11, 31], (**Figure 4**). Estimated neonatal mortality rate (NMR) worldwide ranges from 4 per 1000 live births in HIC countries to 31 per 1000 live births in LMIC countries [1, 3, 31]. The majority (99%) of neonatal deaths are from LMIC [1, 5, 61]. The global estimate of NMR has declined by 28% from 32 per 1000 births in 1990 to 23 in 2010, which is equivalent to an annual average decline of 1.7% [8, 9]. The slow progress in reduction of neonatal mortality has led to increased attention to the newborn health agenda within countries and at the global level [3, 5, 11]. The analysis by Hill et al found that while the rate of

reduction in neonatal mortality is slower than for maternal and under-five mortality, the pace has been accelerated since 2000 [17, 62].

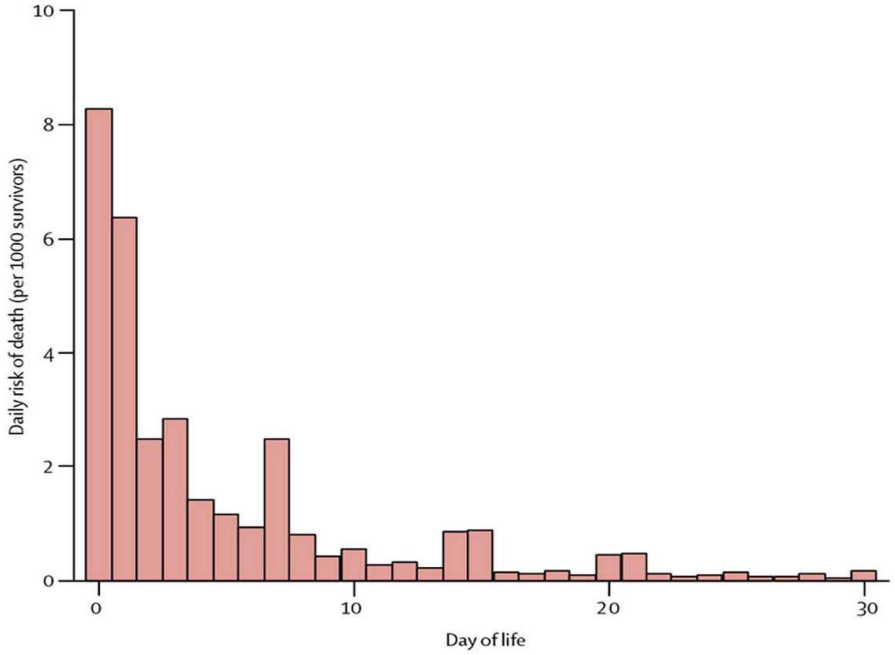

Figure 4: Daily risk of neonatal death during first month of life based on 47 DHS dataset (1995-2003)

Source: Lawn et al 2005 [1].

Africa accounts for 11 per cent of the world's population but have more than 25 per cent of the world's neonatal deaths [21]. Between 1990-2010, NMR dropped by nearly 50% in some regions of the world, whereas, in Africa NMR dropped only by 19%; from 43 per 1000 live births in 1990 to 35 in 2010 [9]. Sub Saharan Africa accounts for more than a third of global neonatal deaths [9]. Declines in late neonatal mortality are faster than declines in early neonatal mortality overall and across all the regions; however the declines are not significant in sub Saharan region [63]. To achieve the Millennium Developmental Goal 4 more efforts and attention is needed in LMIC [1, 8].

In Tanzania 51,000 newborns die each year, accounting for one third of the under-five deaths [26]. In line with global results, the decline in neonatal mortality has been slow; from 35 per 1000 live births in 1990 [24] to 26/1000 births in 2010 [23]. This is equivalent to an annual reduction of 1.3% and less than half of the MDG 4 requirement.

1.1.6 Causes of neonatal deaths

Worldwide, major causes of neonatal death are preterm birth complications "Preterm", intrapartum-related deaths "Asphyxia" and neonatal sepsis or pneumonia "Infection" [1, 10] (**Figure 5**). Deaths due to prematurity and asphyxia dominate the first three days, and deaths due to infection dominate thereafter [3]. The three causes infection, complication of preterm birth, and birth asphyxia together account for nearly 90% of all neonatal deaths [15, 21, 22, 61]. This pattern reflects causes in LMIC [2, 64], while in HIC where mortality is low, preterm birth and congenital malformations are major causes [2].

Preterm birth and related complications is the leading direct cause of neonatal death with around 1.1 mill deaths each year, which makes it the second leading cause of under-five mortality, after pneumonia [10, 20, 65]. Preterm birth also acts as a risk factor for mortality due to other causes, particularly infection [65, 66].

Intrapartum related neonatal deaths (previously denoted birth asphyxia) contribute to around 0.9 mill neonatal deaths each year, which is about 10% of all under-five deaths [13]. The majority of intrapartum related neonatal deaths occur within 24 hours and nearly all within first week of life [67] (see **figure 6**). The causes of intrapartum related neonatal deaths and intrapartum related stillbirths are similar, and are closely linked to maternal complications during labour and delivery, place of delivery, and care given [22, 61, 67-69]. The majority of intrapartum related deaths can be prevented with proper maternal and newborn care.

Infection is a major cause of neonatal mortality, and globally sepsis/pneumonia contribute to 26% of all neonatal deaths [1]. In developing countries infection is

estimated to cause 40% of all neonatal deaths [70]. A review of 32 community based studies in developing countries , suggested that neonatal infection is responsible for 8-80% of all neonatal deaths and as many as 42% of all deaths in the first week of life [71]. A review of 63 studies in developing countries indicated that within first week of life major pathogens are *Klebsiella species*, *Escherichia coli*, *Staphylococcus aureus* and Group B streptococci (GBS) [72]. After the first week of life, *Staphylococcus aureus*, GBS, *Streptococcus pneumonia* and nonthyphoidal *Salmonella* are the most frequent. Risk factors for infection in newborns include lack of antenatal care, maternal infection, premature rupture of membrane, poor hygiene during delivery and cord care, low birth weight, prematurity and delays in recognition of danger signs in both mother and baby [71]. Early identification and treatment of maternal infection, clean delivery and early treatment of newborns with infection or suspected infection by antibiotics reduce mortality related to infection.

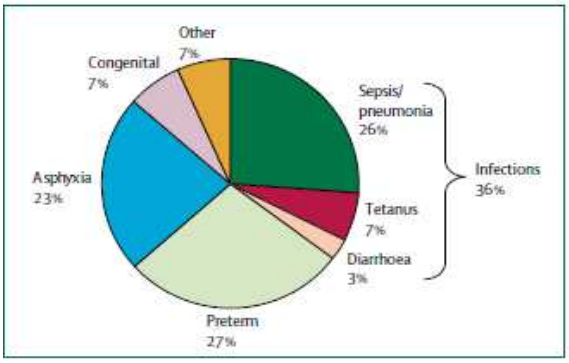

Figure 5: Distribution of direct global causes of neonatal deaths for the year 2000

Source: Lawn et al 2005 [1].

Figure 6: Timing of intrapartum related neonatal deaths based on community studies in rural Nepal

Source: Lawn et al [67].

In Tanzania, the three major causes of neonatal deaths are sepsis/pneumonia (28%), preterm and related complications (27%) and birth asphyxia (26%) (**Figure 7**) [21, 26]. In hospital based studies [50, 73, 74], birth asphyxia and prematurity are the leading causes of neonatal deaths.

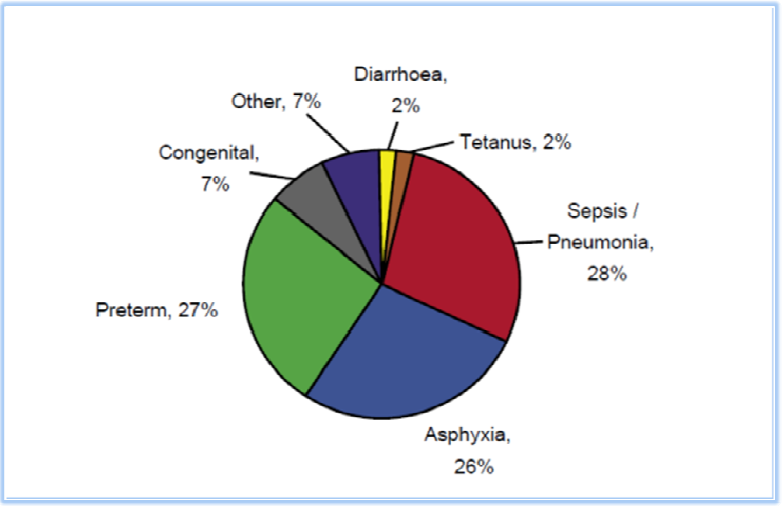

Figure 7: Estimated causes of neonatal death in Tanzania

Source: Manji et al 2009 [26].

1.2 Factors contributing to peri- and neonatal morbidity and mortality

Parental social and demographic characteristics, some maternal diseases, poor antenatal care, complications during labour and delivery, and neonatal conditions are known risk factors of neonatal morbidity and mortality.

1.2.1 Social and demographic characteristics

Social deprivation is associated with poor perinatal outcome such as neonatal care admission [75-79], low birth weight [76, 78, 80, 81] and perinatal mortality [41, 45, 49, 81, 82]. In Tanzania, neonatal mortality is 67% higher in the poorest families compared to better-off families [24, 26]. In developing countries, associations between low social status and poor pregnancy outcome may be due to inadequate access to health care, malnutrition, infection, poor maternal health and a high fertility rate in poor families. Maternal characteristics such as short stature and undernutrition have independent adverse effects on pregnancy outcome such as labour complications

related to cephalopelvic disproportion in women with short stature [83], low birth weight related to intrauterine growth restriction in underweight women [83-85] and perinatal mortality in both conditions [41, 44]. Maternal short stature may be a result of social deprivation during childhood [83], and can therefore be viewed as a socio-economic factor. Other maternal characteristics associated with perinatal morbidity and mortality include; birth to the first child [38, 41, 49, 75], high birth order [34, 41, 45, 49, 86], single marital status [87, 88], teenage mother [34, 89, 90], and maternal age above 35 years [34, 41, 42, 49, 86, 87]. Also paternal characteristics are associated with poor pregnancy outcome, such as low or no education, and unskilled/low skilled worker [41, 77].

1.2.2 Maternal health conditions

Maternal hypertensive disorders such as hypertension before pregnancy, pregnancy-induced hypertension, and preeclampsia/eclampsia increase the risk of preterm delivery, low birth weight, intrauterine growth restriction and perinatal death [66, 89, 91-98]. In developing countries where detection and treatment is limited, it is estimated that the risk of perinatal death after a preeclamptic pregnancy is about 13%, increasing to 28% if the woman develops eclampsia [2].

Pre-gestational and gestational diabetes are known risk factors for neonatal morbidity [75, 99], and stillbirth [100]. Maternal overweight and obesity increase the risk of high birth weight (>4000g), neonatal care admission [101-108], and stillbirth [102-104]. Complications associated with maternal obesity include gestational diabetes and preeclampsia [101, 102, 104-107]. A systematic review and meta-analyses indicated that in obese women there is an increased risk of preterm delivery after induction or caesarean section due to pregnancy complications [109].

In developing countries, a significant proportion of perinatal morbidity and mortality is related to maternal infections such as malaria [85, 110-113], HIV-infection [113-115], and syphilis [85, 113, 116]. A review of infectious disease in pregnancy, found that syphilis, HIV, malaria, toxoplasmosis and bacterial infections are important

causes of stillbirths in developing countries whereas, in developed countries, ascending bacterial infections are the major infectious causes of stillbirths [113]. As for HIV the risk of perinatal deaths increases with untreated or unscreened HIV infection [114]. Similarly, for syphilis the risk of foetal death is high for unscreened [116] or untreated women [117], whereas screened and treated women have no increased risk [85]. A meta-analysis on malaria and perinatal mortality concluded that the risk of stillbirth is higher in the presence of placental malaria [111].

1.2.3 Antenatal care

ANC is a good entry for screening and counselling during pregnancy, and has a potential to improve both maternal and foetal health [118]. ANC visits can be used for addressing other health care needs such as family planning, immunization, tetanus, HIV and malaria prevention, screening for HIV and other infections, and screening and care for diabetic and hypertensive disorders. They also represent an opportunity for women to learn danger signs related to hypertensive disorders and other pregnancy related complications, and an opportunity to encourage women to deliver at a health facility [2, 64, 119]. In a DHS review from 19 countries, women with the recommended number of ANC visits were more aware of danger signs and more often delivered in a health facility [119]. Despite the fact that 96% of the women in a study from Tanzania had attended ANC, less than 50% had attended the recommended number of 4-8 visits, and less than 50% recalled having been counselled on any of the danger signs [24, 120]. The high attendance to ANC combined with poor knowledge might indicate limited quality of ANC with respect to counselling on danger signs.

1.2.4 Complications during labour and delivery

Obstructed/prolonged labour occurs in 3 to 6 per cent of the pregnancies, is estimated to be responsible for 8% of all maternal deaths worldwide [121], and increases the risk of developing asphyxia, birth trauma and perinatal deaths [35, 39, 44, 67, 86, 89, 122, 123]. Premature rupture of membrane (PROM) defined as rupture of membrane before onset of labour occurs in 10% of the pregnancies and increases the risk of preterm

delivery and related complications [124], low birth weight [99, 125], neonatal care admission [99, 126], and perinatal deaths due to sepsis [44, 124, 126, 127]. Consequences of complications are more serious in settings with poor monitoring of labour and in settings without proper emergency obstetric care [39, 57, 86, 128]. A study in a setting with limited resources, indicated that the risk of perinatal death was eight and 13 fold after obstructed/prolonged labour and premature rupture of membrane, respectively [44]. As for PROM, also maternal antibiotic prophylaxis before delivery is important to reduce risk of neonatal sepsis or respiratory distress syndrome [129, 130].

1.2.5 Neonatal conditions

Low birth weight is a result of preterm birth or intrauterine growth restriction, and is estimated to be an underlying factor in about 60-80% of all neonatal deaths [1]. Although birth weight is a predictor of adverse neonatal outcome, the causal relationship between low birth weight and neonatal outcome is questioned [131]. Globally, 15% of babies are born with low birth weight (<2500g) [61, 132]. Preterm birth (<36 weeks) and related complications is responsible for more than 1 million newborn deaths each year and the rate are increasing [65]. Multiple births are at high risk of perinatal morbidity and mortality [32, 34, 86, 133-135]. High birth weight babies (>4000g) are at risk of birth trauma, asphyxia, hypoglycaemia, neural tube defect and neonatal care admission. Babies born with low Apgar score are at risk of developmental disorders and perinatal mortality [50]. Breech or other abnormal presentation increases risk of morbidity and mortality due to birth injury and brain hypoxia as compared to cephalic presentation [34, 49, 86]. In general, male risk of morbidity and mortality exceeds female risk due to biology, preterm delivery and neonatal factors [136]. A review of DHS from developing countries indicated that on average, boys are 28% more likely to die in their first month of life as compared to girls [134].

1.3 Birth registration, perinatal audit and classification of perinatal death

1.3.1 Birth registration and its relevance in epidemiology

In developing countries nearly 90% of children under five are unregistered at birth as compared to only 2% in developing countries [137]. In many developing countries, for example in Sub-Saharan Africa, registration is done mainly for births that occur in health facilities, and there are differences in registration between urban and rural areas [137]. Reporting on disease burden from developing countries is therefore mainly based on Demographic and Health Surveys (DHS) reports, whereas for international estimates mainly statistical modelling are used [8, 19]. In health surveys, some important indicators of child mortality such as birth weight are not well recorded as many babies born at home are not weighted at birth, or due to poor maternal recall [138]. From DHS reports it is indicated that an average of 49-58% of infants are not weighed at birth [137, 138].

In developed countries where vital registration of births and deaths is well established, it is possible to conduct continuously epidemiological surveillance and epidemiological clinical research to understand factors influencing perinatal health outcomes, including health services [139].

In Tanzania birth registration is compulsory and is supposed to cover most of the country. However, because of weaknesses in the vital registration system, Tanzania is among countries in which population and household surveys represent major sources of health information [140]. According to household survey statistics provided by UNICEF in 2005, over 90 per cent of children in Tanzania are unregistered at 5 years of age [137]. The Tanzania DHS 2010 indicated that only 16% of children under five of age are registered of whom about half receive a birth certificate [23]. Children whose mother received medical assistance during delivery are more likely to be registered (14.4%) as compared to children whose mother delivered outside health

facilities (1.9%) [137]. Birth registration is higher in urban areas where 44% of children are registered as compared to 10% in rural areas [23].

Reasons for non-registration in LMIC include too much cost for birth registration, long travelling distance to the registration place, lack of knowledge among the parents about registration, fear of paying fine for late registration and not knowing where to register [137]. Socio-economic characteristics related to non-registration include poverty, home based delivery, birth with unskilled birth attendant, rural residence and long distance to health care facility [137].

1.3.2 Perinatal audit

Perinatal audit is defined as the systematic critical analysis of quality of perinatal care, including procedures used for diagnosis and treatment, the use of resources, and the outcome and quality of life for women and their babies [141]. The aim of perinatal auditing is to identify deficiencies and suggest improvements [141, 142]. Audit of maternal and perinatal deaths can be performed at different levels [143]; by simply recording the number of deaths in an area, by categorizing cause of death, or by identifying potentially avoidable factors or suboptimal care [143]. The use of standard classifications can be helpful in identifying important factors [141]. A meta-analysis by Pattison et al [141] found that after introducing facility based perinatal auditing in low and middle income countries, perinatal mortality declined by 30%.

1.3.3 Classification of perinatal deaths

Several classification systems for stillbirths and perinatal deaths have been designed [144-148]. However, no single system is universally accepted and each has its strengths and weaknesses [149, 150]. Most of the classifications have been designed to include both stillbirths and early neonatal deaths [149]. A general problem is to identify etiological causes for stillbirths, hence many cases remain unexplained [149, 150]. In this thesis we used the Wigglesworth classification of perinatal and neonatal deaths [144] and the Neonatal and Intrauterine Classification of death according to

Etiology (NICE) [145, 151] for classification of cause of neonatal and perinatal deaths, respectively.

2 Rationale of the study

The progress towards Millennium Development Goal 4 (MDG4) in developing countries has been slow. Worldwide, under-five mortality shows a decline in all regions, but the reduction has mainly been for post-neonatal mortality. Globally, birth asphyxia, prematurity, and infection are three major causes which contribute to nearly 90% of neonatal deaths. Although under-five mortality in Tanzania has declined since 2000, Tanzania is among six countries with the highest neonatal mortality in Sub Saharan Africa, and with a slow reduction in neonatal mortality as compared to post neonatal mortality. It is only possible to achieve the MDG4 in Tanzania if neonatal mortality, especially early deaths within first seven days of newborn life, is reduced. We aimed to identify risk factors for neonatal morbidity and causes of perinatal and neonatal deaths in a high risk setting in Northern Tanzania.

2.1 Study Objectives

2.1.1 Main objective

The study aimed to determine risk factors associated with neonatal morbidity and causes of neonatal and perinatal mortality at a tertiary care hospital in Northern Tanzania.

2.1.2 Specific objectives

Paper I

i. To estimate the incidence of newborn transfer to a neonatal care unit

ii. To estimate socio-demographic, maternal and newborn factors associated with newborn transfer to neonatal care unit

Paper II

iii. To estimate major causes of admission to a neonatal care unit and their case fatality

iv. To estimate cause specific neonatal mortality after transfer to neonatal care unit

Paper III

v. To estimate perinatal, stillbirth and early neonatal mortality rates in the selected setting

vi. To assess causes of perinatal death that could be relevant for aetiology and prevention

3 Material and methods

3.1 Study setting

This study was done at the Kilimanjaro Christian Medical Centre (KCMC) in the Kilimanjaro Region in Northern Tanzania. Kilimanjaro region is one of the four regions of Northern zone (**Figure 8**), with a population of nearly 1,4 million according to the 2002 population census [152]. Inhabitants of Kilimanjaro region are mainly Chagga, Pare and Kahe tribes. The KCMC hospital was established in 1971 as a non-profit organization owned by the Good Samaritan Foundation under the Evangelical Lutheran Church of Tanzania. KCMC is one of the four consultant/tertiary referral care hospitals in Tanzania and serves the northern zone; the others are Muhimbili National Hospital in the eastern zone; Bugando Medical Centre in the western zone; and Mbeya referral Hospital which serves the southern Highlands (**Figure 8**). Both consultant hospitals are teaching institutions for medical and paramedical courses and are the only one with specialized neonatal care units [26]. KCMC is a teaching hospital for the Kilimanjaro Christian Medical College and other Allied Health Science institutions.

The hospital has official capacity of 450 beds within several inpatient departments and serves as referral hospital for over 11 million people in Northern Tanzania. The annual number of deliveries is around 3500 of which nearly two thirds are from urban area, and nearly half of them are from Moshi urban. The caesarean section rate at the hospital ranges between 30-35%, of which emergency caesarean sections represent 80% [153, 154].

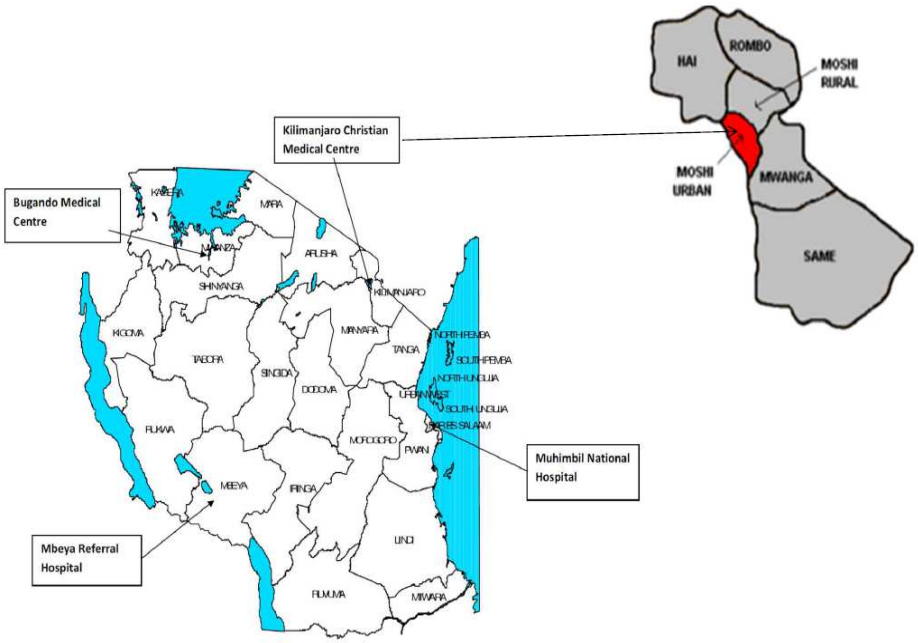

Figure 8: Location of the 4 referral hospitals with specialized neonatal care units and the Kilimanjaro region where KCMC is located

3.2 Source of data

This thesis was based on the data from the KCMC Medical Birth Registry (KCMC-MBR) and neonatal registry. The KCMC-MBR system was established in 1999 as a collaboration between Kilimanjaro Christian Medical College of the Tumaini university, Moshi, Tanzania and the University of Bergen. Officially the KCMC Medical Birth Registry started in July 2000.

3.3 Study subjects

The study population for paper I

The KCMC-MBR data from July 2000 to August 2008 was used. A total of 26 025 deliveries were recorded. Women living outside the urban area who were referred to deliver at KCMC for medical reasons and multiple deliveries, stillbirths, early neonatal

deaths in a labour ward and births with unknown status on survival were excluded. The study population was thus 21 206 singleton live births.

The study population for paper II and III

The KCMC-MBR data from July 2000 to October 2010 was used for paper **II** and **III**.

In paper **II**, we studied a total of 5033 neonates admitted to the neonatal care unit. Clinical diagnosis, gestational age, birth weight, Apgar score, and date of admission/discharge/death were recorded. Clinical diagnoses were recorded in text and up to three diagnoses were recorded. We coded all clinical diagnoses independently. A neonate having more than one diagnosis was recorded in different categories in order to study all causes of admission, case fatality and their contribution to total neonatal mortality. Each neonatal death was classified in a hierarchical order by the modified Wigglesworth classification into one of the five single causes of death groups; 1) congenital malformation 2) prematurity 3) birth asphyxia 4) infection and 5) other causes of death.

In paper **III**, we studied 33 929 neonates of at least 500g, of which 1958 died perinatally. The causes of perinatal deaths were identified and classified using the Neonatal and Intrauterine deaths Classification according to Etiology (NICE) (see **Table 3)**. We performed analyses stratified according to presence or absence of a medical condition as reason for referral. **Table 2** shows a summary of data used and study subjects included in papers **I**, **II** and **III**.

Table 2: Summary of study subjects included in papers I, II and III

	Year of Registry data	Registry used	Total deliveries	Exclusion criteria	Study outcome	Analysis	Sample size
Paper I	July 2000-August 2008	MBR and neonatal registry	26 025	-Medical referral from rural areas -Multiple birth -Missing child status	Transfer to NCU	Generalized linear models	21 206 3190 (15%) transferred
Paper II	July 2000-October 2010	MBR and neonatal registry	34 087	Non admitted neonates	-Deaths in a NCU -Causes of neonatal deaths classified by Wigglesworth classification	Descriptive statistics	5033 neonates admitted (536 neonatal deaths)
Paper III	July 2000-October 2010	MBR and neonatal registry	34 087	Birth weight <500g	-Perinatal deaths -Causes of perinatal deaths classified by NICE classification	Descriptive statistics	33 929 births, (1958 perinatal deaths)

3.4 Data collection

Data collection for the KCMC-MBR was done by midwife nurses who conducted interviews on all eligible subjects using a standardized questionnaire **(Appendix 1)** within 24 hours after delivery or later, depending on the mother's condition in case of a complicated pregnancy. Verbal informed consent was obtained from mothers prior to the interview. The interviews were done on a daily basis including public holidays and weekends. A verbal consent was obtained from the participants prior to the interview. In addition to the interview, the hospital medical records were reviewed and mothers also provided their antenatal (ANC) visit card **(Appendix 2)** for more information. Information collected during the interviews and/or from hospital records includes socio-demographic characteristics, maternal health conditions before pregnancy, during pregnancy and complications during labour and delivery, and pregnancy outcomes such as maternal and newborn health status after birth **(Appendix 1)**.

Information obtained from the ANC card includes; maternal health during pregnancy, HIV status, VDRL result, malaria and anaemia prophylaxis, blood pressure and haemoglobin records during ANC visits **(Appendix 2)**. Detailed information on data collection for the KCMC-MBR has been previously reported [155].

We also used data from the paediatric/neonatal registry form (**Appendix 3**) which is recorded for all neonates delivered at KCMC and transferred to the neonatal care unit. A paediatric nurse working in the neonatal care unit registered all transferred newborns at admission and finalized the record at discharge/death. Information collected in the neonatal registration form includes; primary reasons for transfer, sex, date of birth and admission, management and treatment given, clinical discharge diagnoses and death reports. The form also includes a field for post mortem report to confirm cause of death. Since post mortem examinations are not routinely done due lack of resources, this information is missing.

Data were entered into a Microsoft Access database and checked for quality assurance. The KCMC-MBR and the neonatal registry can be linked using the unique child identification number. In addition, the mother's hospital registration number, baby's birth date together with newborn's birth registration number recorded in both databases can be used for linkage.

3.5 Statistical methods

Descriptive statistics measures such as mean, standard deviation, rate and proportions were calculated in paper I-III.

Paper **I**: Data were analysed using Statistical Package for Social Science (SPSS) program Version 15.0 for Windows (SPSS 15.0 Chicago Inc. III, USA). Generalized linear regression analysis (GML) was used to obtain relative risks (RR) and corresponding 95% confidence intervals. The GLM analysis was based on Poisson regression with robust variances to obtain a valid confidence interval was used when a log-binomial analysis failed to converge [156]. Multivariable analyses were performed in three steps. In the first step (model A) all socio-demographic factors and maternal

health conditions before pregnancy (i.e. pre pregnancy factors) were included. In the second step (model B) we included all factors in model (A) as well as pregnancy and labour-related conditions. In the third and final step (model C), we included all factors in model B as well as neonatal conditions. We report all variables that were statistically significant in any of the three models.

Paper **II**: Data were analysed using Statistical Package for Social Science (SPSS) program Version 18.0 for Window (SPSS 18.0 Chicago Inc. III, USA). Descriptive statistics measures such as mean, standard deviation, rate and proportion were calculated.

Paper **III**: Data were analysed using Statistical Package for Social Science (SPSS) program for Windows Version 19.0 (SPSS 19.0 Chicago Inc. III, USA). Descriptive measures such as mean, standard deviation, rate per 1000 and relative risk were estimated. The relative risk (RR) of perinatal death overall and for each category of cause of death, was calculated as the ratio of perinatal mortality rate among medical referrals to perinatal mortality rate among non-medical referrals.

3.6 Wigglesworth classification

The Wigglesworth classification [144] has been widely used in developed and developing countries, and is considered simple and easy to modify. The classification is aimed at grouping causes of death into groups with clear implications for clinical management [144]. The classification relies on gestational age and time of death, and allows categorizing causes of death according to birth weight. The conventional Wigglesworth is based on five groups, which are hierarchically and mutually exclusive: 1) Normally formed macerated stillbirth (SB) 2) Congenital malformation (SB and END) 3) Conditions associated with immaturity (END) 4) Birth asphyxia (SB and END) and 5) Specific conditions other than 1-4 (to include deaths due to infection or isoimmunisation).

The Wigglesworth classification was further revised to incorporate image findings or autopsy when available, but does not rely on them, and the decision tree (**Figure 9**) was developed to assist in clear categorization of the clinical conditions [157].

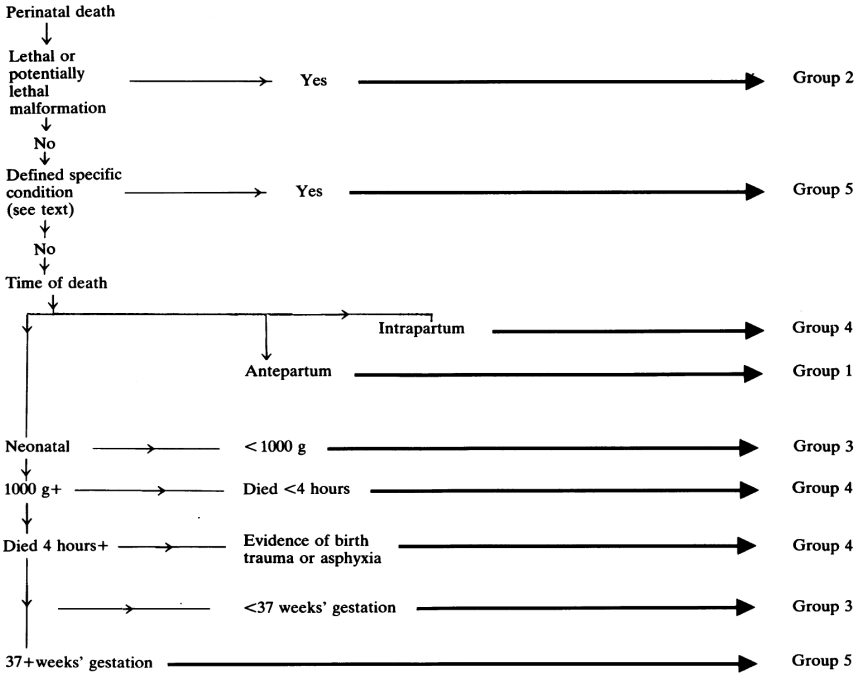

Figure 9: Decision tree for the revised Wigglesworth classification

Source Keeling et al [157].

In our data, up to three clinical diagnoses were recorded for each neonate, and it was important to categorize cause of death in a hierarchical order. We used the modified Wigglesworth classification (paper **II**) to categorize cause-specific neonatal deaths into five major categories; congenital malformations, prematurity, birth asphyxia, infection, and other specific cause of deaths. In a strictly hierarchical approach, each neonatal death was allocated into a single cause category of death. The criteria used to assign babies into single causes of deaths were adapted from both the Wigglesworth

[144] and NICE [145] classification as used by the WHO Child Health Epidemiology Reference Group (CHERG), neonatal group [19] in estimating global causes of neonatal deaths.

Case definition and hierarchy for attributing causes to neonatal deaths

The WHO Child Health Epidemiology Reference Group, neonatal group (CHERG) revised case definition for preterm birth as cause of death and changed from 32 weeks of gestational age and 1800 g in the absence of gestational age [19], (used in paper **II** and **III**), to less than 34 weeks and 2000 g in the absence of gestational age [158]. The changes were done to include the significant number of babies with RDS between 32 and 34 weeks of gestation in the definition of preterm birth. The second reason was to adjust with the widespread use of 2000 g as standard cut off for preterm birth in the absence of gestational age. The proposed hierarchy; congenital malformation, neonatal tetanus, preterm birth, intrapartum related neonatal death (''birth asphyxia''), sepsis/pneumonia, diarrhoea and others was used in our study, except that we did not have a category with neonatal tetanus and diarrhoea.

3.7 Neonatal and Intrauterine death Classification according to Etiology

The Neonatal and Intrauterine death Classification according to Etiology (NICE) (**Table 3**) aims to identify the underlying cause which might have initiated the chain of events leading to death [145, 151]. The classification can be used in a computerized environment, which makes it possible to retrieve information from various sources [145]. The classification includes 31 different characteristics which are categorized into 13 mutually exclusive categories of causes of death. A comparison of Wigglesworth and NICE showed a higher number of unexplained asphyxia and prematurity in the Wigglesworth classification. These deaths were linked to placental abruption, maternal disease and obstetric complication in the NICE classification [145]. **Table 4** presents a summary of characteristics included in the two classification

systems. We used the NICE classification to categorize causes of perinatal deaths into 13 mutually exclusive categories (paper **III**).

The category unexplained small for gestational age was defined as Z-score below -2.5 SD using a formula adapted from [159]; Z= (observed birth weight -mean birth weight)/SD. We calculated separate z-scores for males and females and for singletons and multiple births.

Table 3: The NICE classification

Cause category	Characteristics included
1. Congenital anomalies:	Include stillborn and liveborn infants with lethal malformations or potentially lethal malformations that markedly increase mortality risk.
2. Multiple births:	Includes multiple births other than duplex, or duplex in combination with immaturity (<33 weeks) or intrauterine deaths.
3. Maternal disease:	Includes maternal diabetes mellitus if the infant is stillborn or is large for date (Z>2 SD). Maternal pre-eclampsia, renal disease, hepatosis, epilepsy, systemic lupus erythematosus (SLE) included when combined with an infant either small for date (Z<-2 SD) or immature (<33 weeks), or dead before labour. For maternal SLE also in combination with severe cardiac disease in the infants.
4. Specific fetal conditions:	Include isoimmunization, unexplained hydrops featalis, tumors and specific fetal infections. Accidents included when combined with stillbirth.
5. Unexplained SGA infants:	Infants Z<-2.5 SD without any evidence of maternal disorder.
6. Placental abruption:	If combined with asphyxia, immaturity (<33 weeks) or intrauterine death.
7. Obstetric complications:	Include uterine rupture, disproportion, malpresentation, cord prolapse, cord compression, placenta previa, foetal blood loss and precipitated labour.
8. Unexplained antepartum stillbirths	<37 gestational weeks
9. Unexplained antepartum stillbirths	>36 gestational weeks
10. Specific infant conditions:	Include infants >32 weeks with septicaemia, meningitis or pnaeumonia, includes term infants with respiratory distress syndrome (RDS) or sudden infant death syndrome (SIDS). Accidents included when causing neonatal death.
11. Unexplained asphyxia:	Includes intrapartum death, deaths occur < 4hrs after birth and cases with Apgar score < 4 at 5 min or < 5 in 10 min, where the asphyxia is not explained, and the case does not belong to groups 1–10 above. Immature infants <27 gestational weeks or < 800 g are excluded.
12. Unexplained immaturity:	Includes liveborn infants <33 gestational weeks and 2500 g (or 1800 g if gestational age is unknown) where the immaturity is not explained and the case does not belong to groups 1–11 above.
13. Unclassifiable cases:	Cases not in groups 1–12.

Source: Winbo et al [151].

Table 4: Comparison of the Wigglesworth and NICE classification

NICE	Wigglesworth 1980
Congenital anomalies	Lethal malformations
Multiple births	
Maternal disease	
Specific fetal conditions	Specific conditions
Unexplained SGA infants	
Placental abruption	
Obstetric complications:	
Unexplained stillbirths <37 weeks	Death before the start of labour
Unexplained stillbirths ≥ 37 weeks	
Specific infant conditions	Specific conditions
Unexplained asphyxia in labour	Asphyxia conditions developed in labour
Unexplained immaturity	Conditions associated with immaturity
Unclassifiable cases	Unclassifiable

Source: Winbo et al [151].

3.8 Outcome variables studied in paper I-III

Transfer to neonatal care unit

Transfer was defined as admission of an inborn newborn to the neonatal care unit.

Perinatal death

Perinatal death was defined as stillbirth (birth of dead foetus weighing at least 500 g) or early neonatal death (death of a liveborn within the first week of life). For papers **II** and **III** early neonatal deaths included inborn neonates who died either in labour ward or in the neonatal care unit within the first week of life before hospital discharge.

We calculated *perinatal mortality rate* (PNMR) as the number of perinatal deaths per 1000 births, s*tillbirth rate* (SBR) as the number of stillbirths per 1000 births and *early neonatal mortality rate* (ENMR) as the number of early neonatal deaths per 1000 live births.

Neonatal death

Neonatal death was defined as death of a liveborn before 28 completed days of life. In paper **II** neonatal deaths included inborn neonates who died either in labour ward or in the neonatal care unit before 28 days of life before hospital discharge.

Cause-specific neonatal deaths

Specific causes of neonatal deaths were defined by five single causes of death as classified by the modified Wigglesworth classification.

Causes of perinatal deaths

Causes of perinatal deaths were defined by 13 categories in the Neonatal and Intrauterine deaths Classification according to Etiology (NICE).

3.9 Risk factors studied

The risk factors studied included maternal socio-demographic characteristics such as age at child birth, ethnicity, marital status, education, parity, occupation, residence, maternal height, weight, body mass index (BMI), genital mutilation (FGM), and alcohol intake during pregnancy. Paternal factors included age, ethnicity, education and occupation. Environmental related factors included place of residence, distance from the water source, source of water at home, boiling water for drinking, type of home toilet and season of birth.

Maternal health conditions studied included maternal health before pregnancy such as diabetes mellitus, hypertension, epilepsy, malaria, anaemia, tuberculosis, HIV infection, lung disease, gynaecology disease, sickle cell disease and medical drugs on regular basis. Similar risk factors were studied during pregnancy with additional of gestational diabetic, preeclampsia, eclampsia, bleeding, antenatal care attendance and number of antenatal care visits, and medical drugs during pregnancy. Also studied were complications during labour and delivery which included abruption placenta, premature rupture of membrane, placenta praevia, bleeding, mode of delivery and other unspecified conditions.

Newborn factors studied included gestational age, presentation at birth, sex of the child, birth weight and Apgar score.

Birth weight was categorized in four groups; Very low birth weight (VLBW)- birth weight below 1500 g, Low birth weight (LBW)- birth weight below 2500 g, Normal birth weight (NBW)- birth weight ≥ 2500 g and Large for gestational age (LGA)-birth weight above 4000g.

Gestational age was calculated in complete weeks from the day of last menstrual period (LMP) and was categorized as severe preterm <34 weeks, moderate preterm 34-36 weeks, and term 37+ weeks of gestational age.

Apgar score was categorized as normal Apgar score –a liveborn baby with Apgar score of 7 or more points in the 5th minute after birth, or as low Apgar score – a liveborn baby with Apgar score of less than 7 points in the 5th minute after birth.

3.10 Ethical consideration

The KCMC Medical Birth Registry obtained ethical clearance from the Tanzania Ministry of Health, Institute of Science and Technology, from the Norwegian National ethics committee, the National Institute of Medical Research (NIMR) in Tanzania **(Appendix 4)** and from the Kilimanjaro Christian Medical College (KCM-College) research ethics committee. The protocol for this study was approved by KCM-College research ethics committee **(Appendix 5)**.

4 Results

4.1 Paper I: Transfer of newborns to neonatal care unit: a registry based study in Northern Tanzania

In this paper, we studied 21 206 singleton babies registered at the KCMC-MBR from July 2000-October 2010, of which 3190 (15%) were transferred to neonatal care unit.

In the crude analyses, there were weak associations between socio-demographic factors and transfer to neonatal care unit. Relative risks above 1.2 included single marital status (RR1.3), maternal body height below 150 cm (RR 1.4), father's occupation (RR 1.3 for farmer vs. professional), father's education (RR 1.5 for no education vs. secondary or higher education), and source of water (RR 1.3 for river water vs. tap water). Among the factors related to maternal health before or during pregnancy, the strongest associations (RR 2 or more) were with diabetes before pregnancy (RR 4.7), no ANC attendance (RR 2.3), gestational diabetes (RR 3.1), hypertension during pregnancy (RR 2.0), preeclampsia (RR 2.2), and eclampsia (RR 4.7). Among complications during labour and delivery, the strongest associations were for abruption placenta (RR 4.4), premature rupture of membrane (RR 3.9), bleeding more than 500 ml (RR 2.2) placenta praevia (RR 3.0), other vaginal delivery (i.e. breech, vacuum or forceps) and caesarean section (RR 3.3 and 2.3, respectively). Neonatal factors associated with newborn transfer were birth weight (RR 9.8 for <1500, RR 4.3 for 1500-2499 and RR 7.2 for 4000+ vs. 2500-3999 grams), 5th minute Apgar score less than seven (RR 6.9 vs. above seven), gestational age (RR 5.6 for 25-33, RR 2.2 for 34-36 vs. 37+ weeks), presentation (RR 1.9 for breach, 1.5 for transverse vs. cephalic) and sex (RR 1.2 for males vs. females).

After mutual adjustment of all factors, neonatal factors remained strong predictors of newborn transfer, whereas the associations of pre-pregnancy factors and pregnancy and labour-related complications were weakened or disappeared. Pre-pregnancy factors associated with transfer in the adjusted model were birth to the first baby (RR

1.4), maternal age 26-35 years (RR 1.2), single marital status (RR 1.2), and lack of paternal education (RR: 0.5; 95% CI: 0.3-0.9). Pregnancy and labour-related complications associated with transfer in the adjusted model were preeclampsia (RR 1.3), premature rupture of membrane (RR 2.3), other vaginal delivery (RR 2.2), caesarean section (1.9), referral to ANC (RR 1.3) and few ANC visits (1.3).

4.2 Paper II: Cause-specific neonatal mortality in a neonatal care unit: a registry based cohort study

In this paper we studied a total of 5033 inborn neonates admitted to neonatal care unit from July 2000 to October 2010. Of those admitted 29.0% had a birth weight below <2500 g, and 25.8% were born before 37 weeks of gestation. Leading causes of admission were birth asphyxia (26.8%), prematurity (18.4%), risk of infection (16.9%), neonatal infection (15.4%), and birth weight above 4000 g (10.7%). Babies with respiratory distress syndrome had highest case fatality (52.1%). Case fatality for major causes of admission declined with increasing birth weight, except for congenital malformation.

Of the 5033 neonates, 536 (10.7%, 95% CI 9.8-11.4%) died, of which babies with birth weight below 2500 g constituted 52.1%. Major single causes of neonatal death were birth asphyxia 245 (45.7%), prematurity 188 (35.1%), congenital malformation 49 (9.1%), and infection 46 (8.6%), (**Figure 10**). The mean (SD) for gestational age and birth weight for premature babies who died was 30.3 (3.3) weeks and 1342 (457) grams, respectively. The mean (SD) for babies who died due to birth asphyxia was 38.7 (3.0) weeks and 2843 (705) grams, respectively. Birth asphyxia was the most frequent cause of death in normal birth weight babies (n=179/246, 73.1%) and prematurity in low birth weight babies (n=178/188, 94.7%). Birth asphyxia in normal birth weight and and prematurity in low birth weight each accounted for one third of total deaths. The majority of deaths occurred within 24 hours (304, 56.7%), and 490 (91.4%) within first week of life. There was no clear time trend for overall mortality or within each cause of death.

We repeated the analyses using the new case definition for preterm birth as revised by CHERG (less than 34 weeks gestational age or less than 2000 g in the absence of gestational age). These results did not differ from the reported results based where preterm birth was defined as less than 33 weeks gestational age or less than 1800 g in the absence of gestational age). The proportion of deaths due to preterm birth was unchanged (35.1 and 35.8%), and similar for birth asphyxia (45.7 and 45. 1%).

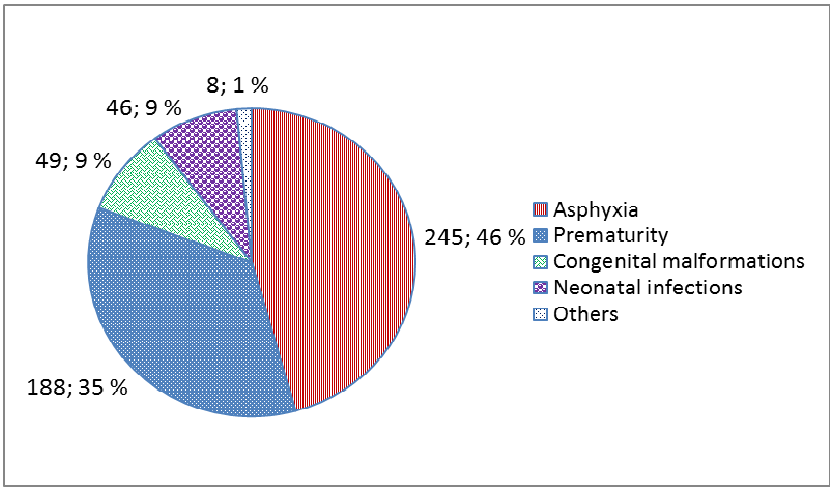

Figure 10: Cause-specific neonatal mortality in a neonatal care unit at KCMC 2000-2010

4.3 Paper III: Causes of perinatal deaths in Northern Tanzania 2000-2010: a registry based study

From the KCMC-MBR and neonatal registry July 2000-October 2010, a total of 33929 births of at least birth weight 500 g were extracted, of which 1958 died perinatally. Overall perinatal mortality was 57.7/1000 births, the stillbirth rate 35.9/1000 births and early neonatal deaths 21.8/1000 live births. Overall and among babies of non-referred mothers, there were no time trends in perinatal mortality from 2000 to 2010 (**Figure 11**). In the group of medically referred, mortality increased from around 80/1000 to

more than 120/1000. Babies with birth weight below 2500 g were more than seven times as likely to die during the perinatal period as compared to normal birth weight babies (224.6 vs. 32/1000). Multiple births were more than twice as likely to die during the perinatal period as compared to singletons (116 vs. 54.5/1000).

Overall, major causes of perinatal mortality were *unexplained asphyxia* (12.5/1000 births) *obstetric complications* (8.9/1000), *maternal disease* (8.5/1000), *unexplained antepartum stillbirth after 37 weeks of gestation* (6.5/1000), and *unexplained antepartum stillbirth before 37 weeks of gestation* (5.4/1000). Obstructed/prolonged labour was present in 82.8% of the perinatal deaths in the *obstetric complications* category, and preeclampsia/eclampsia was present in 88.2% of the deaths in the *maternal disease* category. *Unexplained asphyxia* remained the leading cause even after excluding medical referrals (12.9/1000 births).

Births to women referred for delivery due to medical conditions accounted for 19.1% of all births and 36% of all deaths, with perinatal mortality of 109/1000 births. Excluding medical referrals, perinatal mortality dropped to 45.6/1000 births. The reduction was mainly due to fewer deaths from *obstetric complications* (from 8.9 to 2.1/1000) and *maternal disease* (from 8.5 to 5.5/1000). Major differences in perinatal mortality between referred vs. non-referred women were observed for *obstetric complications* (RR 18.0), *placental abruption* (RR 10.0), and *maternal disease* (RR 4.0).

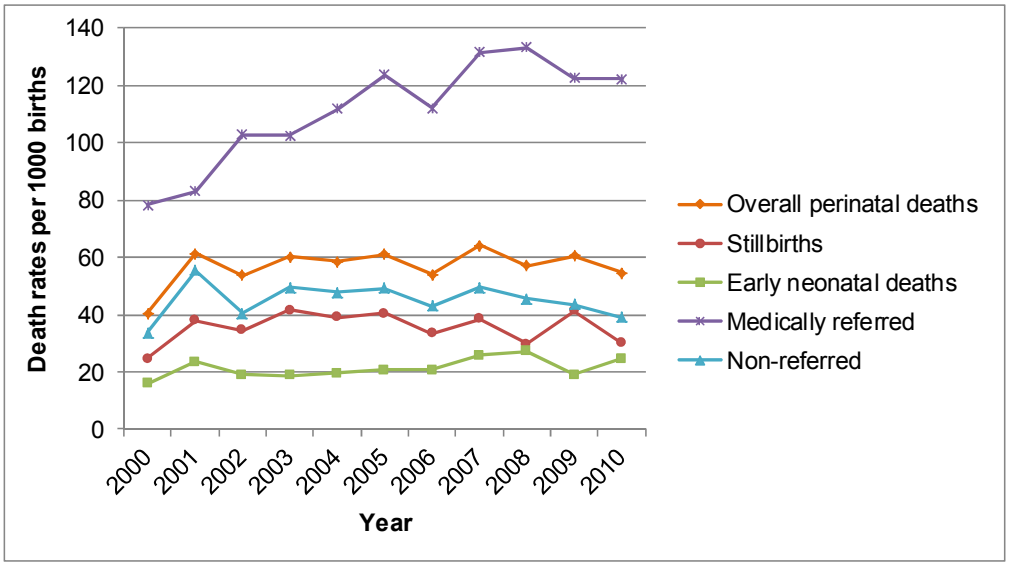

Figure 11: Trend in stillbirths, early neonatal and perinatal deaths at KCMC 2000-2010

5 General discussion and methodological considerations

This thesis presents the risk of neonatal transfer to neonatal care unit and explores causes of neonatal and perinatal deaths at a zonal hospital in Northern Tanzania. This section will consider relevant methodological aspects which might affect our data and our analysis, and discuss the measures taken to increase the validity of the study.

5.1 Methodological considerations

5.1.1 Internal validity

Internal validity refers to which extent the results are valid for the population the data were selected from and is obtained through minimizing systematic errors. Bias is a commonly used term for systematic error. Bias is defined as any systematic error in an epidemiological study that results in an incorrect estimate of the prevalence of a condition or a measure of association between exposure and risk of disease [160]. Our study is hospital based, and we will discuss internal validity with respect to information bias and confounding. The issue of selection bias will be discussed under external validity/generalizability. Most definitions in this section are drawn from Rothman et al. [160].

Information bias

i. General on data collection strategies

Information bias occurs during data collection [161]. Strategies to reduce information bias in the birth registry include;

a. Preparation of a birth registry manual with definition and explanation of the variables in the questionnaire

b. Use of standardized questionnaire to ensure that similar information is collected and recorded for all deliveries

c. Pretesting of questionnaire in a pilot prior to the initial official start

d. Training of the data collection personnel on how to conduct the interview and record the forms

e. Training of the data entry person

ii. Interviewer bias

An interviewer who has knowledge of the diseases (outcome) or the exposure [161, 162], can introduce bias by putting emphasis in different questions or probing for more information. Since the interview of the mothers took place after delivery, there is a risk of interviewer bias. To minimize interviewer bias, the study questionnaire was standardized, and interviewers received training and close supervision with ongoing review of the data by a project consultant from the Norwegian birth registry.

iii. Outcome measures

a. Perinatal mortality

Information on deaths was retrieved from the hospital records. Deaths of neonates who died perinatally after discharge from hospital before seven days, were lost if the baby was not re-admitted to this hospital. Hence, true mortality may be slightly higher than that observed in this study.

b. Causes of death

Paper **II**: Gestational age was missing in 9.1% of the births due to missing information on maternal date of last menstrual period. If gestational age was missing, we used birth weight to classify cause of death. For example, there is a possibility of misclassifying full term, small for gestational age (SGA) babies as *preterm* due to low birth weight.

Paper **III**: The computerized classification of perinatal deaths based on registry data may have lower validity as compared to perinatal audits where data are collected with the specific purpose to study causes of an adverse outcome [151]. However, the regular and systematic collection of data, and the use of detailed information from the two linked registry data sets, allowed us to define categories in a hierarchical order and give an overall picture of causes of perinatal deaths.

Multiple causes can contribute to one neonatal death or stillbirth. There is a possibility of misclassifying important conditions relevant for the classification of cause of death. Gestational age was missing in 12.6% of perinatal deaths; these deaths could be assigned to categories that don't rely on gestational age, i.e. *obstetric complications*, *unexplained asphyxia,* or *others*. Furthermore, uncertainty in last menstrual period may have led to overestimation or underestimation of the *unexplained small for gestational age (SGA)* category, because the calculated Z-score was too low or too high.

Confounding

For a factor to be a confounder it must be associated with the exposure, independent of the outcome, must be a risk factor for the outcome, and must not be an intermediate step in the causal pathway between the exposure and the outcome [163]. Confounding is a situation where a third factor explains all or part of the observed association between the exposure and the outcome in the study by being a cause of both the exposure and the outcome. Confounding in observational studies can be corrected during the study design by restriction or matching, and during statistical analysis by matched analysis, stratification or multivariable analysis [160, 163]. The KCMC birth registry includes all births in the hospital, and no strategies were performed to reduce confounding in the design/data collection phase.

In paper **I**, we restricted the study population to singleton births while studying risk factors of transfer to neonatal care unit. During analysis we controlled for other factors by means of multivariable regression analysis. Adjustments were done in three steps

according to the period the condition occurred; pre-pregnancy, pregnancy, labour and delivery, as well as neonatal factors. The purpose of this was to identify which factors that mediated any association with transfer. It is important to note that the adjustments made in paper **I** not only were performed to adjust for confounding, but also to describe how effects were mediated. For example, relative risk for preeclampsia was 2.2 in the observed data, 2.0 after adjustment for pregnancy and labour complications, and 1.3 after adjustment for neonatal factors. This shows that most of the association between preeclampsia and neonatal transfer was mediated through the condition of the neonate.

In addition to confounders available in the registry data, there may be unknown and unmeasured confounders that we have not been able to account for. For example we found a significantly reduced risk of newborn transfer to neonatal care with low paternal education level. Rather than representing an effect of paternal education per se, it might reflect social differences in the focus on neonatal care. Since this was a historical cohort study we were not able to collect additional data on possible confounders.

5.1.2 External validity (Generalizability)

External validity (or Generalizability) refers to the ability to generalize results and conclusion from the study population to a more general relevant target population. Lack of internal validity will lead to lack of generalizability. Not all women in Kilimanjaro region deliver at the health facilities, as home deliveries are estimated to account for 13-29 per cent of deliveries in Kilimanjaro region [23, 24]. One question would be whether women who give birth at KCMC are representative with respect to socio-demographic characteristics. If women who give birth at KCMC are more privileged with respect to socio-economy, the observed risks may be underestimated as compared to the region. Our findings might be generalized to women who deliver at health facilities. Since our data were retrieved from a registry, the categorization of

causes of deaths may, however, not fully correspond with studies based on perinatal audits or hospital records.

Selection bias

Selection bias occurs when the study population does not represent the target population about which conclusions need to be drawn [160, 161, 163]. Selection bias results from procedures used to select subjects and from factors that influence the study participation. This type of bias is common in hospital based studies. We discuss two mechanisms of selection bias.

i. Selection to hospital birth

Study women recruited for the KCMC Medical Birth Registry were those who came to deliver at this health facility in a certain time period. In most developing countries not all women give birth at a health facility. The recent Tanzania national survey estimate that fifty per cent of births occurred at health facilities and 48% at home [23]. In Kilimanjaro region 86.7% of births occurred in health facilities in 2010 compared with 71% in 2004 [24]. Since the characteristics of women who deliver outside health facility may differ from those who deliver at health facilities, our results may be most representative of women who give birth at similar health facilities.

KCMC is a tertiary care hospital and a non-profit private organization. Not all people who live around KCMC can afford to come for delivery at the centre due to costs, although they acknowledge the high quality of services. Some would rather prefer to deliver at a public health facility where maternal and child health services is free of charge, but with the possibility to be referred to KCMC if complications occur.

ii. Referral

Nearly 20% of deliveries at KCMC are referred due to pregnancy and labour related complications. Since women with complicated pregnancies were more likely to be referred to give birth at this institution, the possibility of overestimation of measures of morbidity and mortality should be considered. Around half of the births at KCMC are

from Moshi urban area. In paper **I**, We combined information on maternal area of residence and referral information, and excluded all medically indicated referrals births from rural areas, suggesting that if it were not for the medical problems they would have delivered in their nearby health facility and not at KCMC. By this exclusion, we expect that women included were those who came to deliver at KCMC either due to the close location or to personal preferences. The excluded cases in paper **I** accounted for 52% of all referrals and 75% of all medical referrals. In paper **II,** we included all inborn neonates who were transferred to the neonatal care unit. Because transfer to the neonatal care unit and management in the neonatal care unit is independent of referral, also neonates of referred mothers were included. Both singletons and multiples were included since management is provided individually. Hence, the outcome measures may not represent the general population but rather reflect the situation in this neonatal care unit, and perhaps in similar units. In paper **III**, we stratified the results into medically indicated referral births and those women who were not referred due to medical reasons. This enabled us to estimate differences in causes of perinatal deaths among women referred and non-referred.

5.2 Discussion of the main findings

The studies forming the basis of this thesis explored several risk factors for neonatal morbidity and causes of neonatal and perinatal mortality in Northern Tanzania. In this section we will discuss main findings from the papers included in this thesis and in consideration of studies from others settings. Related findings from all papers will be combined during discussion

Overall outcome measures

The overall outcomes studied were transfer to neonatal care unit, case fatality for inborn babies admitted to neonatal care unit, neonatal mortality among inborn admitted in a neonatal care unit, and perinatal mortality among inborn neonates. Fifteen per cent of the newborns were transferred to neonatal care unit. Of the admitted neonates 10.7% died. The numbers must be interpreted bearing in mind the

setting, with inborn neonates admitted for care as our study population and with a substantial fraction of deliveries from mothers who were referred due to complications.

Overall perinatal mortality was as high as 58/1000 births. The observed perinatal mortality was similar to previously reported from the same region [46, 164], but higher than reported from a previous study in the same setting [41]. The higher perinatal mortality in the current study may be due to the inclusion of multiple births and rural medical referrals as they were excluded in the previous study [41]. Perinatal mortality was more than twice as high among babies of medically referred as compared to non-medically referred women (45.9 vs. 109/1000 births), and 36% of all perinatal deaths was among babies of medically referred mothers. This reflects the importance of KCMC as a referral hospital in the region, and also the importance of considering referral in the analyses.

Risk factors and neonatal conditions/causes of death

Birth to first child

Birth to first child was associated with a higher transfer rate to NCU as compared to second child; after accounting for complications and neonatal conditions relative risk was 1.4 compared to second birth (paper **I**). A high risk of neonatal transfer of first born babies is also reported in a study from Australia [75]. Birth order is highly correlated with age of the mother at birth and first birth at younger age increases risk of complications, low birth weight and prematurity [134]. In developing countries first births have on average a 33 per cent increased risk of dying during their neonatal period as compared to second births [134]. Nulliparous women are also at high risk of developing preeclampsia [165] and labour related complications such as obstructed labour, caesarean delivery and neonatal care admission [166]. A previous study in our institution indicated that term nulliparous singleton pregnancy were at increased risk of caesarean section delivery [153], which may also partly explain the high transfer

rate of first born babies. Still, the high risk of transfer for first born babies remained after accounting for many of the above mentioned factors.

Antenatal care

Antenatal care (ANC) is most effective in avoiding adverse pregnancy outcomes when it is sought early in the pregnancy and continues throughout delivery [23]. In our data, lack of ANC or a low number of ANC visits and referral to initiate ANC, were associated with neonatal transfer (paper I). In Tanzania there is high ANC coverage, but less than 15% attend ANC before the fourth month of pregnancy, and less than half of the women attend the recommended four ANC visits [23]. Studies from referral hospitals in Tanzania found that eclamptic women were twice as likely to have less than the recommended four ANC visits [96, 97]. The likelihood of women receiving counselling and information on pregnancy complications and to have institutional delivery increases with increasing number of ANC visits [119, 120]. Furthermore, adherence to ANC care visits is associated with reduced risk of perinatal mortality [98].

Hypertensive disorders in pregnancy

Hypertensive disorders in pregnancy include four categories of hypertension in pregnancy; chronic hypertension, gestational hypertension, preeclampsia and eclampsia. Furthermore, abruption placenta is highly linked to hypertensive disorders in pregnancy [167]. These maternal conditions are associated with increased risk of preterm delivery, low birth weight, intrauterine growth restriction, asphyxia and perinatal mortality [89, 91, 93, 96-98]. In paper **I,** hypertension, preeclampsia, eclampsia, and abruption placenta were associated with newborn transfer; this is similar to previously reported in both low and high income countries [75, 91, 99]. Preeclampsia, eclampsia or abruption placenta may have an indirect relation with newborn transfer since these conditions are risk factors for preterm birth and asphyxia, conditions that were directly related to transfer. Our adjusted results showed that most

of the associations between hypertensive conditions and transfer were accounted for by neonatal factors.

In paper **III**, *maternal disease* was among the leading causes of perinatal death. In this category, preeclampsia/eclampsia was present in nearly ninety per cent of perinatal deaths. A high number of deaths related to hypertensive disorders were also previously reported in Tanzania [44, 96, 97]. A more detailed calculation (not previously reported) showed that among the deaths in the *maternal disease* category, 53.6% were preterm (below 36 weeks) and 71.3% were of low birth weight (<2500 g). *Maternal disease* and *placental abruption* were in particular important causes of death among babies of referred women; four times and ten times more likely to cause perinatal death, respectively. This was also observed in a study at Muhimbili National Hospital (MNH) in Tanzania [96]. Lack of awareness and education to recognize obstetric danger signs leading to potentially serious pregnancy complications may contribute to delays in the decision to seek care [119]. Lack of awareness on danger signs in pregnant women is reported in Tanzania [120, 168, 169], and is shown to be associated with unpreparedness for birth and complications. A study in Tanzania indicated more than fifty per cent of the women who attend ANC are not counselled on any danger signs [120].

Obstetric complications

Obstetric complications such as premature rupture of membrane (to be discussed under infection), and obstructed/prolonged labour increases risk of neonatal morbidity and mortality.

Paper **III**: *Obstetric complications* was among the leading causes of death and contributed to 15% of perinatal deaths overall and 35% of perinatal deaths among babies born to mothers who were referred. *Obstetric complications* included malpresentation, obstructed or prolonged labour, uterine rupture, cord prolapse or cord compression and foetal blood loss. All these conditions may lead to asphyxia if emergency care is not available in time. Obstructed/prolonged labour was the most

frequent condition among the *Obstetric complications,* present in more than 80% of the perinatal deaths in this category. Obstructed labour in low income settings is a major cause of intrapartum related asphyxia [39, 43, 44, 170, 171] and may considerably increase the risk of perinatal death; up to factor of 85 in resource limited settings has been reported [67]. A recent study in North-Eastern Tanzania where women residing in Korogwe district were followed through antenatal care visits and seven days after delivery, found that deaths linked to obstructed labour was the major cause of perinatal mortality [98]. A qualitative audit study at Muhimbili National hospital indicated that prolonged labour diagnosed at referring hospitals or at MNH, substantially contributed to perinatal mortality, among which 51.9% of the intrapartum stillbirths had heart beat on arrival. Furthermore, delay in transportation, suboptimal care and poor monitoring of labour were among the factors that contributed to high perinatal mortality [128]. The high number of deaths due to obstetric complications in our setting, especially among referrals, may indicate delay in seeking or in reaching medical care, or delay in recognition of women with abnormal progress of labour.

Intrapartum related asphyxia

Asphyxia-related conditions include low Apgar score (paper **I**), birth asphyxia (paper **II**), and unexplained asphyxia (paper **III**). A fraction of the deaths in the categories *obstetric complications, maternal disease, and placental abruption* (paper **III**) are also made up of such deaths.

Paper **I**: Low Apgar score defined as 5 minute Apgar <7 is a commonly used indicator to identify asphyxia in low income settings. A low Apgar score may be due to asphyxia, prematurity or congenital malformations and is associated with increased risk of morbidity and mortality due to the consequence of brain hypoxia [50]. Babies with low Apgar score had a seven times higher risk of transfer. We calculated that 68.7 % of babies with Apgar score below 7 had a diagnosis of asphyxia (data not reported before). Furthermore, 29.4 % of babies with a diagnosis of asphyxia had low Apgar score, whereas the rest of asphyxiated babies were assigned a normal Apgar score ≥ 7. Corresponding findings, in which not all newborns who died due to birth asphyxia had

low Apgar score, are reported elsewhere [73, 172]. This supports a long term notion that Apgar score is not a reliable measure of birth asphyxia [73].

Paper **II**: Birth asphyxia was the most frequent reported diagnosis among those admitted to neonatal care unit; 26.8% of admitted babies and 59.9 % of babies who died had a diagnosis of asphyxia. The high proportion of admitted babies with asphyxia in our study compared to other hospital based studies from low income countries [173, 174] might reflect the characteristics of our population, which consists of only inborn neonates and a large number of medical referrals. Birth asphyxia was also the leading single cause of neonatal death, accounting for 45.7% of the deaths overall and as much as 72.8% of the deaths among normal birth weight babies. A high number of deaths due to asphyxia in normal birth weight babies reported in Tanzania and in other low income settings [39, 172], may reflect that viable babies die as a result of delayed health care seeking or delayed referral from a lower care level. The majority of deaths due to birth asphyxia occurred within first 24 hours and nearly all within first week, which is consistent to previous findings [67, 73]. Most of the intrapartum related neonatal death die due to encephalopathy and do so mainly in the first days, even in countries with neonatal intensive care units [67].

Paper **III:** *Unexplained asphyxia* defined as intrapartum related deaths (intrapartum related stillbirths and intrapartum related neonatal deaths) which could not be explained by other categories of death, was the leading cause of death category overall and among the non-medical referrals. These are deaths largely linked to obstetric complications and maternal diseases. However information may not be detailed enough or some conditions may not be included in the classifications characteristics to be able to explain aetiology for the rest of intrapartum deaths categorized as unexplained asphyxia. Intrapartum related neonatal deaths, intrapartum related stillbirth and obstructed labour are closely linked to maternal and obstetric complications and services given during labour and delivery [33, 67, 171]. Hence these are deaths largely avoidable by appropriate care during time of labour and delivery including availability of timely caesarean section [171]. Basic resuscitation

provided immediate after birth to asphyxiated newborn have shown to reduce intrapartum related stillbirths [175], intrapartum related neonatal deaths [172, 176] and signs of neurological abnormality [177].

Immaturity

Immaturity related conditions include preterm birth and related complications, among which RDS is most frequently reported. Globally, preterm birth is the leading cause of neonatal mortality [65]. Risk factors of immaturity include preeclampsia, eclampsia, abruption placenta, and low ANC attendance. Cause of death categories that include immaturity are *maternal disease*, *unexplained immaturity*, and *multiple births* (paper **III**).

Paper **I**: Preterm delivery was one of the strongest predictors of transfer; 70.5% of babies below 34 weeks were transferred (RR 5.6 compared to normal) and 27.3% (RR 2.2 compared to normal) between 34-36 weeks. Nearly 30% of babies below 34 weeks were not transferred. The explanation might be that 39% of babies with gestational age <34 weeks had birth weight above 2000 g. These babies were possibly more matured and without other complications and would thus not require neonatal care admission.

Paper **II**: Prematurity was the second most important cause of admission as well as cause of neonatal death. Similar findings have been reported elsewhere [174]. Premature babies who died in the neonatal care unit were severely preterm and of very low birth weight, with mean gestational age 30.3 weeks and mean birth weight 1342 grams. The high case fatality in babies with RDS and severely preterm babies reflects the inadequate care of these neonates in developing countries [177, 178]. Recommended interventions to improve neonatal outcome in preterm and low birth weight babies are prophylactic use of steroids during premature labour, antibiotics for premature rupture of membrane, early breast feeding, treatment of infection, hospital-based kangaroo mother care, prevention of hypothermia and feeding/nutritional support [69, 179, 180]. These interventions are in principle available, but the use of some of these interventions, for example steroids, is limited because women come too

late. A more detailed calculation (not presented previously) shows that only 20 (0.4%) of mothers with babies admitted due to prematurity received steroid prophylaxis prior delivery, of which only one baby had RDS.

Infection

Perinatal infections are common in developing countries. Maternal infections included malaria, HIV, tuberculosis, and syphilis (paper **I**). However, maternal infections were not important risk factors of neonatal transfer. Neonatal outcomes included risk of infection in the neonate and infection as single cause of neonatal death (paper **II**). We also report on PROM (paper **I**) which is associated with maternal and neonatal infection.

PROM in this study was defined as rupture of membrane 18 or more hours before delivery and was associated with three fold risk of newborn transfer. The incidence of early onset disease with group B Streptococcal increases significantly at 18 hour; 18 hr is an appropriate cut off for increased risk of neonatal infection [181]. Babies born to mothers with PROM more than 18 hours who did not receive antibiotic prophylaxis prior to delivery, were transferred to neonatal care unit, put on antibiotic prophylaxis and observed for any sign of sepsis. In paper **II**, risk of infection was one of the leading causes of admission, which reflected babies transferred due to PROM. The outcome of these babies was in generally good. Meta-analysis studies have indicated that antibiotic prophylaxis following PROM reduces risk of neonatal sepsis, and in case of preterm membrane rupture reduces risk of RDS and prolongs latent phase, i.e. time to delivery [129, 130].

Infection was the third leading cause of neonatal death and one of the leading causes of admission. Neonatal mortality due to infection was, however, low as compared to a previous study in the same setting [74]. This might be due to the inclusion of only inborn neonates in our study. The routine transfer to NCU of all inborn neonates at risk of infection due to PROM for antibiotic prophylaxis (paper **I**), has likely played a role in reducing observed mortality due to infections in our study. We did include some

babies who were discharged from hospital and then readmitted of which the majority (67%) were due to infection, but may have lost some cases that developed infection after discharge without being readmitted to our hospital.

Congenital malformations

Paper **II** and **III**, Only 2.2% of those admitted to NCU had a diagnosis of congenital malformation, and 46 out of the 536 neonatal deaths (9.1%) had congenital malformation as single cause of neonatal death. Perinatal mortality due to congenital malformations was 2.5/1000 births. In Tanzania and other developing countries, routine screening for congenital malformation such as early ultrasound scan is not available to the majority of the women. Availability of management/surgery for neonates with severe congenital malformations is limited, and under the prevailing circumstances we suggest that few of these deaths could have been prevented.

Large for gestational age babies (LGA)

In paper **I**, Large for gestational age babies (>4000 g) were seven times more likely to be transferred to neonatal care unit compared to normal birth weight babies. In this setting, high birth weight babies without any other complication are routinely transferred to neonatal care unit for observation and feeding to prevent transient hypoglycaemia. Also, a large fraction of these babies are delivered by caesarean section which is a risk factor for transfer. These babies were observed for 24 hours and discharged from the hospital if blood sugar level was normal and no any other problem detected. The outcome of these babies was in general good (paper **II**).

Unexplained antepartum stillbirths

Antepartum stillbirths contributed to two third of all stillbirths, of which *Unexplained antepartum stillbirths* accounted for half (paper **III**). These are deaths that could not be assigned to the other categories of death based on aetiology. *Unexplained antepartum* stillbirth was one of the major categories of perinatal death and accounted for 20.6% of all perinatal deaths. Similar higher rate of unexplained antepartum stillbirth have been reported from other studies in developed and developing countries [144, 145,

170]. Antepartum stillbirths are associated with maternal infection and foetal growth restriction [56]. Maternal infections such as syphilis, malaria and HIV are associated with high risk for perinatal morbidity and mortality [35, 111, 114, 116], but infection is not included in the NICE classification [145], used in our study. Studies from rural Ghana [170, 182] included maternal infection (malaria, HIV and syphilis) in the maternal disease category. Still, nearly 60% of antepartum stillbirths remained unexplained. This suggests that it is unlikely that infections alone could have explained the large number of unexplained stillbirths in our study. On the other hand, the available information may not be detailed enough to identify the underlying causes for the large fraction of unexplained deaths [145].

6 Study conclusions

Using data generated from the KCMC-MBR, the studies in this thesis identified several risk factors for neonatal morbidity and causes of neonatal and perinatal mortality. Strong associations between neonatal transfer and classical neonatal risk factors for morbidity and mortality were observed. Pregnancy-related and demographic factors were predictors of neonatal transfer in the unadjusted analysis, but these associations were weakened or disappeared after accounting for neonatal factors, except for an excess risk among first births and a reduced risk among babies of father without education. Birth asphyxia, prematurity and infection were the major single causes of neonatal morbidity and mortality. Birth asphyxia in normal birth weight babies and prematurity in low birth weight babies, each accounted for one third of all neonatal deaths. Perinatal mortality was high with no clear time trend overall or among babies of non-referred mothers. Among babies of medically referred mothers, mortality was more than twice as high as compared to non-referred mothers, and increased with time. Major causes of perinatal deaths were *unexplained asphyxia, obstetric complications, maternal disease, and unexplained stillbirths*. The excess risk among babies of medically referred women was particularly high in deaths due to *maternal disease*, *obstetric complications* and *placental abruption*.

We found high numbers of neonatal deaths due to birth asphyxia and prematurity as well as high numbers of perinatal deaths due to *unexplained asphyxia*, *obstetric complications*, *maternal disease, and placental abruption* especially among babies of medically referred women. This may indicate unawareness of danger signs during pregnancy, delay in seeking health care and or inadequate referral mechanism. The lacks of improvements in rates of stillbirths, perinatal and early neonatal deaths over the period 2000 – 2010 are causes of concern. The distributions of the recorded underlying causes of death indicate great potentials for targeting interventions to

reduce perinatal deaths. Possible areas of prevention include improvement of antenatal care and referral system, improved monitoring and intervention when needed during labour and improvement of neonatal care.

7 Recommendations

Routinely and continuously collected information on mothers and their newborn babies are important for understanding the risk factors and causes of perinatal deaths. Although the thesis is based on observational data, the results underscore the need for improved prevention and treatment in order to lower rates of stillbirths and perinatal and early neonatal mortality. The findings, combined with what is known from previous studies, should be utilized for developing public health strategies to monitor and improve perinatal outcomes and may have the following clinical, policy and future research implications.

7.1 Policy implications

In order to reduce neonatal and perinatal mortality related to maternal and obstetric complications there is a an apparent need to;

i. Increase community awareness and ability to recognize obstetric danger signs during pregnancy, and promote early seeking of health services. Though barriers such as lack of resources and poor social conditions may hinder timely access to adequate care, a higher awareness may probably increase birth preparedness.

ii. Increase health workers' awareness and ability to inform and advice pregnant women on danger signs of potential complications during pregnancy through ANC visits.

iii. Reorganization of referral system to ensure timely and proper care.

iv. Establish vital registration systems to record pregnancies and their outcomes to assess the need for future interventions.

7.2 Clinical implications

Areas which probably need to be strengthened in clinical practice include;

i. Securing that fast decisions and appropriate actions are taken for women with pregnancy and labour complications.

ii. Regular re-training and update on the utilization of partograph with early identification and management should be done in cases with risk for foetal distress.

iii. Regular re-training and update on basic resuscitation skills is needed to improve outcome of asphyxiated newborns.

iv. Strengthen perinatal mortality reviews within the institution as well as with surrounding health facilities to ensure proper discussion of all maternal and newborn deaths occurring in the hospital, identify causes, work out preventive measures and give feedback to all the staff involved.

v. Utilize feedback from birth registration systems to identify areas with need of improvement

vi. Utilize birth registration systems to monitor effects of changes in clinical practice.

7.3 Further research

We emphasize the need of further research regarding four major findings:

i. Problem: Hypertensive disorders in pregnancy. Study needed: Intervention study on counselling on danger signs during pregnancy and advocating for early seeking of care within the community.

ii. Problem: High perinatal mortality among births to referred mothers: Study needed: Identify the most important sources of delay in the referral system, and implement feedback mechanisms across the referral levels.

iii. Problem: Obstructed labour and Birth asphyxia. Study needed: Clinical trial to measure effects of partograph use also in peripheral hospitals for early identification of need for emergency care.

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I

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RESEARCH ARTICLE Open Access

Transfer of newborns to neonatal care unit: a registry based study in Northern Tanzania

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Abstract

Background: Reduction in neonatal mortality has been slower than anticipated in many low income countries including Tanzania. Adequate neonatal care may contribute to reduced mortality. We studied factors associated with transfer of babies to a neonatal care unit (NCU) in data from a birth registry at Kilimanjaro Christian Medical Centre (KCMC) in Tanzania.

Methods: A total of 21 206 singleton live births registered from 2000 to 2008 were included. Multivariable analysis was carried out to study neonatal transfer to NCU by socio-demographic factors, pregnancy complications and measures of the condition of the newborn.

Results: A total of 3190 (15%) newborn singletons were transferred to the NCU. As expected, neonatal transfer was strongly associated with specific conditions of the baby including birth weight above 4000 g (relative risk (RR) = 7.2; 95% confidence interval (CI) 6.5-8.0) or below 1500 g (RR = 3.0; 95% CI: 2.3-4.0), five minutes Apgar score less than 7 (RR = 4.0; 95% CI: 3.4-4.6), and preterm birth before 34 weeks of gestation (RR = 1.8; 95% CI: 1.5-2.1). However, pregnancy- and delivery-related conditions like premature rupture of membrane (RR = 2.3; 95% CI: 1.9-2.7), preeclampsia (RR = 1.3; 95% CI: 1.1-1.5), other vaginal delivery (RR = 2.2; 95% CI: 1.7-2.9) and caesarean section (RR = 1.9; 95% CI: 1.8-2.1) were also significantly associated with transfer. Birth to a first born child was associated with increased likelihood of transfer (relative risk (RR) 1.4; 95% CI: 1.2-1.5), while the likelihood was reduced (RR = 0.5; 95% CI: 0.3-0.9) when the father had no education.

Conclusions: In addition to strong associations between neonatal transfer and classical neonatal risk factors for morbidity and mortality, some pregnancy-related and demographic factors were predictors of neonatal transfer. Overall, transfer was more likely for babies with signs of poor health status or a complicated pregnancy. Except for a possibly reduced use of transfer for babies of non-educated fathers and a high transfer rate for first born babies, there were no signs that transfer was based on non-medical indications.

Background

Progress on United Nations' Millennium Development Goal 4 (MDG4) to reduce the under-five mortality has been slower than anticipated due to high neonatal mortality in developing countries. Worldwide, about 4 million neonatal deaths occur each year, of these three quarter occur in the first week of life with the highest risk at the first day of life [1]. Estimated neonatal mortality in Tanzania is about 35 per 1000 live births, and neonatal deaths are estimated to account for 28% of the under-five mortality [2]. Both the infant mortality rate and the under -five mortality rate have decreased from 1990 to 2004; by 31% (from 99 to 68 deaths per 1000 live births) and 24% (from 147 to 112 deaths per 1000 live births), respectively. This decline was, however, observed for post-neonatal mortality only, while neonatal as well as maternal mortality remained unchanged [2,3]. Adequate neonatal care may therefore be an important factor for continued improvement. Socio-economic deprivations are known to cause poor perinatal outcome such as neonatal care admission [4-7], low birth weight [8-10] and increased perinatal mortality [10-13]. A review of international evidence in socio-economic inequalities in childhood mortality in low and middle income countries showed higher childhood mortality in low socio-economic groups within each country

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[14]. Absolute inequalities were found to be higher for infant mortality than for child mortality. It was also estimated that 20-25% of under-five mortality inequalities arise in the neonatal period [14]. Making sure that health care is provided independent of social status is important for overall improvement in health.

Most studies on neonatal health in developing countries have focused on mortality rather than morbidity. However, in order to reduce neonatal mortality it is also of importance to consider factors associated with neonatal morbidity. Transfer of babies to neonatal care unit (NCU) may represent an indicator of morbidity that can be used for designing and implementing interventions aimed at improving health and increasing neonatal survival. Although previous studies have reported on the relationship of socio-demographic, maternal, or neonatal factors with neonatal admission [5,6,15], the combined effect of socio-demographic, maternal health factors and neonatal factors in relation to admission to NCU has not been well explored.

Referral in pregnancy and child birth can be categorised as self-referral or referral performed by health workers [16]. Self-referral implies that a woman (perhaps with the help of her family) seeks care at a health centre or a hospital. A study of 415 maternity admissions in Tanzania found that about 70% of the admissions could be categorized as self-referrals [16].

The presence of a NCU at the hospital gives an opportunity for all at risk babies to be admitted and managed by a paediatrician. The paediatric department at KCMC has established guidelines for care and management of newborns based on the condition of the newborn. Decision for transfer is usually done by midwives or a paediatrician based on the condition of the newborn; low Apgar score, prematurity, birth weight <1800 or birth weight >4000 g, congenital malformation and suspected infection. In addition, some obstetric conditions may necessitate baby transfer because they could represent a risk to the newborn. When a pregnancy complication indicates that the baby needs to be seen by a paediatrician, the paediatrician is informed in advance and attends the delivery to take care of the newborn in the labour ward or in NCU if transfer is necessary. The parents are usually informed about the reason for babies transfer but they are not asked for decision. Although KCMC is a private hospital, payment for the hospital bill is not considered as initial criteria for transfer or management of admitted newborns, therefore, all admitted babies receive same quality of care irrespective of the social background. The social welfare department within the hospital usually takes care of the hospital bills for families unable to pay.

The aim of our analysis was to estimate the influence of social background, pregnancy-related conditions and the condition of the newborn in relation to neonatal transfer to NCU. We explore these associations in a structured series of analyses, expecting most of the associations to be explained by the condition of the newborn. First, we expect social conditions to impact the likelihood of transfer by their effects on pregnancy complications and the condition of the newborn. Then we expect pregnancy complications to impact the likelihood of transfer by their effects on the condition of the newborn. Deviations from these expectations will appear as residual effects of social background and pregnancy complications after we adjust for the condition of the newborn. Such deviations will be inspected further since they could represent priority-settings or clinical judgment that incorporates social background or the background history of the delivery.

Methods

Setting

This study was done at Kilimanjaro Christian Medical Centre (KCMC) in Northern Tanzania. The hospital is a zonal hospital serving more than 13 million people from 4 regions namely; Kilimanjaro, Arusha, Tanga and Manyara. We established a cohort of babies based on records from the Medical Birth Registry comprising all deliveries at the hospital from July 2000 to September 2008 and followed the cohort in a registry of neonates transferred from the labour ward to NCU. The KCMC Medical Birth Registry system was established in 1999 as a collaboration between Kilimanjaro Christian Medical College, Tumaini University and the University of Bergen, Norway. The annual number of deliveries is around 3000 of which nearly two thirds are from urban area. Approximately 10-15% of the neonates are transferred to NCU for observation and management.

A total of 26 025 births were recorded in the Medical Birth Registry from July 1st 2000 to September 30th 2008. We excluded multiple deliveries, stillbirths, neonatal deaths in labour ward and neonates with missing child status record after delivery (Figure 1). In order to obtain a study group that reflected the general population, we excluded deliveries where mothers residing in rural areas had been referred for delivery at KCMC for medical reasons. Women residing in Moshi urban were not excluded since they could have delivered at KCMC anyway. KCMC is located in Moshi Urban and that 50% of the deliveries at KCMC are from Moshi Urban district [11]. We finally analyzed a total of 21 206 singleton live births.

Data collection

Information from all mothers who delivered at KCMC were collected within the first 24 hours after delivery. Trained midwife nurses conducted the interviews on a daily basis with all eligible subjects using a standardized

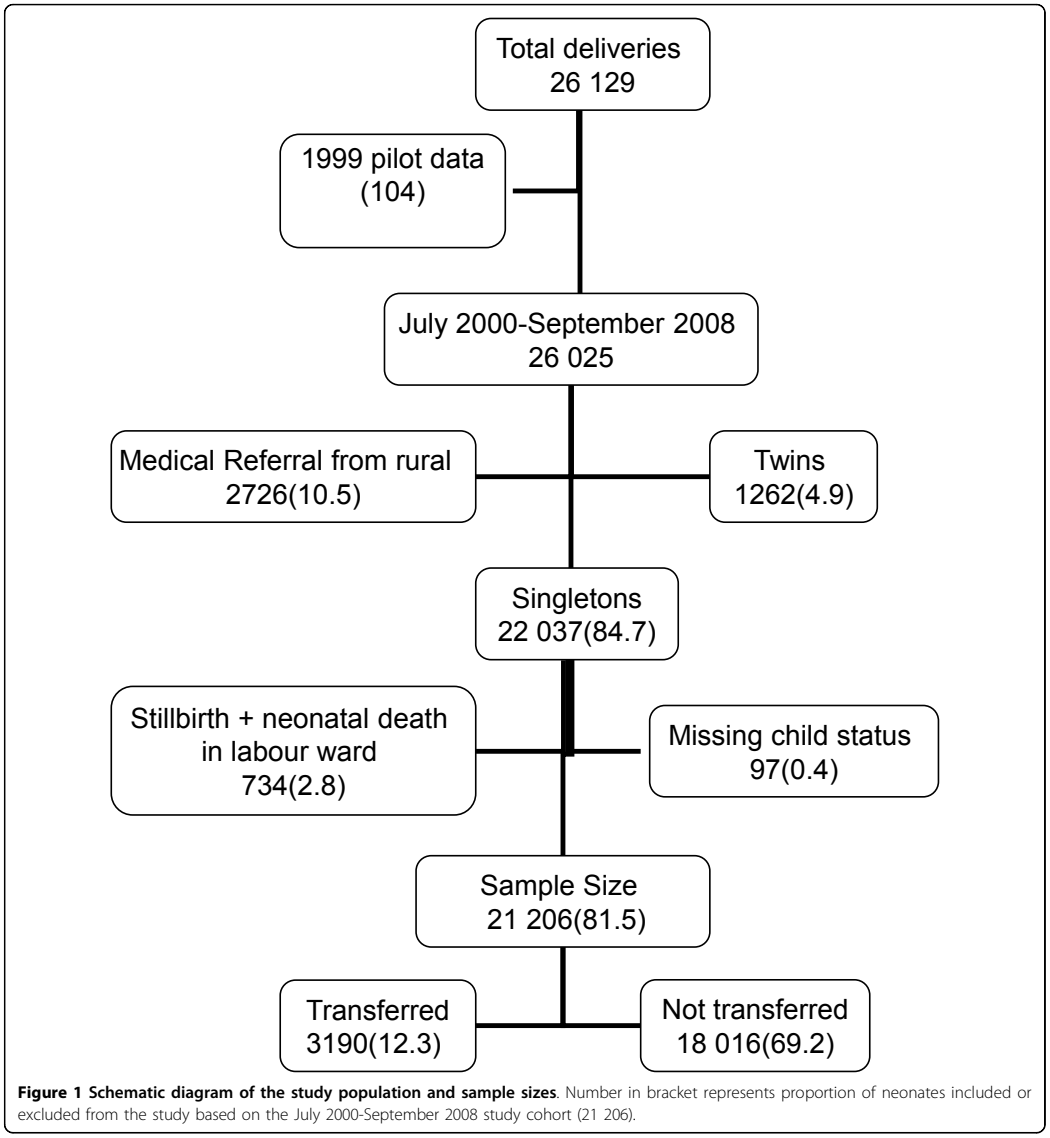

Figure 1 Schematic diagram of the study population and sample sizes. Number in bracket represents proportion of neonates included or excluded from the study based on the July 2000-September 2008 study cohort (21 206).

questionnaire. A verbal consent was obtained from the participants prior to the interview. Mothers also provided their antenatal visit card for more information such as date of first ANC visit, immunization history, malaria prophylaxis, drugs, illnesses recorded during follow up, weight at first ANC visit, number of ANC visits, as well as referral to ANC (self-referred or referred by health worker).

Information in the birth registry includes maternal health conditions before and during pregnancy, parents' socio-demographic characteristics, complications during labour and delivery, and information on the newborn; sex, gestational age, birth weight, Apgar score, and child status in four categories: 1) live born 2) live born transferred to NCU 3) neonatal death in labour ward, 4) stillborn.

The paediatric registry form was recorded in the NCU for all neonates who were transferred. The neonatal registry includes information on primary reasons for transfer, management, and discharge/death diagnoses. The two databases were linked using the unique child identification number, the mother's hospital registration, and the newborn's birth registration number.

Variable definition

Transfer to NCU was the main outcome. Independent variables include socio-demographic characteristics including maternal, paternal and environmental factors, maternal health conditions before and during pregnancy, and complications during labour and delivery, as well as condition of the newborn (Tables 1, 2 and 3).

Data analysis

Data were analyzed using Statistical Package for Social Science (SPSS) program Version 15.0 for Windows (SPSS 15.0 Chicago Inc. III, USA). Cross tabulations and generalized linear models were used to obtain relative risks (RR) and corresponding 95% confidence intervals. From the bivariate analyses we present all variables with p-value less than 0.1, which were then entered into the multivariable analysis. Three steps were involved in the multivariable analysis. In the first step (model A) all socio-demographic factors and maternal health condition before pregnancy were included. In the second step (model B) we included all variables in step one as well as pregnancy and labour-related conditions. In the third and final step (model C), we included all variables in step two as well as neonatal conditions. We used Poisson regression with robust variances to obtain a valid confidence interval when a log-binomial analysis failed to converge [17]. A priori we also considered some maternal conditions to be important and included in the final analysis, these were hypertensive conditions (preeclampsia, eclampsia and abruption placenta) and diabetes (pre-gestational or gestational).

Ethical approval

The birth registry at Kilimanjaro Christian Medical Centre obtained ethical clearance from the Tanzania Ministry of Health, Institute of Science and Technology, from the Norwegian National ethics committee and from the Kilimanjaro Christian Medical College (KCM-College) research ethics committee in 1999. The protocol for this study was approved by KCM-College research ethics committee, with certificate no. 333 of 15th July 2010.

Results

A total of 21 206 live-born singletons were analysed. The majority of the mothers were married (89.7%), were residing in urban areas (61.9%), had primary school education (61.3%), and belonged to the *Chagga* tribe (58.2%). Mean maternal age at child birth was 27.4 (SD = 6.1) years, and 38.8% of the mothers had their first born child. Mean maternal pre-pregnancy weight and height were 62.7 (SD = 12.5) kilograms and 160.0 (SD = 6.7) centimetres, respectively. The mean number of antenatal care visits per women was 5 (SD = 2.1). Mean gestational age and birth weight were 39.1 (SD = 2.5) weeks and 3090 (SD = 544 grams), respectively.

A total of 3190 (15%) were transferred to NCU. Descriptive associations between transfer and socio-demographic, pregnancy-related and neonatal factors are shown in Tables 1, 2 and 3.

Socio-demographic characteristics and pre pregnancy conditions

After mutual adjustment of the socio-demographic and maternal pre-pregnancy health factors, most of the factors remained associated with neonatal transfer (Table 4; model A). First born babies and fourth or later born babies (RR 1.3; 95% CI: 1.2-1.4 and 1.2; 95% CI: 1.0-1.3, respectively) were shown to have a high risk of being transferred compared with second born babies. Babies of single mothers were more likely to be transferred compared to babies of married mothers (RR 1.3; 95% CI: 1.1-1.5). Both maternal overweight and obesity increased the risk of babies transfer. Babies born from families who do not boil water for drinking had increased risk of being transferred to NCU (RR 1.2; 95% CI: 1.1-1.3).

Pre-gestational diabetes mellitus was strongly associated with neonatal transfer to NCU (RR 4.4; 95% CI: 3.3-5.8). A history of acute or chronic lung disease other than tuberculosis showed a weaker association (RR 1.2; 95% CI: 1.1-1.4).

Pregnancy, labour and delivery

Factors related to pregnancy, labour and delivery were included in the multivariable model in B. Hypertensive conditions such as eclampsia and preeclampsia (RR 2.8; 95% CI:1.7-4.4 and 2.0; 95% CI: 1.7-2.3, respectively), labour-related complications such as premature rupture of membrane and abruption placenta (RR 2.9; 95% CI: 2.6-3.4 and 2.6; 95% CI: 1.6-4.1, respectively), and other vaginal delivery (i.e. breech, vacuum or forceps) and caesarean section delivery (RR 2.9; 95% CI: 2.3-3.6 and 2.1; 95% CI: 1.9-2.3, respectively) were all associated with transfer (Table 4; model B). Gestational diabetes increased the risk of babies transfer by 40% although not statistically significant. Referral to ANC and few ANC visits were also found to be important predictors of neonatal transfer to NCU (RR 1.3; 95% CI: 1.1-1.4 and 1.3; 95% CI: 1.2-1.4), respectively.

Table 1 Transfer to neonatal care unit (n = 3190) among 21 206 live-born according to socio-demographic factors

Risk factors	Number live-born deliveries	Proportion (%) live-born babies transferred to NCU	RR (95% CI)	p-value
Maternal factors[x]				
Maternal age (years)				0.106
Under 18	480	17.9	1.2 (1.0-1.5)	
18-25	8328	14.5	1.0	
26-35	10 272	15.3	1.0 (1.0-1.1)	
Over 35	2070	15.7	1.0 (1.0-1.2)	
Mother's tribe				0.032
Chagga	12 311	14.5	1.0	
Pare	2496	16.2	1.0 (1.0-1.2)	
Others	6355	15.6	1.0 (1.0-1.2)	
Marital status				<0.0001
Married	19 016	14.6	1.0	
Single	2086	18.6	1.3 (1.2-1.4)	
Birth order				<0.0001
1st Child	8220	16.4	1.2 (1.1-1.3)	
2nd Child	5985	13.4	1.0	
3rd Child	3287	16.5	1.0 (0.9-1.1)	
4th or more	3714	13.5	1.2 (1.1-1.4)	
Mother's education				0.060
No education	348	17.8	1.2(1.0-1.7)	
Primary	12 990	15.3	1.0(1.0-1.1)	
Sec/higher	7819	14.4	1.0	
Mother's occupation				<0.0001
Professional	3355	14.3	1.0	
Business	4821	14.8	1.0 (0.9-1.2)	
Service	1538	15.4	1.1 (0.9-1.2)	
Farmer	4003	16.3	1.1 (1.0-1.3)	
Housewife	5401	15.4	1.1 (1.0-1.2)	
Others	1955	13.3	1.0 (0.8-1.1)	
Body height (cm)				<0.0001
<150	1505	18.3	1.4 (1.2-1.5)	
150+	18 342	14.1	1.0	
BMI (kg/m^2)				0.013
<18.5	1277	14.1	1.1 (0.9-1.2)	
18.5-24.9	4787	14.8	1.0	
25-29.9	6793	13.3	1.1 (1.0-1.2)	
30+	1496	16.2	1.2 (1.1-1.4)	
Genital mutilation				0.086
Yes	4752	15.8	1.0 (0.9-1.0)	
No	16 389	14.8	1.0	
Drinking in pregnancy				0.033
Yes	8278	14.4	1.0	
No	12 882	15.4	1.1 (1.0-1.2)	
Paternal factors[x]				
Father's age (years)				0.003
Under 26	3002	16.7	1.1 (1.1-1.3)	
26-35	11 794	14.6	1.0	
36-45	5428	14.5	1.0 (0.9-1.1)	
Over 45	827	17.7	1.2 (1.0-1.4)	

Table 1 Transfer to neonatal care unit (n = 3190) among 21 206 live-born according to socio-demographic factors *(Continued)*

Father's tribe				0.004
Chagga	11 157	14.2	1.0	
Pare	2463	16.0	1.1(1.0-1.3)	
Others	7451	15.8	1.1(1.0-1.2)	
Father's Occupation				<0.0001
Professional	4483	14.0	1.0	
Business	6798	14.8	1.1 (1.0-1.2)	
Service	4321	15.0	1.1 (1.0-1.2)	
Farmer	2070	18.7	1.3 (1.2-1.5)	
Skilled	2808	14.1	1.0 (0.9-1.1)	
Others	643	15.9	1.1 (0.9-1.4)	
Father's education				0.013
No education	110	20.9	1.5 (1.0-2.1)	
Primary	10 563	15.5	1.1 (1.0-1.2)	
Sec/higher	10 446	14.4	1.0	
Environmental factors[x]				
Type of toilet				0.006
Pit latrine	12 515	15.6	1.1 (1.0-1.2)	
Flush	8608	14.2	1.0	
Source of water				0.030
Tap water	19 555	14.9	1.0	
Well	459	16.6	1.1 (0.9-1.4)	
River	432	19.7	1.3 (1.1-1.6)	
Spring	644	16.0	1.1 (0.9-1.3)	
Boil drinking water				<0.0001
Yes	6672	13.3		
No	14 449	15.8	1.2 (1.1-1.3)	

x-The total in some variables does not sum to 21 206 due to missing data

Significant factors in model A continued to be independent predictors for neonatal transfer also in model B, except for maternal body height below 150 cm. However, addition of variables in model B slightly reduced the relative risk for most factors.

Neonatal factors

In model C, neonatal factors were added into the multivariable model. All the selected neonatal factors were significantly associated with transfer to NCU, with the highest relative risks being for birth weight above 4000 g (RR 7.2; 95% CI: 6.5-8.0) and five minutes Apgar score below 7 (RR 4.0; 95% CI: 3.4-4.6) (Table 4; model C).

After inclusion of the neonatal factors, some pre-pregnancy factors, such as women giving birth to their first babies (RR 1.4; 95% CI: 1.2-1.5), maternal age 26-35 years (RR 1.2; 95% CI: 1.1-1.3), and single marital status (RR 1.2; 95% CI: 1.0-1.3) were still significantly associated with neonatal transfer. Lack of paternal education (RR: 0.5; 95% CI: 0.3-0.9) was negatively associated with transfer to NCU. Birth to fourth or later born babies, maternal overweight or obesity, pre-gestational diabetes and epilepsy were no longer significantly associated with neonatal transfer.

Discussion

In this registry based study from a tertiary hospital in Tanzania, we identified patterns of neonatal transfer to NCU. In a three-step analysis we studied socio-demographic factors, maternal health factors, and neonatal factors in relation to transfer. A particular aim was to assess whether socio-demographic factors were related to transfer to NCU beyond their association with well-defined medical risks. The analyses showed that neonatal factors by far had the strongest association with neonatal transfer, but that pre-pregnancy and pregnancy factors were also independently associated with transfer.

The incidence of neonatal transfer in this study was 15%, which is slightly higher than reported in previous studies both from developed [4,5] and developing countries [7,18].

Neonatal factors

The studied neonatal factors included classical risk factors for morbidity and mortality, such as birth weight,

Table 2 Transfer to neonatal care unit (n = 3190) among 21 206 live-born according to maternal health conditions

Risk factors	Number live-born deliveries	Proportion (%) live-born babies transferred to NCU	RR (95% CI)	p-value
Before pregnancy[a]				
Medication regular	493	18.9	1.3 (1.1-1.5)	0.013
Diabetes	49	69.4	4.7 (3.9-5.6)	<0.0001
Hypertension	143	21.7	1.5 (1.1-2.0)	0.021
Epilepsy	64	25.0	1.7 (1.1-2.6)	0.026
Gyn. Disease	1122	17.5	1.2 (1.0-1.4)	0.020
Lung disease	1950	16.6	1.1 (1.0-1.2)	0.040
Malaria	12 258	14.9	1.0 (0.9-1.1)	0.899
Anaemia	406	17.0	1.2 (0.9-1.5)	0.267
Tuberculosis	77	18.2	1.3 (0.7-2.2)	0.703
During pregnancy[a]				
No ANC attendance	137	34.3	2.3 (1.8-2.9)	<0.0001
Referred to ANC[§]	2284	21.0	1.5 (1.4-1.6)	<0.0001
ANC < 5 visits	13 168	16.2	1.3 (1.2-1.4)	<0.0001
Anaemia	449	18.3	1.2 (1.0-1.5)	0.050
Gestational Diabetic	17	47.1	3.1 (1.9-5.2)	<0.0001
Hypertension	72	30.6	2.0 (1.4-2.9)	<0.0001
Preeclampsia	711	32.1	2.2 (2.0-2.5)	<0.0001
Eclampsia	27	70.4	4.7 (3.7-6.0)	<0.0001
Bleeding	239	23	1.5 (1.2-2.0)	<0.0001
Malaria	4314	14.4	1.0 (0.9-1.0)	0.167
Tuberculosis	414	15.0	1.0 (0.8-1.3)	0.969
HIV infection	784	16.1	1.0 (0.8-1.1)	0.528
Complications[a]				
Abruptio placenta	29	65.5	4.4 (3.4-5.7)	<0.0001
PROM	468	54.7	3.9 (3.5-4.2)	<0.0001
Bleeding >500 mls	36	33.3	2.2 (1.4-3.5)	0.001
Placenta previa	51	45.1	3.0 (2.2-4.1)	<0.0001
Caesarean section	6472	24.2	2.3 (2.2-2.5)	<0.0001
Other Vaginal delivery	317	33.4	3.2 (2.7-3.8)	<0.0001
Other unspecified	373	24.7	1.7 (1.4-2.0)	<0.0001

a- Numbers for reference categories not given, each variable had complete data

§- First ANC visit triggered by health workers

preterm delivery, Apgar score and sex, and were as expected strongly related to neonatal transfer. Although the causal effect of birth weight is controversial [19] low birth weight is a good predictor of need for neonatal care. Low birth weight has been proposed to contribute to 40-80% of neonatal morbidity and mortality [20,21]. Preterm delivery is estimated to account for 28% of all neonatal deaths [20].

We also found a very high admission rate of newborns with a birth weight above 4000 g. Fetal macrosomia is associated with obstetric complications and neonatal morbidity such as injuries, respiratory distress and hypoglycaemia. Observation for transient or persistent hypoglycaemia is a common reason for admission of high birth weight babies to NCU [22]. At KCMC, such babies will be discharged within 24 hours if there is no risk of persistent hypoglycemia and the blood glucose level is normal. The outcome is in general good for these babies, and one may speculate whether observation without transfer to NCU for many of these babies would represent a better use of resources.

In general, male neonatal morbidity exceeds female morbidity, partly due to a higher occurrence of preterm birth and other neonatal risk factors [23]. The male-to-female ratio of transfer 1.24, declining to 1.18 in the adjusted analyses, corresponds well with the established higher risk in males, and does not indicate a difference in care according to infant sex.

Table 3 Transfer to neonatal care unit (n = 3190) among 21 206 live-born according to newborn health conditions

Risk factors[x]	Number live-born deliveries	Proportion (%) live-born babies transferred to NCU	RR (95% CI)	p-value
Birth weight (g)				<0.0001
500-1499	173	95.4	9.8 (9.3-10.4)	
1500-2499	1652	41.5	4.3 (4.0-4.6)	
2500-3999	18 607	9.7		
4000-6000	714	69.7	7.2 (6.7-7.7)	
Apgar score 5 min				<0.0001
<7	442	91.9	6.9 (6.6-7.2)	
7+	20 590	13.4		
Gestation age (weeks)				<0.0001
25-33	447	70.5	5.6 (5.2-6.1)	
34-36	1401	27.3	2.2 (2.0-2.4)	
37+	17 603	12.5	1.0	
Presentation				<0.0001
Cephalic	20 862	14.8	1.0	
Breech	238	28.2	1.9 (1.6-2.3)	
Transverse	28	21.4	1.5 (0.7-3.0)	
Sex				<0.0001
Male	10 904	16.6	1.2 (1.2-1.3)	
Female	10 162	13.3	1.0	

x-The total in some variables does not sum to 21 206 due to missing data

Pregnancy, labour and delivery

Risk of neonatal transfer was high in mothers with preeclampsia, eclampsia and abruption placenta, however no or weak effects were observed after inclusion of neonatal factors in the model. Hypertensive conditions in pregnancy are associated with preterm birth and low birth weight [15,24-27], and many cases of abruption placenta occur at a low gestational age, which explain the indirect association between these complications and neonatal transfer. The direct cause of transfer would be the preterm birth.

Other conditions, such as premature rupture of membrane, caesarean section and operative vaginal delivery, showed a high risk of neonatal transfer also after accounting for the neonatal condition of the baby. The high rate of transfer for babies born with mothers having PROM is similar to what is reported elsewhere [15]. Premature rupture of the membrane (PROM) is associated with preterm delivery and low birth weight [15,27]. A previous study at KCMC reported a high prevalence (38%) of low birth weight babies after PROM [27]. Such babies are at higher risk of developing neonatal infection. Antibiotic prophylaxis given to mothers with PROM has shown to reduce risk of infection in the newborn [28,29]. The high transfer rate after PROM in our data is likely to be explained by the fact that a majority of mothers with a history of PROM did not receive antibiotic prophylaxis prior to delivery, due to late arrival to the centre.

Mothers with less than five antenatal care visits were more likely to have their baby transferred and this association persisted after we took into account our measures of the condition of the newborn. Amount of antenatal care plays a role in neonatal outcome [30-32], and each additional ANC visit has previously been found to offer a protective effect on neonatal outcome [31]. When the mother had been referred for antenatal care, however, the risk of transfer was increased.

Pre pregnancy factors

Among diseases that the mothers had before the pregnancy, only lung disease remained significantly associated with neonatal transfer when pregnancy conditions and neonatal conditions were accounted for (Table 4, model C). Pre-gestational diabetes was strongly related to transfer in models A and B, but the association disappeared after accounting for the neonatal conditions in model C. Noteworthy, gestational diabetes had a weak and non-significant association with transfer, and the relative risk was not affected by adjustment for neonatal factors. The low risk of transfer in babies born to mothers with gestational diabetes compared to babies of mothers with pre-gestational diabetes is also reported elsewhere [5,15,33].

Women giving birth to their first child and single mothers were more likely to have their baby transferred to NCU, also after accounting for pregnancy conditions and neonatal conditions. Birth to a first child and single

Table 4 Linear regression model risk factors for neonatal transfer to neonatal care unit

	Model A[a]	Model B[a]	Model C[a]
Risk factors	**RR (95%CI)**	**RR (95%CI)**	**RR (95%CI)**
Pre-pregnancy factors			
Maternal age (Ref. 18-25 years)			
Under 18 years	1.0 (0.8-1.4)	1.0 (0.8-1.4)	0.9 (0.7-1.2)
26-35 years	1.3 (1.1-1.4)**	1.2 (1.1-1.3)**	1.2 (1.1-1.3)**
Over 35 years	1.1 (0.9-1.3)	1.0 (0.8-1.3)	1.0 (0.8-1.2)
Birth order (Ref. 2nd child)			
1st child	1.3 (1.2-1.4)**	1.3 (1.2-1.5)**	1.4 (1.2-1.5)**
3rd child	1.0 (0.8-1.1)	1.0 (0.9-1.1)	1.0 (0.9-1.1)
4th or more	1.2 (1.0-1.3)	1.3 (1.1-1.4)**	1.1 (1.0-1.3)
Body mass index(Ref 18.5-24.9)			
Underweight (<18.5)	1.0 (0.9-1.2)	1.0 (0.9-1.2)	1.0 (0.9-1.2)
Overweight (25-29.9)	1.2 (1.1-1.3)**	1.2 (1.0-1.3)**	1.1 (1.0-1.2)
Obesity(30+)	1.3 (1.1-1.5)**	1.2 (1.1-1.4)**	1.1 (1.0-1.3)
Single marital status	1.3 (1.1-1.5)**	1.2 (1.1-1.4)*	1.2 (1.0-1.3)*
Body height <150 cm	1.2 (1.1-1.4)*	1.0 (0.9-1.2)	1.1 c(0.9-1.2)
Paternal age (Ref 26-35 years)			
Under 26 years	1.2 (1.0-1.3)	1.1 (1.0-1.3)	1.2 (1.0-1.3)*
36-45 years	1.0 (0.9-1.1)	0.9 (0.8-1.0)	0.9 (0.8-1.1)
Over 45 years	1.1 (0.9-1.4)	1.1 (0.9-1.4)	1.1 (0.9-1.3)
Father's education (Ref sec/high)			
No education	1.2 (0.7-2.3)	0.8 (0.5-1.5)	0.5 (0.3-0.9)*
Primary school	1.0 (0.9-1.1)	1.0 (0.9-1.1)	1.0 (0.9-1.1)
Pre-gestational diabetic	4.4 (3.3-5.8)**	3.5 (2.6-4.7)**	1.6 (0.7-3.3)
Maternal Lung disease	1.2 (1.1-1.4)**	1.2 (1.1-1.4)**	1.2 (1.0-1.3)*
Maternal Epilepsy	1.6 (1.0-2.6)	1.9 (1.2-2.9)**	1.4 (0.9-2.2)
Not boiling drinking water	1.2 (1.1-1.3)**	1.1 (1.0-1.3)**	1.1 (1.0-1.2)
Pregnancy, labour and delivery			
Mother referred to ANC[§]	-	1.3 (1.1-1.4)**	1.2 (1.0-1.3)*
ANC < 5 visits	-	1.3 (1.2-1.4)	1.2 (1.1-1.3)**
Gestational Diabetic	-	1.4 (0.6-3.4)	1.4 (0.5-4.5)
Hypertension		1.5 (0.9-2.4)	1.2 (0.7-1.9)
Preeclampsia		2.0 (1.7-2.3)**	1.3 (1.1-1.5)**
Eclampsia	-	2.8 (1.7-4.4)**	0.9 (0.6-1.6)
Abruptio placenta	-	2.6 (1.6-4.1)**	1.1 (0.7-1.8)
Premature rupture of membrane	-	2.9 (2.6-3.4)**	2.3 (1.9-2.7)*
Caesarian section	-	2.1 (1.9-2.3)**	1.9 (1.8-2.1)**
Other vaginal delivery	-	2.9 (2.3-3.6)**	2.2 (1.7-2.9)**
Other unspecified complications	-	1.8 (1.4-2.3)**	1.5 (1.2-1.9)**
Neonatal factors			
Birth weight >4000 g	-	-	7.2 (6.5-8.0)**
Birth Weight 1500-2500 g	-	-	2.8 (2.5-3.1)**
Birth weight <1500 g	-	-	3.0 (2.3-4.0)**'
Gestational age below 34 weeks	-	-	1.8 (1.5-2.1)**
Gestational age 34-36 weeks	-	-	1.3 1.3 (1.1-1.5)**
Five minutes Apgar score <7	-	-	4.0 (3.4-4.6)**
Male sex			1.2 (1.1-1.3)**

*p-value less than 0.05

**p-value less than 0.01

[a] In each step variables entered were all which had p-value of < 0.1 in univariable analysis including maternal age although p-value was slightly above 0.1 (0.106). The lowest risk category in each group was used as a reference. Results are presented for all variables which were significant at least once in any of the three steps.

Model A, first step; adjusted for pre pregnancy factors

Model B, second step; variables in model A plus conditions in pregnancy, labor and delivery

Model C, third step; variables in model B plus neonatal factors

§- First ANC visit triggered by health workers

motherhood are classical risk factors for neonatal morbidity and mortality [9,10,12,18,34,35]. However, the 40% higher risk of admission for a first born child in the fully adjusted model (model C), is higher than what one would expect according to previous knowledge on morbidity and mortality associated with first delivery. In a previous study from the same hospital, perinatal mortality was not associated with birth order except for a higher perinatal mortality in offsprings of mothers with three or more previous pregnancies [11]. To further elaborate this finding, we performed a regression analysis with a finer categorization of Apgar score. In this model, the parity effect was still statistically significant, however reduced. In a setting with limited obstetric services, the generally higher neonatal stress on first born babies might be even more evident.

In line with previous findings [36-38] we found that overweight and in particular obese mothers had a high risk of having their baby transferred to NCU. Maternal obesity is associated with some pregnancy complications [33,36-40] and overweight or obese mothers are more likely to have high birth weight babies [37,38,40]. A meta-analysis review showed a lower risk of low birth weight among babies of overweight or obese mothers compared to normal weight mothers, however the risk of very low birth weight and extremely low birth weight was increased due to more induced preterm deliveries in overweight or obese mothers [41]. In our data, the association of neonatal transfer associated with maternal overweight and obesity was weakened but still statistically significant after adjustment for pregnancy conditions, however disappeared after adjustment for neonatal conditions. Hence, pregnancy conditions and neonatal conditions seem to be mediators in the association between maternal overweight and neonatal transfer. A similar pattern was seen for mothers of short stature, where an increased risk seen in model A seemed to be linked to a higher rate of pregnancy complications for these mothers.

Drinking unboiled water was one of the factors associated with neonatal transfer. Waterborne disease including diarrhoea and dysentery is prevalent in Tanzania, therefore, it is recommended to boil water for drinking including tap water. In our study 92% of the participants used tap water, however only 31% boiled water for drinking. In a study from Tanzania, lack of boiling water prior to consumption was more common in households with low income, and lack of proper knowledge on the importance of how to handle and store water safely was associated with E.coli occurrence [42]. Both ignorance and poverty might be the major barriers to boiling drinking water.

Lack of paternal education was associated with a low chance of neonatal transfer (RR = 0.5; 95% CI: 0.3-0.9) in the fully adjusted model. Although our results should be interpreted with care due to the low numbers (110 fathers with no education) and a confidence interval close to one, the findings could reflect low focus on neonatal health care in deprived families. A previous study using the same birth registry reported that paternal socio-demographic factors seemed to be more important predictors of perinatal mortality than maternal socio-demographic factors in this area [11]. However, such an interpretation is not compatible with the principle that transfer mechanisms should be unaffected by parental and family influence.

Strengths and limitations

The study was based on a hospital based birth registry, where data are carefully collected according to standardized procedures, ensuring complete coverage of births on a daily basis including weekends and holidays. Information was collected by designated midwives using a structured questionnaire-based interview, and medical records were used to verify the information from the questionnaire. The sample size was relatively large and enabled us to study many risk factors in relation to neonatal transfer. Hence, the data allowed us to study the relationship between socio-demographic characteristics, maternal health and complications during delivery, and neonatal characteristics, with transfer to neonatal intensive care unit. Selection bias was reduced by excluding all medically indicated referral births from rural areas where the mother would not probably deliver at KCMC if not referred. The excluded cases accounted for 52% of all referrals and 75% of all medical referrals.

About 29% of the deliveries in the Kilimanjaro region occur at home [20], and the study results may not be representative of the entire population within the area. Although women who give birth at the hospital largely differ with respect to socio-demographic status, the socio-demographic variation in the community may be even larger and towards a less privileged population. It is therefore possible that the observed risks are underestimated as compared to the region.

We applied an analytical approach where the various classes of variables were included in regression models through three steps. The purpose of this was to identify which factors that mediated any association with transfer. Our analyses are based on a limited set of variables, and there may be important risk factors of neonatal transfer that we have not been able to account for. Hence, the effects obtained in the models may represent a mixture of effects of the studied factors and effects of factors not accounted for. In particular, our measures of the condition of the newborn were probably too crude to fully account for the clinical judgement of the baby's condition and the need for transfer.

Despite these limitations, we believe that our study, based on structured collection of information with a hospital based design combined with careful considerations of possible biases, represent findings of importance. True population data are difficult to collect in sub-Saharan Africa. Investment in competence building and data collection should start with key hospitals, and efforts should be done to include well-defined populations, in order to generate relevant and representative data to address the important public health issues within the general population.

Conclusions

Our study has demonstrated the combined effect of socio-demographic, maternal health conditions and neonatal factors in predicting transfer to NCU. The relationship between socio-demographic, maternal health characteristics and neonatal factors observed in this study reflects traditionally known predictors of neonatal morbidity and mortality. As for the pre-pregnancy factors, most of the associations with transfer were accounted for by pregnancy complications and neonatal factors. An exception from this was a possibly reduced use of transfer for babies of non-educated fathers. The potential effect of paternal social status both on neonatal health and on access to health care for mother and baby needs more attention. Another exception that needs to be further explored is the 40% higher rate of transfer among first born babies. With respect to neonatal factors, one might speculate whether the high number of babies above 4000 g transferred to the NCU represents an optimal use of resources, as the outcome of these babies is in general good.

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Authors' contributions

BTM: Study design, methodology, data analysis and manuscript writing. RTL, GSK, RO, GK, AKD: Study design, methodology, manuscript writing. All authors approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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Cause-specific neonatal mortality in a neonatal care unit in Northern Tanzania: a registry based cohort study

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Abstract

Background: The current decline in under-five mortality shows an increase in share of neonatal deaths. In order to address neonatal mortality and possibly identify areas of prevention and intervention, we studied causes of admission and cause-specific neonatal mortality in a neonatal care unit at Kilimanjaro Christian Medical Centre (KCMC) in Tanzania.

Methods: A total of 5033 inborn neonates admitted to a neonatal care unit (NCU) from 2000 to 2010 registered at the KCMC Medical Birth Registry and neonatal registry were studied. Clinical diagnosis, gestational age, birth weight, Apgar score and date at admission and discharge were registered. Cause-specific of neonatal deaths were classified by modified Wigglesworth classification. Statistical analysis was performed in SPSS 18.0.

Results: Leading causes of admission were birth asphyxia (26.8%), prematurity (18.4%), risk of infection (16.9%), neonatal infection (15.4%), and birth weight above 4000 g (10.7%). Overall mortality was 10.7% (536 deaths). Leading single causes of death were birth asphyxia (n = 245, 45.7%), prematurity (n = 188, 35.1%), congenital malformations (n = 49, 9.1%), and infections (n = 46, 8.6%). Babies with birth weight below 2500 g constituted 29% of all admissions and 52.1% of all deaths. Except for congenital malformations, case fatality declined with increasing birth weight. Birth asphyxia was the most frequent cause of death in normal birth weight babies (n = 179/246, 73.1%) and prematurity in low birth weight babies (n = 178/188, 94.7%). The majority of deaths (n = 304, 56.7%) occurred within 24 hours, and 490 (91.4%) within the first week.

Conclusions: Birth asphyxia in normal birth weight babies and prematurity in low birth weight babies each accounted for one third of all deaths in this population. The high number of deaths attributable to birth asphyxia in normal birth weight babies suggests further studies to identify causal mechanisms. Strategies directed towards making obstetric and newborn care timely available with proper antenatal, maternal and newborn care support with regular training on resuscitation skills would improve child survival.

Keywords: Neonatal mortality, Neonatal deaths, Neonatal morbidity, Birth asphyxia, Prematurity, Causes of death

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Background

The aim of the United Nations' Millennium Development Goal 4 (MDG4) is to reduce under-five mortality worldwide to 30 deaths per 1000 live births by 2015. Globally, an estimate of 10.6 million children under five years died in 2000 [1], declining to 8.8 million in 2008 [2] and further to 7.7 million in 2010 [3]. At the same time, methods of estimation and available sources of information for under-five mortality have improved [1-4]. However, share of neonatal deaths increased from 37% in 2000 [1,5] to 41% in 2008 [2]. The slow decline in neonatal mortality as compared to post-neonatal mortality calls for attention and efforts to reverse this trend. Within the neonatal period an estimated 50% of all deaths are within the first 24 hours while 75% are within the first week of life [5]. Given that a large fraction of these deaths are preventable, a focus on mortality in the first week of life is important in order to accelerate the millennium goal.

Worldwide, the most important single causes of neonatal deaths are preterm birth, birth asphyxia, sepsis and pneumonia [2,5,6]. This reflects the mortality pattern in low income countries where neonatal mortality is high, whereas, in high income countries where mortality is low, preterm birth and congenital malformations are the leading causes of death [7]. The World health organization (WHO) estimates that birth weight below 2500 g indirectly contributes to about 15% of the neonatal mortality, ranging from 6% in high income countries to 30% in low income countries, with preterm birth and related complications being the underlying cause [8].

Tanzania is among the countries with insufficient progress towards achieving the MDG4 showing slow decline in under-five mortality rate [4]. Neonatal mortality in Tanzania is estimated to account for 28-34% of deaths in children younger than five years [2,3,9], with the most frequent single causes of death being prematurity, birth asphyxia, sepsis and pneumonia [2,10].

Globally, it has been estimated that ninety nine percent of neonatal deaths occur in developing country where also vital registration is limited [5]. The UNICEF report in 2002 estimated that only 5% of Tanzanian children aged five years are registered, with marked difference in percentage between rural (3%) and urban (22%) areas [11]. A recent country survey in Tanzania reported consistently low registration rate for under-five years children (16%), of whom about half (8%) receive birth certificate [12]. Also this survey indicated the difference in the birth registration rate between rural (10%) and urban (44%) areas.

Identification of cause-specific mortality in a particular setting is important to design interventions directed to improve neonatal survival. Therefore, in order to address neonatal mortality in Tanzania and possibly identify areas of prevention, we studied causes of neonatal admission and cause-specific neonatal mortality in a cohort of neonates delivered at the KCMC tertiary hospital and admitted to NCU.

Methods

Setting

The primary study unit was the neonatal care unit (NCU) at the Kilimanjaro Christian Medical Centre (KCMC) in Northern Tanzania. As a tertiary and a referral hospital for the four regions in the Northern part of the country, the NCU at KCMC receives high risk babies delivered within the institution and referrals from other health facilities or from home. The NCU has bed capacity of 40 babies. The babies are nursed in locally made baby cots and there are heaters to keep the room as well as the babies warm. The unit has no mechanical ventilator or any continuous positive airway pressure machine. The babies receive oxygen through nasal prongs or face masks. There is no central oxygen supply; instead oxygen is usually stored in big cylinders. In addition, there are four portable oxygen concentrators. The midwives in the labour ward are responsible for the initial resuscitation of normal deliveries. Doctors from the paediatric department are called to the labour ward to attend the at risk pregnancies. Normal babies are put on the breast as soon as they recover from the birth trauma which is usually within the first four hours after delivery. Babies in the nursery rooms are either fed on expressed breast milk if the mothers are around or formula in the absence of the mothers. Feeding is given either through nasal gastric tube, syringe or cup and spoon. For neonates with feeding difficulties, parenteral feeding with either 10% or 5% dextrose depending on the gestational age is used.

The neonatal care unit has 3 nursery rooms, one for preterm babies, one for term babies with non-infectious conditions and the third is reserved for bacterial as well as viral infections. Kangaroo mother care is being encouraged in the unit and a special room has been allocated for that purpose. Two other rooms are available for stable babies who are given to their mothers and to continue treatment under the supervision of the unit nurses, pending discharge when fully recovered.

We have previously reported that approximately15% of the births within the KCMC hospital were transferred to neonatal care unit for admission [13]. Criteria for transfer to neonatal care unit were found to be low Apgar score, prematurity, birth weight <1800 or birth weight >4000 g, congenital malformation, suspected infection or risk of infection, as well as for observation in case of poor maternal outcome or poor obstetric history.

Study design and subjects

This is a birth registry based cohort study. Neonates registered in the Medical Birth Registry and admitted to

the neonatal care unit at KCMC, were included. The KCMC Medical Birth Registry was established in 1999 as collaboration between Kilimanjaro Christian Medical College, Tumaini University and the University of Bergen, Norway. The Medical Birth Registry and neonatal registry were officially established in July 2000.

From July 2000 to October 2010, a total of 34087 births were registered in the birth registry, of which 5033 (14.8%) neonates were admitted to the neonatal care unit. These neonates formed our study population.

Data collection

Information from all mothers who delivered at KCMC was collected within the first 24 hours after delivery based on a standardized questionnaire as well as antenatal records. Detailed information collected for the Medical Birth Registry are described elsewhere [13].

The neonatal registry form was recorded for all neonates who were transferred for admission in the NCU. The data collection form was administered by a trained paediatric nurse who worked in a neonatal care unit. The collection of information for neonates admitted to the NCU was done during admission and finalized after discharge or death. Information collected in the neonatal registry includes child's ID-number, date of admission, reasons for admission, investigations done, management given, clinical details at discharge and death reports. The information collected from the Medical Birth Registry and neonatal registry were finally entered into a computerized database where they can be linked using the child's ID-number.

On arrival in the NCU, the baby is examined by a medical officer. Estimation of the gestational age is done using the Finnstrøm maturity score, which is a simple method for assessing maturity based on external characteristics. Tables for maturity score and transformation to gestational age are included in the KCMC Paediatric management schedule [14]. The diagnosis of birth asphyxia is based on Apgar score below 7 at five minutes and severity of neonatal condition at admission, based on the presence of convulsions within the first 24 hours. A diagnosis of infection is based on clinical symptoms and signs, evidence of focal lesions, or laboratory findings including blood cultures. Thin and thick blood slides are taken in order to rule out congenital malaria if suspected. A diagnosis of congenital malformation is based on the child's clinical presentation at admission and screening with the aid of X-ray, ultrasound scan, echocardiography and CT scan when applicable. Up to three clinical diagnoses are recorded for each neonate. The two conditions Respiratory Distress Syndrome (RDS) and Necrotizing Enterocolitis (NEC) were frequently reported as preterm complications and were mainly diagnosed clinically followed by X-ray investigation. Other preterm complications such as Intraventricular haemorrhage (IVH) may be underreported in the clinical discharge or death diagnosis reports as brain ultrasound investigation is not routinely done for preterm babies. Management of all admitted neonates follows the KCMC Paediatric Management Schedules [14]. This book was prepared by past and present paediatricians in the department by adapting the WHO guidelines for management of common illnesses in limited resource settings [15]. During the study period there was no documented change in clinical practice and management specifically for prematurity and birth asphyxia. As for neonatal infections, the department observed a high rate of staphylococcal isolates from newborns blood culture sensitive to cloxacilline and gentamycine in early 2000 also observed and recommended by Klingenberg et al., [16]. Therefore, treatment guidelines for neonatal infection changed from gentamycine and ampicilline to gentamycine and cloxacilline [14]. Surfactant treatment is not available in the neonatal unit at the moment. Therefore, babies with RDS are managed as severely preterm babies with oxygen therapy, thermal care, nutritional support, antibiotic treatment and vitamin K [14]. In addition, aminophylline is given for babies with apnoea attacks not responding to tactile stimulation.

Data analysis

We first coded clinical diagnoses independently depending on the presence of any diagnosis; a neonate having more than one diagnosis was recorded in different categories in order to study all causes of admission, case fatality and their contribution to total neonatal mortality. Case fatality was computed as number (percentage) of deaths within each clinical discharge diagnosis among admitted babies with the same condition.

Secondly, the Wigglesworth classification with the revised decision tree [17,18] with modifications from the Neonatal and Intrauterine deaths Classification according to Etiology (NICE) [19] was used to classify neonatal deaths in a hierarchical order. The criteria described in Table 1, adapted and modified from elsewhere [20] were used in order to assign babies to a single cause of death. Fourteen neonates who had symptoms recorded as discharge/death diagnosis were reassigned a cause of death after reviewing the birth history and clinical presentation. Finally, in hierarchical order, each neonatal death was classified into one of the five single causes of death groups; 1) congenital malformation 2) prematurity 3) birth asphyxia 4) infection and 5) other causes of death. The single causes of death were then stratified into 5 birth weight categories in order to study birth weight specific mortality.

Data were analyzed using Statistical Package for Social Science (SPSS) program Version 18.0 for Window (SPSS

Table 1 Criteria used for case definition to identify cause-specific mortality*

Causes of death	Case definition	Search criteria for clinical diagnosis in registry
Congenital malformation	lethal congenital malformation (congenital heart, spinal bifida, congenital syndromes, gastrointestinal malformation)	– multiple congenital malformation
		– congenital heart disease
		– spinal bifida/hydrocephalus
		– congenital syndromes or syndrome baby and deaths due to systemic conditions such as-renal failure or gastrointestinal system
Birth asphyxia	birth asphyxia, hypoxic ischaemic encephalopathy Apgar based definition	– birth asphyxia weight >1000 g or gestational age >27 weeks
		– birth asphyxia and prematurity with gestational age ≥33wks and birth weight ≥2500 g or birth weight ≥ 1800 g if gestational age unknown
		– hypoxic ischaemic encephalopathy five minutes Apgar less than 7
Prematurity	prematurity, respiratory distress syndrome in preterm, necrotizing enterocolite in preterm birth	– prematurity
		– prematurity and asphyxia with gestational age < 33 weeks and birth weight < 2500 g or birth weight < 1800 g if gestational age is unknown
		– respiratory distress syndrome in preterm
		– necrotizing enterocolitis
		– birth asphyxia gestational age <27 weeks or birth weight <1000 g
		– infection with gestational age <33 weeks
Infection	neonatal infection, sepsis/septicaemia, meningitis, pneumonia	– neonatal infection
		– sepsis/septicaemia
		– meningitis
		– pneumonia
		– impetigo neonatorum
Others	other specific causes not classified above	– neonatal jaundice
		– meconium aspiration syndrome
		– respiratory distress syndrome in term babies

*The criterion was adapted from modified Wigglesworth classification and the revised decision tree [17,18], and NICE classification [19] as used by Lawn et al. in classifying causes of neonatal deaths [20] with minor modifications.

18.0 Chicago Inc. III, USA). Descriptive statistics measures such as mean, standard deviation, rate and proportions were calculated.

Ethical approval

The birth registry at Kilimanjaro Christian Medical Centre obtained ethical clearance from the Tanzania Ministry of Health, Institute of Science and Technology, from the Norwegian National ethics committee and from the Kilimanjaro Christian Medical College (KCM-College) research ethics committee in 1999. Informed consent was obtained from mothers prior to the interview. The protocol for this study was approved by KCM-College research ethics committee, with certificate no. 333 of 15th July 2010.

Results

Characteristics of mothers and neonates

A total of 5033 inborn neonates were admitted, of these 2806 (55.8%) were males, (Table 2). Most of them 4583 (91.1%) were singletons. The mean (SD) birth weight and gestational age were 2899 (857) grams and 38 (3.5) weeks, respectively. Babies with missing data on birth weight and gestational age accounted for (0.8% and 9.1%) of all admissions, respectively. The majority of mothers 4871 (96.8%) had booked for antenatal care, and 49.0% of the babies were born after caesarean section. The mean (SD) maternal age and number of antenatal care (ANC) visits were 27.6 (6.2) years and 4.3 (2.0) visits, respectively.

Causes of admission

The leading causes of admission were birth asphyxia 1351 (26.8%), prematurity 930 (18.4%), risk of infection 852 (16.9%), neonatal infection 776 (15.4%), and large for gestational age (birth weight above 4000 g) 538 (10.7%), (Table 3). Of those admitted 1459 (29.0%) were low birth weight (<2500 g) and 1178 (25.8%) were born before 37 weeks of gestation.

Case fatality

Among the admitted neonates, 536 (10.7%, 95% CI 9.8 - 11.6) died. High case fatality was observed for babies with Respiratory Distress Syndrome (RDS), 52 (52.5%), congenital malformations 49 (43.6%), birth asphyxia 321 (23.8%) and prematurity 208 (22.4%), (Table 3). Large

Table 2 Characteristics of admitted neonates

Characteristics	n (%)	Characteristics	Mean (SD)
Child		**Child**	
Males	2806 (55.8)	Birth weight	2899 (857) gm
Female	2227 (44.2)	Birth length	47.5 (3.6) cm
Singletons	4583 (91.1)	Gestational age	38.0 (3.5) wks
From labour/obstetric ward	4788 (95.1)	**Maternal**	
From home/other facilities	245 (4.9)	Mean maternal age	27.6 (6.2) years
Born by caesarean section	2468 (49.0)	Mean ANC visits	4.3 (2.0)
Low birth weight (<2500 g)	1459 (29.0)		
Gestational age <37 weeks	1178 (25.8)		
Maternal			
Below 18 years	136 (2.7)		
18-25 years	1879 (37.3)		
26-35 years	2450 (48.7)		
Over 35 years	558 (11.1)		
First born	2119 (43.6)		
Single mother	60 (12.5)		
Antenatal care booking	4871 (96.8)		

for gestational age babies had the lowest case fatality (0.9%) in which the five cases that died had birth asphyxia as the underlying cause. Except for congenital malformations, case fatality decreased with increasing birth weight (Figure 1).

Table 3 Clinical discharge diagnosis, case fatality and contribution to overall mortality in a neonatal care unit (N = 5033). Ranked according to case fatality

Diagnosis**	Admitted	Case fatality	Proportion of deaths
	n (%)	n (%)	(%)
RDS	99 (2.0)	52 (52.5)	9.7
Congenital malformation	111 (2.2)	49 (44.1)	9.1
Asphyxia	1351 (26.8)	321 (23.8)	59.9
Prematurity	930 (18.4)	208 (22.4)	38.8
MAS	103 (2.0)	8 (7.9)	1.5
Neonatal infection	776 (15.4)	58 (7.5)	10.8
Other conditions	230 (4.6)	8 (3.5)	1.5
Neonatal jaundice	174 (3.5)	5 (2.9)	0.9
Risk of infection	852 (16.9)	11 (1.3)	2.1
LGA (>4000 g)	538 (10.7)	5 (0.9)	0.9
Normal for observation	368 (7.3)	0	0
TTN	132 (2.6)	0	0
Growth characteristics			
Birth weight <2500 g	1459 (29.0)	279 (19.1)	52.1
Gestational age <37 weeks	1178 (25.8)	217 (18.4)	40.5

**A neonate having more than one diagnosis is counted more than once; therefore proportion of deaths exceeds 100%. Abbreviations: *LGA* (Large for gestational age), *MAS* (meconium aspiration syndrome), *RDS* (Respiratory Distress Syndrome), *TTN* (Transient Tachpnoea of Newborn).

Cause-specific neonatal mortality

The leading single causes of neonatal death were birth asphyxia 245 (45.7%), prematurity 188 (35.1%), congenital malformations 49 (9.0%), and infections 46 (8.6%), (Figure 2). During the study period, there was no clear trend observed over time for overall mortality or within each cause of death (Figure 3).

The mean (SD) for gestational age and birth weight for premature babies who died was 30.3 (3.3) weeks and 1342 (457) grams, respectively. On the other hand, the mean (SD) for babies who died due to birth asphyxia was 38.7 (3.0) weeks and 2843 (705) grams, respectively. Of the babies who died due to asphyxia 143 (58.4%) had 5-minute Apgar score below 5 whereas, 102 (41.6%) had 5-minute Apgar score above 7. The majority of deaths attributed to asphyxia (179/245, 73.1%) occurred in normal birth weight babies (Table 4). Birth asphyxia in

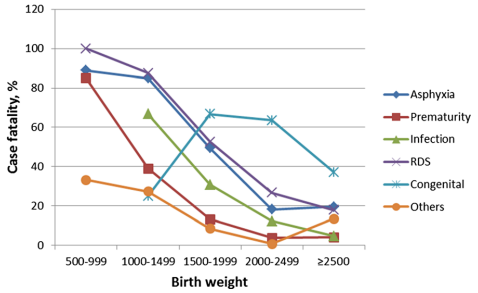

Figure 1 Case fatality according to clinical discharge diagnosis, in relation to birth weight (N = 5033 neonates).

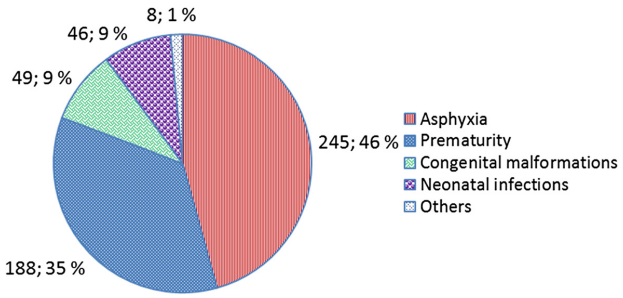

Figure 2 Single causes of neonatal deaths in a NCU (N = 536 neonatal deaths).

normal birth weight babies and prematurity in low birth weight babies each contributed to about one third of all deaths; 179/536 (33.4%) and 178/536 (33.2%), respectively. Mortality decreased with increasing birth weight.

Most babies (304, 56.7%) died within the first 24 hours, and as many as 491 (91.6%) within the first week (Table 5). Birth asphyxia and prematurity accounted for 86.8% of all deaths within the first 24 hours.

Discussion

The motive of our study was to identify morbidity and causes of neonatal death of inborn neonates admitted to

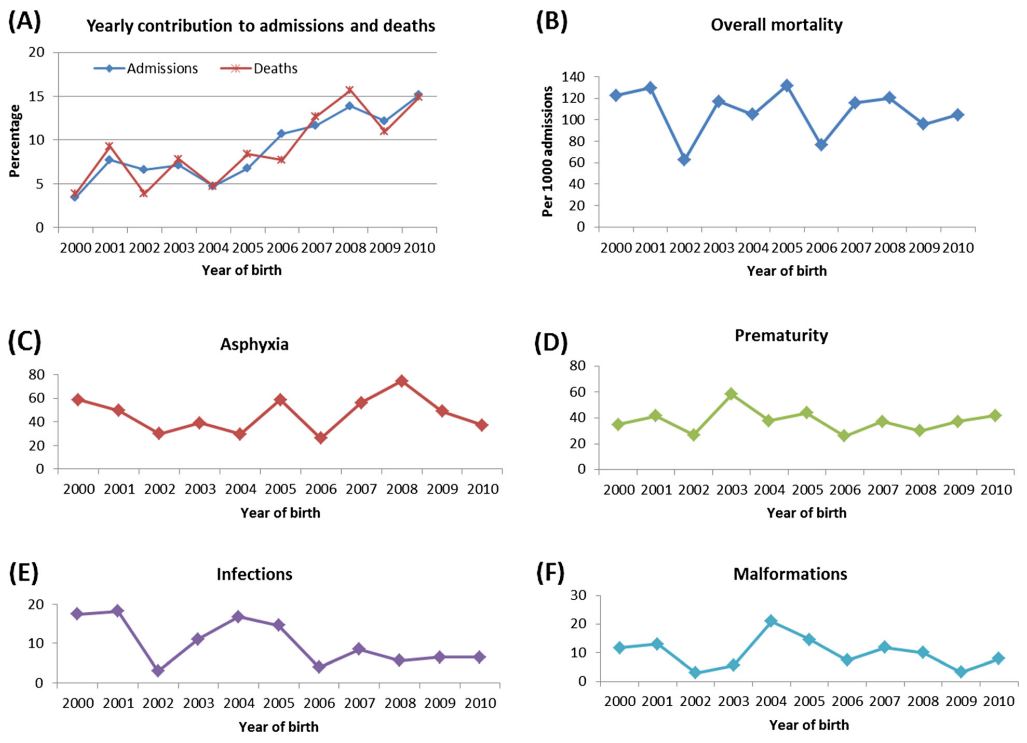

Figure 3 Graphs showing percentage contribution to overall admissions and overall deaths for each year (A), trend in death rate per 1000 admissions according to year of birth for overall (B) and in each category of cause-specific of deaths (C-F).

Table 4 Single causes of neonatal death by birth weight (N = 536)

Causes	Total deaths	Birth weight in grams					
		500-999	1000-1499	1500-1999	2000-2499	2500+	Unknown
No. admitted	5033	43	254	552	612	3535	37
Congenital	49	0	1	4	14	29	1
Prematurity	188	37	85	52	4	3	7
Asphyxia	245	0	11	19	34	179	2
Infection	46	0	4	6	6	29	1
Other	8	0	0	0	2	6	0
Total deaths	**536**	**37**	**101**	**81**	**60**	**246**	**11**
(%) deaths	(10.7)	(86.0)	(39.8)	(14.7)	(9.8)	(7.0)	(29.7)

a neonatal care unit at a tertiary hospital in Northern Tanzania. Our main results are largely consistent with the global pattern of mortality [2,5], with birth asphyxia, prematurity, and infection as the most important single causes of neonatal death. Our results should be interpreted bearing in mind that it includes only inborn neonates delivered at a tertiary health facility. Neonates who are admitted at a tertiary hospital NCU represent the important subgroup of neonates who have high risk of morbidity and mortality.

Overall mortality

Overall, 10.7% of the admitted neonates died in the neonatal period. This is similar to a study done in a regional referral hospital in Sudan where also only inborn neonates were included [21]. Most other studies include both outborn and inborn neonates, where in general mortality is higher [22-24]. A previous study from KCMC NCU in 2003 including both inborn and outborn neonates reported 19% neonatal mortality [16]. A study from Nigeria reported overall mortality of 25.5%; 20.3% among inborn neonates and 64.2% among outborn neonates [22]. A study from Bangladesh [23] reported 8% mortality in inborn neonates and 25.6% in outborn neonates. The variations in mortality probably reflect local and national differences in care pattern of newborn babies.

Table 5 Single causes of neonatal deaths in relation to time of death (N = 536)

Diagnosis	Total	Day 0-1	Day 2-7	After day 7
Congenital	49	23	20	6
Prematurity	188	109	59	20
Asphyxia	245	152	87	6
Infection	46	16	17	13
Other	8	4	4	0
Total (%)	**536 (100.0)**	**304 (56.7)**	**187 (34.9)**	**45 (8.4)**

Causes-specific mortality

Our finding that birth asphyxia was the leading cause of death is consistent with a previous study from a university and tertiary care hospital in Tanzania [10]. In contrast, the global pattern and studies from university and tertiary care hospitals find prematurity to be the leading cause of death [5,22-24]. One explanation of the high number of deaths due to asphyxia in our data may be the definition criteria for asphyxia that we used, which included some of the preterm babies. In some studies [21,24], all preterm babies who die are classified with prematurity as cause of death. Of particular interest is the high number of deaths attributable to asphyxia in normal birth weight infants in our study (one third of all deaths) because they may represent a potential for prevention. Basic training on newborn resuscitation skills and proper newborn resuscitation immediate after birth has proved to reduce mortality among babies born with birth asphyxia up to 40% [25-27]. A recent study in six developing countries showed that training on Essential Newborn Care which includes training on basic resuscitation had no effect on early neonatal mortality. However, there was a significant reduction in the rate of stillbirths primarily fresh, most likely as an effect of resuscitation of babies who would have been misclassified as stillbirths before training [28]. On the other hand, there was no additional effect of training in the Neonatal Resuscitation Program once the Essential Newborn Care training was already in place [28]. Training on newborn resuscitation immediately after birth is highly needed in Tanzania, where only 16% of health care services reported that they offer newborn respiratory support [29].

Prematurity was the second most important cause of death. Management of premature babies requires high specialized equipment, highly trained personnel and financial support [26,30]. In high income countries where ventilation technology and the use of surfactant have been implemented, the survival of premature babies has improved [30]. RDS is a known very frequent complication of preterm babies due to lung immaturity, and babies with RDS had the highest case fatality in our study, which is also reported elsewhere [16,24,31,32]. The high case fatality in babies with RDS reflects the inadequate care of these neonates in developing countries [30,33].

Some specific and simple measures has been identified which could be implemented to reduce deaths related to low birth weight and preterm in low income countries [27,34,35]. These include among others prophylactic use of steroid during premature labour, antibiotic for premature rupture of membrane, early breast feeding, treatment of infection, hospital-based kangaroo mother care, prevention of hypothermia, feeding and nutritional support. A recent meta-analysis review found hospital-based

Kangaroo mother care (skin-to-skin contact) implemented within the first week of life for stable preterm and low birth weight neonates was effective and could reduce neonatal mortality up to 51% [36].

Mortality due to infection was low compared to the global pattern as well as the pattern in low income countries [10,16,23,25]. The low number of deaths due to infection might in part be explained by the inclusion of only inborn neonates, since appropriate treatment of infection or suspected infection can start with a minimum of time delay after delivery.

In a previous study from the same NCU where both inborn and outborn neonates were included one fifth of the deaths were due to infection [16]. Furthermore, the use of Gentamycin and Cloxacillin instead of Gentamycin and Ampicillin [14] introduced in the early 2000 for neonatal infections in the department may have played a role in increased survival in infected neonates. A similar change in antibiotic treatment in Nigeria resulted in a 32% reduction in mortality associated with septicaemia [25]. The routine transfer to NCU of all neonates at risk of infection or suspected infection due to premature/prolonged rupture of membrane for antibiotic prophylaxis [13], might also have contributed to low mortality due to infection in this setting. We have previously shown that babies of mothers with premature/prolonged rupture of membrane had a 2 fold risk of being transferred to NCU for antibiotic prophylaxis due to risk of infection [13].

The majority of women in low income countries do not access early ultrasound scan for screening of congenital malformation, and there are very few early terminations of pregnancies due to severe/fatal congenital malformations. Availability of management/surgery for neonates with severe congenital malformations is limited, and under the prevailing circumstances we suggest that few of these deaths could have been prevented.

Time of death

The majority of neonatal deaths occurred during the first day after admission and more than 90% within the first week of life. We found that birth asphyxia and prematurity were the major causes of death within the first 24 hours, whereas deaths related to infections were more frequent after first week. These results are similar to what has previously been observed [25,34].

Strengths and limitations

This study used a large Medical Birth Registry with a complementary neonatal registry of neonates admitted to NCU where data are collected using standardized questionnaires. The data set contains a substantial number of neonates to be studied. All admitted neonates were given at least one discharge diagnosis and all information from the NCU could be linked to their information recorded in the birth registry. The modified Wigglesworth classification used to classify single causes of neonatal death was selected because it is simple to apply and since causes of death according to this classification have clear implications for clinical management. The classification gives the opportunity to identify areas of health care provision in need of prevention or improvement in management and care to improve neonatal survival. Since KCMC is a tertiary care hospital and included only inborn neonates, the results may not be generalized to all hospitals in Kilimanjaro or to the population.

Conclusions and recommendations

Birth asphyxia, prematurity and infection were the major single causes of neonatal morbidity and mortality. Birth asphyxia in normal birth weight babies and prematurity with low birth weight, each accounted for one third of all deaths, and some of these deaths may be preventable. First, strategies directed towards strengthening screening and identification of mothers at risk and early referral mechanisms for care and support is needed. Second, regular and continuous training of health personnel on essential newborn care to ensure basic knowledge on resuscitation skills and immediate actions needed for asphyxiated newborns should be strengthened. Care of premature babies should include in hospital kangaroo mother care for stable preterm and low birth weight babies, thermal care, feeding and nutritional support, as well as prevention and treatment of infections.

Decline in neonatal mortality might have been hampered by insufficient feedback mechanisms within the hospital or between the hospital and peripheral health facilities where patients are referred from. Therefore, all deaths occurring in the hospital whether maternal or newborn should be reviewed and discussed between obstetricians and paediatricians; the cause identified, preventive measures worked out, and feedback given to all the staff involved within the institution as well as surrounding health facilities through existing outreach programs.

Regular review of neonatal deaths using simple classifications within a particular setting will help to understand the magnitude of the problem and review the strategies for better improvement. Reviews should be directed towards identifying areas where screening, prevention and therapeutic interventions need to be strengthened.

Efforts should be done to further develop registration systems in order to collect information that can be used to understand maternal and newborn health

outcomes and serve as guidance for further preventive measures.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
BTM: Study design, methodology, data analysis and manuscript writing. RTL, RO, MJM, GK, AKD: Study design, methodology, manuscript writing. RTL and AKD approved the manuscript for final submission. All authors approved the final manuscript.

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III

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Causes of perinatal death at a tertiary care hospital in Northern Tanzania 2000--2010: a registry based study

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Causes of perinatal death at a tertiary care hospital in Northern Tanzania 2000–2010: a registry based study

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Abstract

Background

Perinatal mortality reflects maternal health as well as antenatal, intrapartum and newborn care, and is an important health indicator. This study aimed at classifying causes of perinatal death in order to identify categories of potentially preventable deaths.

Methods

We studied a total of 1958 stillbirths and early neonatal deaths above 500 g between July 2000 and October 2010 registered in the Medical Birth Registry and neonatal registry at Kilimanjaro Christian Medical Centre (KCMC) in Northern Tanzania. The deaths were classified according to the Neonatal and Intrauterine deaths Classification according to Etiology (NICE).

Results

Overall perinatal mortality was 57.7/1000 (1958 out of 33 929), of which 1219 (35.9/1000) were stillbirths and 739 (21.8/1000) were early neonatal deaths. Major causes of perinatal mortality were unexplained asphyxia (n=425, 12.5/1000), obstetric complications (n=303, 8.9/1000), maternal disease (n=287, 8.5/1000), unexplained antepartum stillbirths after 37 weeks of gestation (n= 219, 6.5/1000), and unexplained antepartum stillbirths before 37 weeks of gestation (n=184, 5.4/1000). Obstructed/prolonged labour was the leading condition (251/303, 82.8%) among the obstetric complications. Preeclampsia/eclampsia was the leading cause (253/287, 88.2%) among the maternal conditions. When we excluded women who were referred for delivery at KCMC due to medical reasons (19.1% of all births and 36.0% of all deaths), perinatal mortality was reduced to 45.6/1000. This reduction was mainly due to fewer deaths from obstetric complications (from 8.9 to 2.1/1000) and maternal conditions (from 8.5 to 5.5/1000).

Conclusion

The distribution of causes of death in this population suggests a great potential for prevention. Early identification of mothers at risk of pregnancy complications through antenatal care screening, teaching pregnant women to recognize signs of pregnancy complications, timely access to obstetric care, monitoring of labour for fetal distress, and proper newborn resuscitation may reduce some of the categories of deaths.

Keywords

Perinatal mortality, Perinatal deaths, Maternal disease, Obstetric complication, NICE classification

Introduction

Perinatal mortality refers to the death of a fetus or death during first week of life, and is thought to reflect maternal pre-pregnancy health as well as maternal, obstetric, and newborn care. It is widely used as a health indicator in international comparisons, and within countries and regions to estimate temporal trends [1]. Globally, approximately 5.9 million perinatal deaths occur annually, of which 3.2 million stillbirths (SB) and 2.7 million early neonatal deaths (END) [2]. The highest burden of perinatal deaths is in developing countries which account for about 98% of all deaths [2].

Tanzania like other Sub Saharan African countries, has a high perinatal mortality estimated to be 69/1000 births in 2004 [2]. A recent national survey reported perinatal mortality for

pregnancies lasting seven months or more to be 36/1000, ranging between 24/1000 and 60/1000 in the different zones [3]. In studies, estimates of perinatal mortality in Tanzania vary depending on the geographical area, the type of study, and information collected, ranging from 27–124 deaths/1000 births [4-10].

Causes and determinants of early neonatal deaths and stillbirths differ from causes of postneonatal deaths [1,11,12]. Many perinatal deaths are the consequence of a chain of events [13], in which complications such as obstructed labour and fetal malpresentation are common [1,12]. Globally, one third of all stillbirths (1.2 million) are estimated to occur during labour/delivery, while one third of all early neonatal deaths (0.9 million) are due to birth asphyxia [12]. These two causes of perinatal mortality represent intrapartum related perinatal deaths and are examples of deaths that are largely linked to quality of care around the time of delivery [1,2,12].

Several classification systems of perinatal deaths have been developed. The usefulness of these systems varies considerably due to dissimilarities in recording system and information collected [14]. The Wigglesworth classification [15] has also been used for classification of perinatal and neonatal deaths in developing countries because it is simple and does not require sophisticated investigations, aimed at subdividing cases into groups with clear implications for clinical management. The Neonatal and Intrauterine deaths Classification according to Etiology (NICE) is developed to uncover the underlying etiology which might have initiated the chain of events leading to death, in terms of maternal, obstetric, fetal and neonatal conditions [13,16]. Compared to Wigglesworth, the NICE classification is found to reduce the proportion of intrauterine deaths, deaths from asphyxia, and deaths from immaturity linked to maternal disease, abruption placenta or obstetric complications [13].

Due to lack of good vital registration systems, reports on perinatal and neonatal mortality in developing countries are mainly based on public health surveillance such as demographic and health surveys. Ninety percent of the children under the age of five in Tanzania are unregistered [17]. In high income countries where all births and deaths are registered, the information obtained has been continuously used for planning and implementation of prevention strategies. In low income countries, hospital records may be an available source of information, but these are usually difficult and time consuming to retrieve, and are not designed to fit into classification systems.

The Kilimanjaro Christian Medical Centre (KCMC) Medical Birth Registry system was established in 1999 as collaboration between Kilimanjaro Christian Medical College, Moshi, Tanzania and the University of Bergen, Norway through the support of the Norwegian Council for Higher education program for Development Research (NUFU) project. The birth registry at KCMC is a daily activity including public holidays with integrated neonatal registry for neonates admitted to a neonatal care unit. The KCMC Medical Birth Registry and neonatal registry include maternal, obstetric, fetal, and neonatal characteristics which give us the opportunity to classify perinatal deaths into etiologically based groups. The aim of this study was to identify and classify causes of perinatal deaths by using the Neonatal and Intrauterine death Classification according to Etiology (NICE), and possibly identify causal mechanisms relevant for prevention.

Methods

Setting

This study is based on data collected at KCMC hospital in Northern Tanzania. The hospital is a tertiary care and zonal referral hospital which serves about 10 million people from mainly four regions in Northern Tanzania, namely Kilimanjaro, Arusha, Tanga and Manyara. Being a tertiary referral hospital the KCMC labour ward receives normal deliveries as well as high risk mothers with maternal or obstetric complications referred at various stages of pregnancy or labour from Moshi urban area or from other health facilities in the Northern zone.

The KCMC obstetrics and gynaecology department has a team on call which includes one specialist or consultant obstetrician, one obstetric resident and one intern doctor, two anaesthesiologists and 3 midwives who take care of the department outside regular working hours for comprehensive emergency obstetrics and gynaecological care. The department has two operative theatres in labour ward for emergency caesarean sections. In the Kilimanjaro region 70% of all births take place at health facilities [18]. Around 50% of the deliveries at KCMC are from Moshi urban area. The caesarean section rate at the institution is about 33% [19].

Based on records from the birth registry linked to the neonatal registry from July 2000 to October 2010 [20], we established a cohort of births with birth weight 500 g or more. A total of 34087 births were recorded of which 158 (0.4%) the birth weights were either missing or below 500 g (Figure 1). Therefore, our study population was 33929 births with birth weight 500 g or more, of which 1958 died perinatally.

Figure 1 Description of the study population. Numbers in brackets are proportions of all births 2000–2010 (N=34087)

Data collection

Information on all mothers who delivered at KCMC was obtained through a structured questionnaire and the mothers being interviewed within the first 24 hours after delivery. Informed consent was obtained from mothers prior to the interview. Information was also extracted from the antenatal care record cards. Detailed description of the data collection procedure and data collected for the birth registry and neonatal registry have been previously published [20,21].

For stillbirths, time of death was recorded as before labour, during labour, or unknown. The status of the fetus was also recorded, whether it was a macerated stillbirth or fresh one. The information was also sought whether the fetus died before or after admission to labour ward. Reporting of early neonatal deaths included date of death, time of death (died within first 24 hours, died within first week), and up to three diagnoses of cause of death [20].

Variable definitions

Early neonatal deaths include newborns that die during first week of life. We define perinatal mortality as stillbirth or early neonatal death with birth weight 500 grams or more [22]. Perinatal mortality rate (PNMR), stillbirth rate (SBR) and early neonatal mortality rate

(ENMR), were calculated as follows: PNMR = (stillbirths + early neonatal deaths/total births) × 1000, SBR = (stillbirths/total births) × 1000 and ENMR = (early neonatal deaths/live births) × 1000.

Outcome was perinatal death, overall and according to cause of death. Causes of death were classified on the basis of maternal, obstetric, fetal and neonatal characteristics identified in the linked registry data, according to the NICE classification [23], with a mild modification of the *unexplained asphyxia* category (Table 1) based on our previous modification [20]. In a strictly hierarchical order, each stillborn or early neonatal death was classified into one of the 13 specific, mutually exclusive causes of death. For the two causes of death categories *maternal disease* and *obstetric complications*, we also investigated co-morbidity.

Table 1 Definitions of the characteristics included in the 13 categories of causes of perinatal deaths by NICE classification

Causes	Characteristics*
1. Congenital anomalies:	Include stillborn and liveborn infants with lethal malformations or potentially lethal malformations that markedly increase mortality risk.
2. Multiple births:	Includes multiple births other than duplex, or duplex in combination with immaturity (<33 gestational weeks) or intrauterine deaths.
3. Maternal disease:	Maternal diabetes mellitus if the infant is stillborn or is large for date (Z-score >2 SD). Maternal pre-eclampsia, renal disease, hepatosis, epilepsy, systemic lupus erythematosus (SLE) included when combined with an infant either small for date (Z-score <−2 SD) or immature (<33 gestational weeks), or dead before labour.
4. Specific fetal conditions:	Isoimmunization, unexplained hydrops featalis, tumors and specific fetal infections. Accidents included when combined with stillbirth.
5. Unexplained SGA infants:	Infants Z-score <−2.5 SD without any evidence of maternal disorder.
6. Placental abruption:	If combined with asphyxia, immaturity (<33 gestational weeks) or intrauterine death.
7. Obstetric complications:	Uterine rupture, disproportion, malpresentation, cord prolapse, cord compression, placenta previa, foetal blood loss and precipitated labour.
8. Unexplained antepartum stillbirths	<37 gestational weeks
9. Unexplained antepartum stillbirths	>36 gestational weeks
10. Specific infant conditions:	Liveborn infants >32 gestational weeks with septicaemia, meningitis or pnaeumonia, includes term infants with respiratory distress syndrome (RDS) or sudden infant death syndrome (SIDS). Accidents included when causing neonatal death.
11. Unexplained asphyxia:	Intrapartum death, deaths occur < 4 hrs after birth and cases with **Apgar score <7 at 5 min**, where the asphyxia is not explained, **clinical diagnosis Hypoxic ischaemic encephalopathy (HIE) or severe birth asphyxia where Apgar score is missing** and the case does not belong to groups 1–10 above. Immature infants 27 gestational weeks or **< 1000 g** are excluded.
12. Unexplained immaturity:	Liveborn infants <33 gestational weeks and 2500 g (or 1800 g if gestational age is unknown) where the immaturity is not explained and the case does not belong to groups 1–11 above.
13. Unclassifiable cases:	Cases not in groups 1–12.

*Characteristics included in the 13 categories adapted and modified from Winbo et al. [23]. Modifications are bolded

Main results were stratified according to referral status (mother referred for delivery due to medical condition yes/no). The following conditions recorded in the birth registry were considered; obstructed labour, malpresentation, prolonged labour, retained twin, fetal distress, cord prolapse, premature/prolonged rupture of membrane, abruption placenta, placenta previa, antepartum haemorrhage, ruptured uterus, preeclampsia, eclampsia, gestational or diabetic mellitus, hypertension, and malaria. Referral due to previous caesarean section without any of the complications above was not regarded a medical referral.

Data analysis

Data were analyzed using Statistical Package for Social Science (SPSS) program for Windows Version 19.0 (SPSS 19.0 Chicago Inc. III, USA). Descriptive measures such as mean, standard deviation, rate per 1000 and relative risk were calculated.

Ethical approval

The protocol for this study was approved by Kilimanjaro Christian Medical college (KCM-College) research ethics committee, with certificate no. 333 of 15th July 2010.

Results

Among the 1958 perinatal deaths 1026 (52.4%) were males, 917 (46.8%) were females, 15 (0.8%) had unknown sex, 1017 (51.9%) were below 2500 g, and 781 (39.9%) were born before 37 weeks of gestation. Mean (SD) birth weight and gestational age were 2335 (944) g and 36 (4.7) weeks, respectively. Mean (SD) maternal age and number of ANC visits were 28.2 (6.4) years and 3.8 (2.0), respectively. Gestational age was missing in 247 (12.6%) perinatal deaths (151 stillbirths and 96 early neonatal deaths), and Apgar score at 5 minutes was missing in 12 (1.6%) early neonatal deaths. Mode of delivery for the perinatal deaths was spontaneous vaginal delivery (55.6%), cesarean section (35.3%), assisted breech delivery (5.6%), vacuum extraction (1.7%), destructive operative delivery (0.2%), and unknown (1.5%). Corresponding numbers for all births were 64.5%, 32.8%, 1.2%, 1%, 0.01% and 0.4%. In addition, 0.02% of all births were delivered by forceps.

Overall perinatal mortality was 57.7/1000 births (1958 out of 33 929) (Table 2), of which 1219 (35.9/1000) were stillbirths and 739 (21.7/1000) were early neonatal deaths. The majority of the stillbirths (799, 65.5%) were antepartum stillbirths, while 420 (34.5%) were intrapartum stillbirths. Overall and among non-referred, there were no time trends in perinatal mortality from 2000 to 2010 (Figure 2). In the referred group, mortality increased from around 80/1000 to more than 120/1000.

Table 2 Number and rate of stillbirths and early neonatal deaths by birth weight among 1958 perinatal deaths at KCMC 2000-2010

		Birth weight in grams		
	Total	<1500	1500-2499	>=2500
	n (/1000)	n (/1000)	n (/1000)	n (/1000)
Total births	**33929**	**741**	**3787**	**29401**
Perinatal deaths	***1958*** (***57.7***)	***459*** (***619.4***)	***558*** (***147.3***)	***941*** (***32.0***)
Stillbirths	1219 (35.9)	283 (381.9)	383 (101.1)	553 (18.8)
Antepartum (Macerated) stillbirths	799	204	272	323
Intrapartum (Fresh) stillbirths	420	79	111	230
Early neonatal deaths	739 (21.8)	176 (237.5)	175 (46.2)	388 (13.2)
Apgar <7	395	97	73	215
Apgar ≥7	332	77	98	167
Missing Apgar score	12	2	4	6
Total singletons	**32165**	**552**	**2916**	**28697**
Perinatal deaths	1752 (54.5)	348 (630.4)	491 (168.4)	913 (31.8)
Total multiple births	**1765**	**190**	**871**	**704**
Perinatal deaths	206 (116.7)	111 (584.2)	67 (76.9)	28 (39.8)

Figure 2 Trends in stillbirths, early neonatal deaths and perinatal deaths at KCMC 2000–2010

Trends in stillbirths, **early neonatal deaths and perinatal deaths at KCMC 2000–2010**

Causes of perinatal death

Overall, major causes of perinatal death were *unexplained asphyxia* (n=425, 12.5/1000), *obstetric complications* (n=303, 8.9/1000), *maternal disease* (n=287, 8.5/1000), *unexplained antepartum stillbirths after 37 weeks of gestation* (n= 219, 6.5/1000), and *unexplained antepartum stillbirths before 37 weeks of gestation* (n=184, 5.4/1000), (Table 3). In the large group of *unexplained asphyxia*, 236 (55.5%) were early neonatal deaths and 189 (44.5%) were intrapartum stillbirths. A further analysis of co-morbidities showed that obstructed/prolonged labour was present in more than 80% of the deaths in the *obstetric complications* category, and that preeclampsia/eclampsia was present in nearly 90% of the deaths in the *maternal disease* category.

Table 3 Causes of stillbirths and early neonatal deaths by Neonatal and Intrauterine Classification of death according to Etiology (NICE) (N=1958, birth weight ≥500 g)

		Medical referral		
	All	No	Yes	RR
Number of births	33929	27460	6469	
Identified causes	n (/1000)	n (/1000)	n (/ 1000)	
1. Congenital anomalies	84 (2.5)	53 (1.9)	31 (4.8)	2.5
2. Multiple birth	156 (4.6)	110 (4.0)	46 (7.1)	1.8
3. Maternal disease	287 (8.5)	150 (5.5)	137 (21.8)	4.0
4. Specific fetal conditions	1 (0.03)	1 (0.04)	0	0
5. Growth restriction	70 (2.1)	52 (1.9)	18 (2.8)	1.5
6. Placental abruption	75 (2.1)	23 (0.8)	52 (8.0)	10.0
7. Obstetric complications	303 (8.9)	57 (2.1)	246 (38.0)	18.1
8. Unexplained antepartum stillbirth <37 weeks	184 (5.4)	144 (5.2)	40 (6.2)	1.2
9. Unexplained antepartum stillbirth ≥37 weeks	219 (6.5)	173 (6.3)	46 (7.1)	1.1
10. Specific infant conditions	33 (1.0)	29 (1.1)	4 (0.6)	0.6
11. Unexplained asphyxia	425 (12.5)	353 (12.9)	72 (11.1)	0.9
12. Unexplained immaturity	46 (1.4)	39 (1.4)	7 (1.1)	0.8
13. Unexplained	75 (2.1)	69 (2.5)	6 (0.9)	0.4
Total	1958 (57.7)	1253 (45.6)	705 (109)	2.4

RR =PMR medical referral/PMR non referral

Births to mothers referred for delivery due to medical conditions accounted for 19.1% of all births and 36% of all deaths. Perinatal mortality was 45.6 per 1000 in the non-referred group and 109 per 1000 in the referred group (RR 2.4). In the group of non-referred, *unexplained asphyxia* still was the most common cause of death, while deaths from *obstetric complications* and *maternal disease* were largely reduced. High relative risks for referred vs. non-referred group were observed for *obstetric complications* (38/1000 vs. 2.1/1000, RR= 18.1), *placental abruption* (RR 8/1000 vs. 0.8/1000, RR=10.0), and *maternal disease* (21.8/1000 vs. 5.5/1000, RR= 4.0).

Discussion

In this study of perinatal deaths at a zonal hospital in Northern Tanzania during 2000–2010, overall perinatal mortality was 57.7 per 1000 and with no time trends. Among 13 hierarchical categories of perinatal death, major causes were *unexplained asphyxia*, *unexplained stillbirth*, *obstetric complications*, and *maternal disease*. Nearly 20% of the mothers in our study were referred to the hospital for medical reasons, and perinatal mortality in this group was 109 per 1000. Still, perinatal mortality was as high as 45.6 per 1000 in the non-referred group. Mode of delivery of the perinatal deaths corresponded with the figures for all births. The observed distribution of causes suggests a high burden of avoidable deaths if adequate resources were available.

Overall mortality is similar to previous reports from community studies in Kilimanjaro region [7,8], but higher than the National estimates (36-42/1000 births) [3,17]. Mortality is higher

than reported in previous studies from the same hospital since both multiple births and births to women referred to the hospital for medical reasons are included in our study, [6].

Maternal disease and abruption placenta

Nearly ninety percent of the deaths in the *maternal disease* category were affected by preeclampsia/eclampsia. Inadequate screening and women's unawareness of danger signs in pregnancy means that serious maternal complications may go unrecognized leading to a delay in seeking and receiving necessary delivery care. In the Tanzanian demographic and health survey 2004–05, only 47% of the women who attended antenatal clinics recalled having been informed about any danger sign during pregnancy [18]. In a recent study in Rufiji district in Tanzania, 42% of the women who attended antenatal clinics were not informed of any danger signs, whereas only 8.7% were informed of all seven danger signs (vaginal bleeding, severe headache/blurred vision, severe abdominal pain, swollen hands and face, fever, baby stopped or reduced movement, and excessive tiredness or breathlessness) [24]. The risk of perinatal death due to *maternal disease* was in particular high in the referred group (21.8/1000 vs. 5.5/1000, RR=4.0). Also deaths due to *placental abruption*, which is associated with hypertension in pregnancy [25] were more frequent in the referred group (8.0/1000 vs. 0.8/1000, RR=10.0). Screening as well as raised awareness of signs of hypertensive disease in pregnancy among the women and their families could improve pregnancy outcome in this study setting. A study in rural Tanzania indicated that only 9% of all women screened for hypertension by health workers were informed about their blood pressure results [26]. Furthermore, health workers were able to detect high blood pressure level only in four out of the 12 patients with elevated blood pressure levels, of which only one received appropriate counseling. Lack of providers' ability to screen, counsel and inform women on danger signs seen in rural Tanzania may be present on our area, too. Other threats to improved care are lack of transport, financial constraints, poor compliance with referral, and lack of birth preparedness [27,28].

Unexplained antepartum stillbirths

Unexplained antepartum stillbirths accounted for around half of all antepartum stillbirths. These are deaths largely linked to maternal health conditions before pregnancy, complications of pregnancy, such as preeclampsia, and placental dysfunction, without being able to establish the cause [1]. Antepartum stillbirths are also largely linked to maternal infection and fetal growth restriction [29]. Maternal and fetal infections are estimated to cause about 10-25% of stillbirths in high income countries, whereas, the rate is expected to be higher in low income countries [30]. Studies in low income countries found maternal infections such as syphilis, malaria and HIV are associated with high risk for perinatal morbidity and mortality [31-34]; but infection is not included among the causes of death in the NICE classification. Furthermore, the available information may not be detailed enough to identify the underlying causes for the large fraction of unexplained deaths [13].

Obstetric causes

In consistence with previous studies from Tanzania [5,7] and other African countries [34-36], obstructed/prolonged labour was present in a majority of the deaths due to *obstetric complications* (80%). Worldwide, obstructed/prolonged labour is the most frequent obstetric complication leading to perinatal mortality [12]. A study in Western Tanzania found

obstructed/prolonged labour accounted for 18.5% of perinatal deaths [5]. The risk of perinatal death associated with obstructed labour was 2-fold in Uganda [35], and 8-fold in Kenya [36]. *Obstetric complication* was the category with the largest relative difference between births to non-referred vs. referred women (38.0/1000 vs. 2.1/1000, RR=18.1). It is likely that delay in referral, transportation problems, and delay in taking action for emergency care are responsible for a large fraction of these deaths in the referred group [5,9].

Unexplained asphyxia

Unexplained asphyxia includes intrapartum related stillbirths and intrapartum related neonatal deaths, and was the largest category among births to non-referred mothers. These are deaths closely linked to obstetric and maternal complications and services given during labour and delivery [11,12]; hence they are largely avoidable by appropriate care during time of labour and delivery. The majority of intrapartum stillbirths and early neonatal deaths with Apgar score below 7 at 5 minutes were babies of normal birth weight. These are viable fetuses and babies who would have survived with proper care during labour and delivery. We have previously shown that birth asphyxia was the leading cause of deaths in a neonatal care unit, and that most babies who died due to birth asphyxia had normal birth weight and were born at term [20]. Among interventions recommended to reduce intrapartum stillbirths and deaths related to asphyxia are; appropriate care at birth, the use of partograph for monitoring labour and proper resuscitation for asphyxiated newborns [37]. A qualitative audit study in Tanzania found lack of appropriate fetal heart monitoring during labour in more than 40% of the perinatal deaths [9].

Strengths and limitations

A major strength of the study is that data is retrieved from a birth registry where the information is collected on a daily basis including holidays with use of a standardized questionnaire. The birth registry is linked to a neonatal registry at the neonatal intensive care unit at the same hospital, where causes of death are routinely registered in a specially designed form. By means of the NICE classification we were able to identify cause of death in more than 50% of the stillbirths. Furthermore, we analyzed a large number of births over a period of 11 years, reducing the possibility of chance findings.

Since the study is based on births in a tertiary care hospital, the results may not be representative for the population because some women are selected to give birth at this level of care due to complications. This might affect overall perinatal mortality as well as the distribution of causes of death. Another limitation is that perinatal mortality may be underestimated since deaths of newborn who were discharged from hospital before seven days were lost if the death occurred at home or in another health facility. Although the standardized birth registry form is designed to collect detailed information, maternal conditions may be underreported due to poor diagnostic procedures in pregnancy, and obstetric conditions may be underreported especially in emergency situations.

Conclusion and recommendations

Our results indicate that even for deliveries in a tertiary care hospital where emergency obstetric care and neonatal care is available to a larger extent than at lower care levels, there is a huge room for improvement in perinatal outcomes.

First, the high number of deaths in the category of unexplained asphyxia, which also applies to births to women who were not referred for medical reasons, may indicate inadequate monitoring of labour, or inadequate skills on newborn resuscitation immediately after birth. At the hospital level, retraining through ongoing continuous medical training programmes in use of partograph during labour, how to interpret abnormal progress of labour, and basic resuscitation skills might reduce the number of these deaths. Furthermore, feedback mechanisms and regular reviews involving both the obstetric and the neonatal staff should be encouraged. Second, the high number of deaths related to obstetric complications, in particular in the group of referred women, may indicate delay in referral, insufficient referral mechanisms, or delay in seeking health care before labour. Reorganization of the referral system to ensure timely and proper referral, and promoting women and their families to seek health care in time might reduce the number of these deaths. Further studies are needed to identify the most important sources of delay in the referral system, as to be able to implement preventive measures and feedback mechanisms across the referral levels. Third, the high number of deaths related to preeclampsia/eclampsia may indicate unawareness of danger signs related to hypertensive disorders during pregnancy. Both proper screening and counseling on danger signs in connection with antenatal care are relevant measures which may reduce deaths related to maternal conditions.

In conclusion, a future decline in perinatal mortality depends on interventions at different levels. Recommended interventions need to be implemented at the hospital level, with respect to the referral system, and with respect to antenatal care and community education so as to improve perinatal outcomes as soon as possible. The causes of perinatal death identified through the birth registry and the neonatal registry represent valuable information which should be systematically utilized in order to monitor causes of perinatal mortality.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

BTM: Study design, methodology, data analysis and manuscript writing. RTL, AKD: Study design, methodology, manuscript writing. RO, MJM, OO: manuscript writing. All authors approved the final manuscript.

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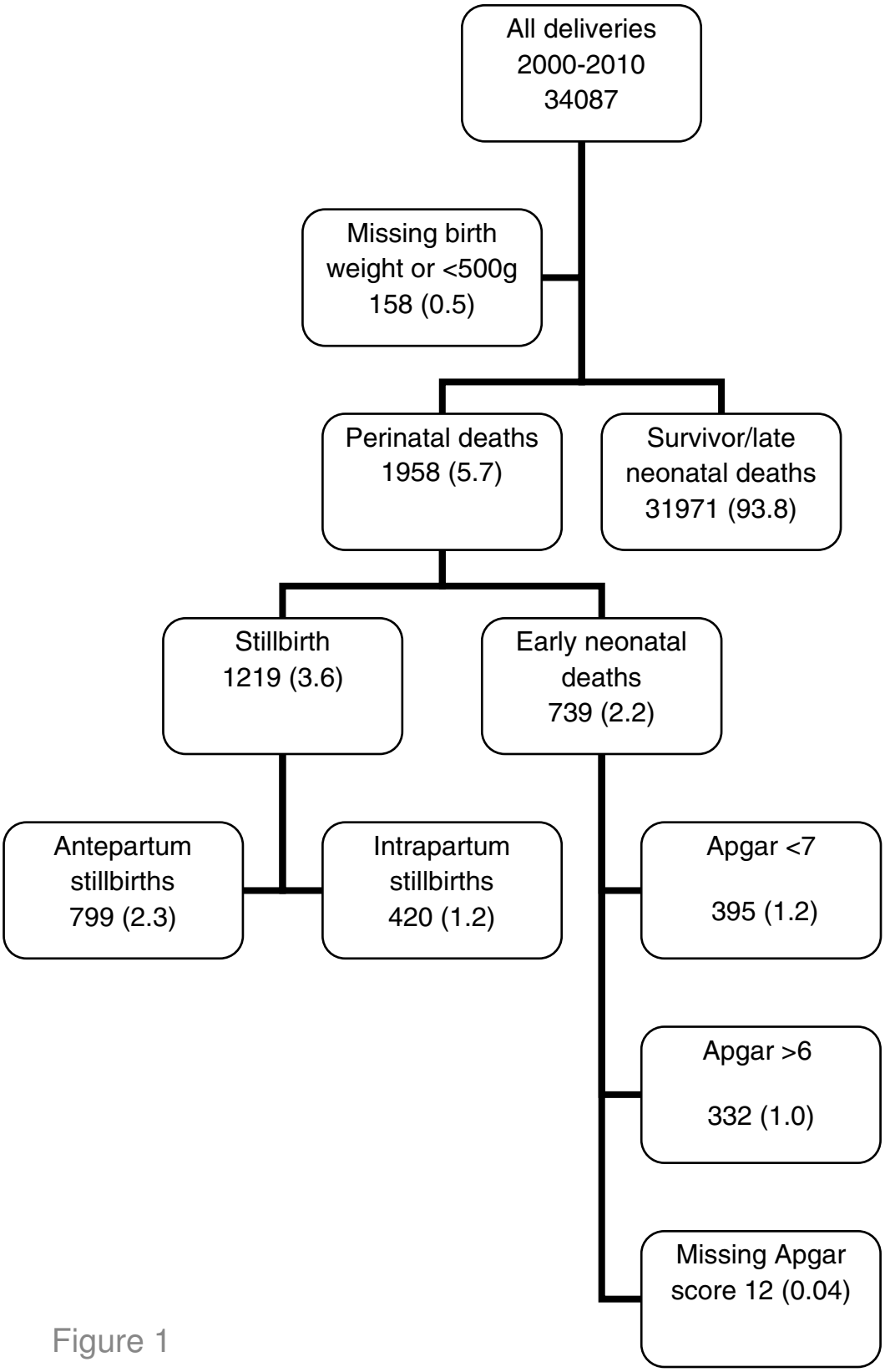

All deliveries
2000-2010
34087
Missing birth weight or <500g
158 (0.5)
Perinatal deaths
1958 (5.7)
Survivor/late neonatal deaths
31971 (93.8)
Stillbirth
1219 (3.6)
Early neonatal deaths
739 (2.2)
Antepartum stillbirths
799 (2.3)
Intrapartum stillbirths
420 (1.2)
Apgar <7
395 (1.2)
Apgar >6
332 (1.0)
Missing Apgar score 12 (0.04)

Figure 1

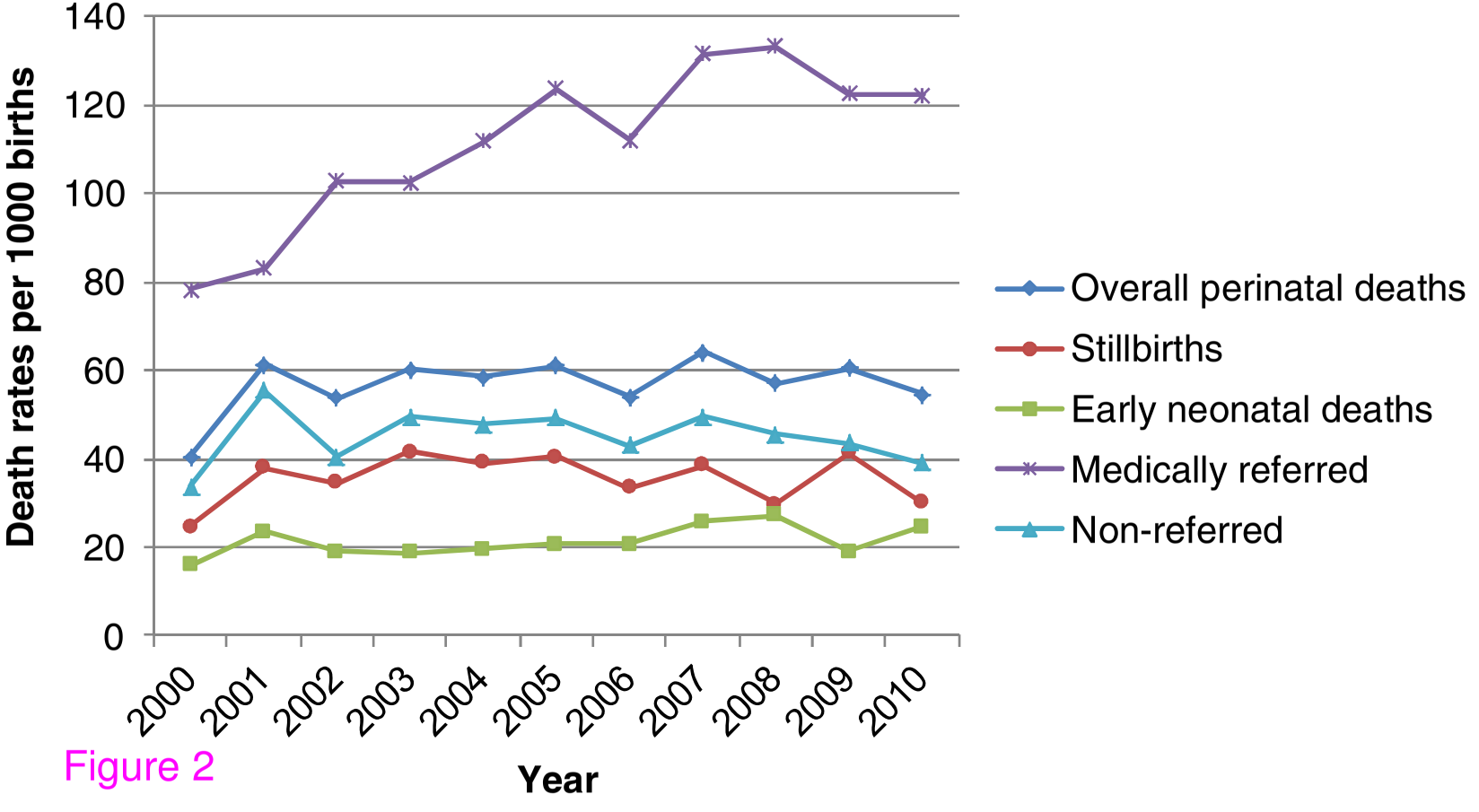

Death rates per 1000 births
140
120
100
80
60
40
20
0
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
Year
Overall perinatal deaths
Stillbirths
Early neonatal deaths
Medically referred
Non-referred

Figure 2

Appendices

10.1 KCMC Medical Birth Registry interview questionnaire

K.C.M.C **KCMC Medical Birth Registry**

Version 5 - November 2004

1 Basic information concerning mother

1.1 **Mothers date of birth:** _ _ _ _ _ _ **Age:** _ _

1.2 **Mothers name:**

1.3 **Address:**

1.4 **Hospital number:** _ _ _ _ _ _

1.5 **Date of interview:** _ _ _ _ _ _

1.6 **Birth number:** _ _ _ _

1.7 **Interview by:**

1.8 **Date of admission:** _ _ _ _ _ _

Referred for delivery: ☐ 1 Yes ☐ 2 No (*self referral*) If yes: ⇒

Referred from: ☐ 1 Home ☐ 2 Regional hospital ☐ 3 District hospital ☐ 4 Other, specify:

Referred during labour: ☐ 1 Admitted in labour ☐ 2 Admitted before labour

Reason for referral:

1.9 **Official date of discharge:** _ _ _ _ _ _

1.10 **Date leaving hospital:** _ _ _ _ _ _

1.11 **Current residence:** ☐ 1 Rural ☐ 2 Urban ☐ 3 Semi urban

Area of mother's residence:

1.12 **Mothers childhood residence:** ☐ 1 Rural ☐ 2 Urban ☐ 3 Semi urban

Area of mother's childhood residence:

1.13 **Highest educational level:** ☐ 1 None ☐ 2 Primary (1-7) ☐ 3 Secondary (8-11) ☐ 4 Higher (12+)

1.14 **Current occupation:** ☐ 1 Housewife ☐ 2 Farmer ☐ 3 Service ☐ 4 Business ☐ 5 Professional ☐ 6 Student ☐ 7 Others ⇒

1.15 **Current marital status:** ☐ 1 Married Age at first marriage: _ _ ☐ 2 Single ☐ 3 Widowed ☐ 4 Remarried ☐ 5 Divorced ☐ 6 Polygamous family Add wife number: _ _

No of previous pregnancies _ _

1.16 **Regular menstrual periods:** ☐ 1 Yes ☐ 2 No Age at menarche: _ _

1.17 **Genital mutilation** *(Circumcision)* ☐ 1 Yes ☐ 2 No **If yes, at age:** _ _ **If yes, type:** ☐ 1 Type one ☐ 2 Type two ☐ 3 Type three ☐ 4 Other types

1.18 **Mother's tribe:** ☐ 01 Chagga ☐ 02 Pare ☐ 03 Masai ☐ Other ⇒

1.19 **Religion:** ☐ 1 Catholic ☐ 2 Protestant ☐ 3 Muslim ☐ 4 Others ⇒

2 Questions concerning the father of the child:

2.1 **Father's name:**

2.2 **Father's age:** _ _

2.3 **Current occupation of father:** ☐ 01 Farmer ☐ 02 Business ☐ 03 Skilled worker ☐ 04 Unskilled worker ☐ 05 Service ☐ 06 Official ☐ 07 Professional ☐ 08 Student ☐ 09 Unemployed ☐ 10 Other ⇓

2.4 **Father's educational level:** ☐ 1 None ☐ 2 Primary (1-7) ☐ 3 Secondary (8-11) ☐ 4 Higher (12+)

2.5 **Father's tribe:** ☐ 1 Chagga ☐ 2 Pare ☐ 3 Masai ☐ 4 Others ⇒

3 Questions concerning home conditions:

3.1 **Source of drinking water:** ☐ 1 Tap water ☐ 2 Well ☐ 3 River ☐ 4 Spring ☐ 5 Other, specify

3.2 **Boiling of drinking water:** ☐ 1 Yes ☐ 2 No

3.3 **Distance to water, if not tap:** ☐ 1 Less than 1 km (less ½ hour walk) ☐ 2 More than 1 km, specify in km: _ _

3.4 **Home toilet:** ☐ 1 Pit latrine ☐ 2 Flush ☐ 3 Others ⇒

4 Mothers health before and during present pregnancy

4.1 Body weight (kg): (before pregnancy) ____

4.2 Body height (cm): ____

4.3 Blood transfusions ☐ 1 Yes ☐ 2 No

4.4 Serious diseases

- ☐ 01 Diabetes
- ☐ 02 Hypertension
- ☐ 03 Heart diseases
- ☐ 04 Epilepsy
- ☐ 05 Malaria
- ☐ 06 Anaemia
- ☐ 07 Gynaecological disease
- ☐ 08 Liver disease (jaundice)
- ☐ 09 Kidney disease
- ☐ 10 Lung disease
- ☐ 11 Tuberculosis
- ☐ 12 Sickle cell
- ☐ 13 Other, specify ⇓

4.5 Have you ever practised family planning: ☐ 1 Yes ☐ 2 No

Months trying to get pregnant: ____

If yes, what kind of prevention

- ☐ 01 Pills
- ☐ 02 Injections
- ☐ 03 IUD
- ☐ 04 Condoms
- ☐ 05 Implant
- ☐ 06 Lactation
- ☐ 07 Withdrawal
- ☐ 08 Natural
- ☐ 09 Abstinence
- ☐ 10 Traditional
- ☐ 11 Other specify ⇓

4.6 Antenatal care in this pregnancy: ☐ 1 Yes ☐ 2 No

If yes: First medical appointment date: ____

If date unknown, estimate first appointment :

- ☐ 1 0-12. week of gestation
- ☐ 2 13-20. week
- ☐ 3 21-30. week
- ☐ 4 After 31. week

Number of visits: ____

4.7 L.M.P: ____

4.8 Ultrasound ☐ 1 Yes ☐ 2 No

4.9 E.D.D. based on clinical estimate: ____

4.10 Do you smoke? ☐ 1 Yes ☐ 2 No

If yes: how many cigarettes per day: ____

Smoking during this pregnancy: ☐ 1 Yes ☐ 2 No

Chewing tobacco ☐ 1 Yes ☐ 2 No

Chewing tobacco during this pregnancy: ☐ 1 Yes ☐ 2 No

4.11 Do you drink alcoholic beverages? ☐ 1 Yes ☐ 2 No

If yes:

- ☐ 1 Every day
- ☐ 2 More than once a week
- ☐ 3 Once a week
- ☐ 4 Occasionally

Did you also drink alcoholic beverages during this pregnancy? ☐ 1 Yes ☐ 2 No

If yes:

- ☐ 1 Every day
- ☐ 2 More than once a week
- ☐ 3 Once a week
- ☐ 4 Occasionally

4.12 Drugs on regular basis? ☐ 1 Yes ⇒ ☐ 2 No ____

If yes:

- ☐ 1 Modern
- ☐ 2 Traditional

Did you take any drugs during this pregnancy: ☐ 1 Yes ⇒ ☐ 2 No ____

If yes, specify:

- ☐ 1 Modern
- ☐ 2 Traditional

Did you take any drugs at time of conception or during first trimester: ☐ 1 Yes ⇒ ☐ 2 No ____

Drugs for infertility: ☐ 1 Yes ☐ 2 No ____

4.15 Blood group (AB0) ____

Rh: ____

Anti-D in previous pregnancies: ☐ 1 Yes ☐ 2 No ☐ 3 Unknown

VDRL status ☐ 1 Positive ☐ 2 Negative ☐ 3 Unknown

Hb ____

Hb measurement done:

- ☐ 1 On Admission
- ☐ 2 Last visit to ANC

HIV test recorded ☐ 1 Yes ⇒ ☐ 2 No

If yes, result:. ☐ 1 Negative ☐ 2 Positive

Treatment during this pregnancy: ☐ 1 Yes ☐ 2 No Specify ____

4.16 Diseases and complications during present pregnancy, including accidents: ☐ 1 Yes (specify below) ☐ 2 No

- ☐ 01 Gestational diabetes
- ☐ 02 Diabetes
- ☐ 03 Hypertension
- ☐ 20 Preeclampsia, mild
- ☐ 21 Preeclampsia, severe
- ☐ 05 Eclampsia
- ☐ 06 Epilepsy
- ☐ 07 Bleeding
- ☐ 08 Anaemia
- ☐ 09 Hyperemesis
- ☐ 10 Malaria
- ☐ 11 Jaundice
- ☐ 12 Schistosomiasis
- ☐ 13 Gynaecological disease
- ☐ 14 Tromboembolic disease
- ☐ 15 Heart disease
- ☐ 16 Tuberculosis
- ☐ 17 Lung disease
- ☐ 18 Infections, specify
- ☐ 19 Others, specify ↓

____

5 Questions concerning the delivery

5.1 At birth ☐ 1 Single birth ☐ 2 Multiple birth⇒ If multiple, add no. of children: ☐ Weight on admission: ☐

5.2 Complications during delivery ☐ 1 PROM ☐ 2 Bleeding > 500 ml ☐ 3 3-4. degree tear ☐ 4 Abruption of placenta ☐ 5 Placenta previa ☐ 6 Other complications

5.3 Induction of labour ☐ 1 Yes ☐ 2 No If yes: ☐ 1 Amniotomy ☐ 2 Oxytocin ☐ 3 Prostaglandin

5.4 Others ☐ 1 Episotomy ☐ 2 Symphysiotomy

5.5 Analgesia: ☐ 1 Yes ☐ 2 No

5.6 Anaesthesia: ☐ 1 General ☐ 2 Spinal/Epidural

5.8 Blood Loss (ml) ☐

Specify type other type of complication

5.9 Mother's health after delivery ☐ 1 Good ☐ 2 Fair ☐ 3 Bad ☐ 4 **Maternal death**

Cause of death:

5.7 Gestational age at birth clinical estimate ☐

Post mortem: ☐ 1 Yes ☐ 2 No

6 Status of 1. child (Always fill inn)

6.1 Date of delivery ☐

6.2 Time of delivery ☐

6.3 Sex ☐ 1 Male ☐ 2 Female ☐ 3 Unknown, unspec.

6.4 Birth weight (gram) ☐

6.5 Length (cm) ☐ **6.6 Head circum** ☐

6.7 Presentation: ☐ 1 Cephalic ☐ 2 Breech ☐ 3 Transverse ☐ 4 Other

6.8 Status ☐ 1 Live born ☐ 2 Live born transferred to paediatrics dept ☐ 3 Stillborn ☐ 4 Neonatal death

Cause of death

6.9 If stillborn: ☐ 1 Dead before labour ☐ 2 Dead during labour ☐ 3 Unknown, unspec.

If stillborn, also specify: ☐ 1 Dead before admission ☐ 2 Dead after admission

And: ☐ 1 Fresh ☐ 2 Macerated

Post mortem: ☐ 1 Yes ☐ 2 No

6.10 Apgar score: 1min ☐ 5 min ☐ 10 min ☐

If neonatal death: ☐ 1 Died within first 24 hours ☐ 2 Died within first week

Date of death: ☐

6.11 Mode of delivery: ☐ 1 Spontaneous ☐ 2 Vacuum, vaginal ☐ 3 Forceps, vaginal ☐ 4 CS elective ☐ 5 CS others ☐ 6 Assisted breech ☐ 7 Destructive operative

Indication when caesarean section: Primary / Secondary

6.12 Failed intervention ☐ 1 Vacuum ☐ 2 Forceps

6.13 Does the child have any of these conditions? ☐ 1 Birth defects ☐ 2 Injuries ☐ 3 Diseases ☐ 4 HIV Positive

Status on 2. child (For multiple births – not for singletons, if more than twins add extra copy of this page)

6.1 Date of delivery ☐

6.2 Time of delivery ☐

6.3 Sex ☐ 1 Male ☐ 2 Female ☐ 3 Unknown, unspec.

6.4 Birth weight (gram) ☐

6.5 Length (cm) ☐ **6.6 Head circum** ☐

6.7 Presentation: ☐ 1 Cephalic ☐ 2 Breech ☐ 3 Transverse ☐ 4 Other

6.8 Status ☐ 1 Live born ☐ 2 Live born transferred to paediatrics dept ☐ 3 Stillborn ☐ 4 Neonatal death

Cause of death

6.9 If stillborn: ☐ 1 Dead before labour ☐ 2 Dead during labour ☐ 3 Unknown, unspec.

If stillborn, also specify: ☐ 1 Dead before admission ☐ 2 Dead after admission

And: ☐ 1 Fresh ☐ 2 Macerated

Post mortem: ☐ 1 Yes ☐ 2 No

6.10 Apgar score: 1min ☐ 5 min ☐ 10 min ☐

If neonatal death: ☐ 1 Died within first 24 hours ☐ 2 Died within first week

Date of death: ☐

6.11 Mode of delivery: ☐ 1 Spontaneous ☐ 2 Vacuum, vaginal ☐ 3 Forceps, vaginal ☐ 4 CS elective ☐ 5 CS others ☐ 6 Assisted breech ☐ 7 Destructive operative

Indication when caesarean section: Primary / Secondary

6.12 Failed intervention ☐ 1 Vacuum ☐ 2 Forceps

6.13 Does the child have any of these conditions? ☐ 1 Birth defects ☐ 2 Injuries ☐ 3 Diseases ☐ 4 HIV Positive

7 Previous pregnancies including abortions in chronological order

C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14
Preg. no	Year	Outcome	Months	Birth weight	Sex	Lact.ation months	Delivery where	Attended by	Mode	ANC	Alive/ Death	Cause of death	Age
1													
2													
3													
4													
5													
6													
7													
8													
9													
10													
11													
12													
13													
14													
15													
16													
17													
18													
19													
C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14

C1 Pregnancy number.
C2 Year of pregnancy. (Birth or other termination) PP: Present pregnancy.
C3 Outcome of pregnancy: (L) Live born, (S) Stillborn, (A) Spontaneous abortion, (I) Induced abortion, (E) Ectopic, (M) Molar, (T) Twins or other multiples *, (O) Other
C4 Months of gestation at birth or other termination.
C5 Birth weight in grams
C6 Sex: (M) Male, (F) Female, (U) Unknown
C7 Lactation: In months
C8 Delivered where: (1) At home, (2) At hospital, (3) At health post, (4) During transport) , (5) Other / unknown
C9 Attended by whom: (R) Relative, (N) Nurse, (M) Midwife, (D) Doctor, (T) Traditional birth attendant
C10 Mode: (S) Spontaneous, (V) Vacuum, (F) Forceps, (C) Cesarean section, (B) Breech, (O) Other, (9) Unknown
C11 Antenatal care: (Y) Yes, (N) No
C12 Child's current status: (A) Alive, (D) Dead
C13 Cause of death: Specify
C14 Age: (1) Less than one week, (2) Less than one month, (3) Less than one year, (4) More than one year

* Multiple births (Twins, Triples...) are filled in on subsequent lines

10.2 Antenatal care card for Pregnancy women attending clinics in Tanzania (Swahili version)

REKODI YA MAHUDHURIO YA MAMA BAADA YA KUJIFUNGUA HADI WIKI 6

Baada ya kujifungua mama ahudhurie kliniki mara tatu au zaidi . Kwa mama na mtoto wasio na matatizo wanahitaji mahudhurio matatu: ndani ya siku 7, 28, 42

Chunguza yafuatayo, weka (√) au Ndiyo au Hapana panapohusika. Pale unapogundua tatizo mpeleke kwa Mganga au Hospitali

A. REKODI YA MAHUDHURIO		Hudhurio la kwanza (Siku 7)	Hudhurio la pili (Siku 28)	Hudhurio la tatu (Siku 42)
TAREHE				
Joto la Mwili (38°C na zaidi)				
Blood Pressure 160/100 na zaidi (mmHg)				
Hb chini ya 60% (8.5gm/dl)				
MATITI				
• Maziwa yanatoka?	Ndiyo / Hapana			
• Mtoto ananyonya?	Ndiyo / Hapana			
• Chuchu zina vidonda?	Ndiyo / Hapana			
• Yamejaa sana ?	Ndiyo / Hapana			
• Yana jipu?	Ndiyo / Hapana			
• Chunguza unyonyeshaji, toa ushauri				
TUMBO LA UZAZI				
• Linanywea? (Involution)	Ndiyo / Hapana			
• Kuna matatizo yoyote?	Ndiyo / Hapana			
• Maumivu makali ?				
SEHEMU ZA UKE				
Msamba				
• Hakuchanika ?	Ndiyo / Hapana			
- Alichanika (Tear) ?				
- Aliongezwa njia (Episiotomy)?				
• Kidonda Kimepona?	Ndiyo / Hapana			
- Kina usaha ?	Ndiyo / Hapana			
- Kimeachia ?	Ndiyo / Hapana			
• **LOKIA** – Inatoa harufu?	Ndiyo / Hapana			
Kiasi: Nyingi / Wastani / Kidogo				
- Rangi gani?				
HALI YA AKILI				
• Timamu / Siyo Timamu				
UZAZI WA MPANGO				
• Ushauri umetolewa?	Ndiyo / Hapana			
DAWA ZA KINGA				
• Ferrous Sulphate				
• Folic Acid				
• Pepopunda: -Chanjo amepata ya ngapi? TT1, TT2, TT3, TT4, TT5.				
• Vitamini A (Amepata/Hajapata)				
Tiba nyingine				
Matatizo mengineyo				
Tarehe ya kurudi				
Jina la Mhudumu				
Cheo cha Mhudumu				

*Iwapo mama ana matatizo aonwe kliniki kulingana na mahitaji

KADI HII HAIUZWI RCH 4

Jamhuri ya Muungano wa Tanzania
Wizara ya Afya na Ustawi wa Jamii

KADI YA KLINIKI YA WAJA WAZITO

Jaza au weka (√) panapohusika

JINA LA KLINIKI	NAMBA YA UANDIKISHAJI		
	NAMBA YA HATI PUNGUZO		
JINA LA MAMA	UMRI:	KIMO (CM):	JUU YA 150 ☐ CHINI YA 150 ☐
	ELIMU:	KAZI:	
JINA LA MUME / MWENZI	UMRI:	ELIMU:	
	KAZI:		
KIJIJI/KITONGOJI/MTAA:	JINA LA MWENYEKITI:		
WILAYA:	KATA		

HABARI KUHUSU UZAZI ULIOTANGULIA

MIMBA YA NGAPI ..... AMEZAA MARA NGAPI ..... WATOTO WALIO HAI.....

Mimba Zilizoharibika	Mwaka	Umri wa Mimba	Mimba Zilizoharibika	Mwaka	Umri wa Mimba

TAREHE YA KWANZA YA HEDHI YA MARA YA MWISHO (LNMP).....

TAREHE ANAYOTAZAMIA KUJIFUNGUA (EDD).....

CHUNGUZA VIDOKEZO VIFUATAVYO KWA MAMA AJAPO KWA MARA YA KWANZA

A **WEKA ALAMA (√) PANAPOHUSIKA. MPELEKE KITUO CHA AFYA AU HOSPITALI KWA UCHUNGUZI / USHAURI ZAIDI ENDAPO MAMA ANA:**

UMRI CHINI YA MIAKA 20 ☐
MIAKA 10 AU ZAIDI TOKEA MIMBA YA MWISHO ☐
KUJIFUNGUA KWA KUPASULIWA ☐
KUZAA MTOTO MFU/KIFO CHA MTOTO MCHANGA (Wk 1) ☐
KUHARIBIKA KWA MIMBA 3 AU ZAIDI ☐
UGONJWA WA MOYO ☐ KISUKARI ☐ KIFUA KIKUU ☐

B **WEKA ALAMA (√) PANAPOHUSIKA. MSHAURI AENDE KITUOCHA AFYA AU HOSPITALI KWA KUJIFUNGUA ENDAPO ANA:**

MIMBA YA 5 AU ZAIDI ☐ MIMBA YA KWANZA ZAIDI YA MIAKA 35 ☐
KIMO CHINI YA CM 150 ☐ KUZALISHWA KWA KUPASULIWA AU VAKUM ☐
KILEMA CHA NYONGA ☐ KUTOKA DAMU NYINGI BAADA YA KUJIFUNGUA ☐
KONDO LA NYUMA KUKWAMA ☐

VIPIMO MAALUM VYA MAABARA:

DAMU: GROUP ..... Rh..... VDRL/RPR ..... PMTCT .....

VIPIMO VINGINE: .....

Toleo 2006

* Iwapo mama ana matatizo aonwe kliniki kulingana na mahitaji

REKODI YA MAHUDHURIO

CHUNGUZA VYOTE KILA HUDHURIO MPELEKE KITUO CHA AFYA /HOSPITALI IWAPO KIWANGO KINAZIDI AU KUPUNGUA ILIYO KWENYE MABANO

Mimba isiyo na matatizo mama anahitaji mahudhurio 4: chini ya wiki 16, kati ya wiki 20-24, 28-32, 36-40*.

TAREHEYA HUDHURIO						
UZITO (Kilo)						
BLOOD PRESSURE (140/90mmHg)						
ALBUMIN KWENYE MKOJO (+)						
DAMU/Hb (8.5 gm/dl)						
SUKARI KWENYE MKOJO (+)						
UMRI WA MIMBA KWA WIKI						
KIMO CHA MIMBA (BAADA YA WIKI 20 (cm)						
MLALO WA MTOTO (KUANZIA WIKI YA 36)						
KITANGULIZI (KUANZIA WIKI YA 36)						
MTOTO ANACHEZA BAADA YA WIKI 20 (NDIYO / HAPANA)						
MAPIGO YA MOYO WA MTOTO (BAADA YA WIKI 20) YAPO (Y), HAKUNA (H)						
KUVIMBA MIGUU "Oedema" (+ +)						
DAWA ZA KINGA:						
Ferrous Sulphate (2 Kila siku);						
*Folic acid (1 kila siku)						
Mebendazole (500mg start)						
Sulphadoxine/Pyrimethamine (SP) vidonge 3 baada ya wiki 16, rudia dozi hii baada ya wiki nne. (*Baada ya kumeza SP, mama asitumie Folic Acid kwa wiki moja).*						
PEPOPUNDA: Angalia Kadi Kama Amepata Chanjo (*jaza amepata ya ngapi*) TT1, TT2, TT3, TT4, TT5						
MAMA AMESHAURIWA KUHUSU:						
• Maandalizi ya kujifungua						
• Dalili za Hatari						
• Uzazi wa Mpango						
• Unyonyeshaji maziwa ya mama						
• Huduma ya PMTCT/ART (PMTCT 0, PMTCT -, PMTCT 1 PMTCT 2, PMTCT 1N, CTC Pre - ART, CTC on ART)						
• Magonjwa yatokanayo na kujamiana						
Tarehe ya kurudi						
Jina la Mhudumu						
Cheo cha Mhudumu						

C **VIDOKEZO VYA MIMBA VYA KUANGALIA KATIKA KILA HUDHURIO. WEKA ALAMA (✓) PANAPOHUSIKA NA MPELEKE HOSPITALI / MGANGA**

BP 140/90 AU ZAIDI ..... ☐	UMRI WA MIMBA ZAIDI YA WIKI 40 ..... ☐
Hb Chini ya 60%(8.5gm/dl) ..... ☐	MTOTO KUFIA TUMBONI ..... ☐
ALBUMIN KWENYE MKOJO ..... ☐	MTOTO AMELALA VIBAYA BAADA YA WIKI 36 .... ☐
SUKARI KATIKA MKOJO ..... ☐	KUVIMBA MIGUU ..... ☐
MAMA ANAZO DALILI ZA HATARI.... ☐	ANA MAPACHA ..... ☐
KIMO CHA MIMBA KIKUBWA ZAIDI AU KIDOGO ZAIDI KULIKO UMRI WAKE ..... ☐	

MAMA AMESHAURIWA AZALIE WAPI: .....

*Baada ya wiki 40 mama ahudhurie kliniki kila wiki.

REKODI YA UCHUNGU

JINA LA KITUO .....

KULAZWA Tarehe ..... Saa.....

UCHUNGU UMEANZA: Tarehe ..... Saa .....

CHUPA IMEPASUKA: NDIYO / HAPANA: Tarehe ..... Saa .....

UMRI WA MIMBA: (Wiki) ..... KIMO CHA MIMBA (Wiki) .....

MLALO WA MTOTO ..... KITANGULIZI .....

UPIMAJI WA NYONGA: - Sacral Promontory inafikiwa? Ndiyo/Hapana
- Ischial Spines zimetokeza? Ndiyo/Hapana
- Outlet: Finyu? Ndiyo/Hapana
- Nyonga ni kubwa ya kutosha? Ndiyo/Hapana

MAONI YA MPIMAJI: .....

JINA LA MHUDUMU ..... CHEO .....

CHUNGUZA VIDOKEZO HIVI WAKATI WA KUMLAZA - WEKA ALAMA (✓) PANAPOHUSIKA. MPELEKE HOSPITALI AU MWARIFU DAKTARI HARAKA.

KIDOKEZO A AU B KATIKA UJAUZITO	☐	HOMA ZAIDI YA 38Centigrade	☐
CHUPA IMEPASUKA BILA UCHUNGU	☐	KONDO LA NYUMA KUKWAMA	☐
UCHUNGU KABLA YA WIKI 34	☐	KIFAFA CHA MIMBA AU BP ZAIDI YA 140/90	☐
NI ZAIDI YA SAA 12 TOKEA UCHUNGU ULIPOANZA.....	☐	UPUNGUFU WA DAMU CHINI YA (8.5 gm/dl)	☐
MLALO/KITANGULIZI KIBAYA CHA MTOTO.....	☐	NYONGA NYEMBAMBA AU MTOTO MKUBWA.....	☐
KUTOKA DAMU UKENI.....	☐	MECONIUM	☐
MAPIGO YA MOYO WA MTOTO YANABADILIKA BADILIKA (Chini ya 120 au zaidi ya 160 kwa Dak.)...	☐		

BAADA YA KUZAA

KUCHANIKA VIBAYA KWA MSAMBA	☐	KUPOTEZA DAMU ZAIDI YA ML500	☐
VITAMIN A IMETOLEWA: NDIYO/HAPANA	☐		

MAELEZO YA UZAZI

KUJIFUNGUA: Tarehe..... Saa .....

NJIA YA KUJIFUNGUA .....

KAMA AMEPASULIWA: SABABU ZA KUPASULIWA .....

KONDO LIMETOKA: Tarehe ..... Saa .....

KONDO NA MEMBRENI ZIMETOKA KAMILI? NDIYO/HAPANA.....

DAMU ILIYOTOKA.....ML ERGOMETRINE/SYNTOMETRINE/OXTOCIN..... im

MSAMBA : HAUKUCHANIKA☐ UMECHANIKA☐ ULICHANWA (EPISIOTOMY) ☐

JINA LA ALIYESHONA MSAMBA ..... CHEO .....

BP BAADA YA KUJIFUNGUA..... (mmHg)

MUHTASARI: HATUA YA 1 Saa..... Dakika..... HATUA YA 2 Saa..... Dakika.....

HATUA YA 3 Saa..... Dakika.....

JINA LA MZALISHAJI ..... SAINI .....

MENGINEYO MUHIMU.....

MTOTO: Jinsia ..... Uzito ..... Kgs

APGAR SCORE 1 dakika. ..... 5 dakika. .....

Amepewa ARV .....(kama Mama ni PMTCT 1N)

VIDOKEZO VYA HATARI KWA MTOTO BAADA YA KUZALIWA

*** Weka alama (√) panapohusika. Mpeleke Hospitali**

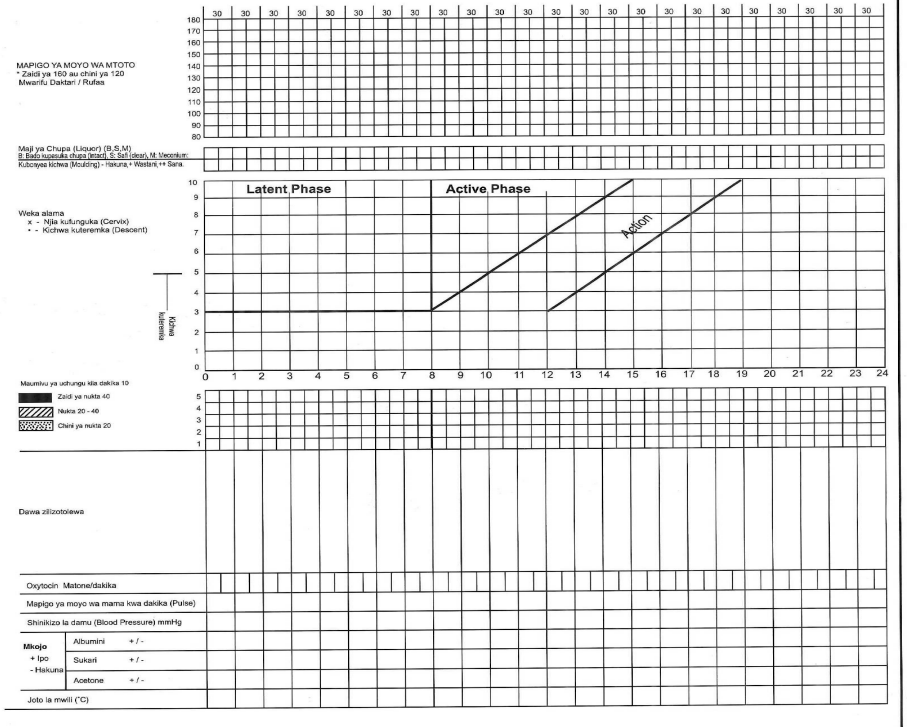
Uzito chini ya kilo 2.5☐ Homa kali zaidi ya digri 38°☐Mtoto kushindwa kunyonya ☐

Mtoto kushindwa kupumua vizuri (APGAR SCORE chini ya 5 baada ya dakika 5) ☐

Chunguza maumbile ya mtoto tokea kichwani hadi miguuni

Grafu ya Uchungu

TAREHE _____ SAA_____



10.3 Paediatrics disease register form and death report

Paediatric department KCMC

Version 1 - August 2003

Disease register form and death record

(1) Basic information concerning patient

1.1 Name of the patient……

1.2 Hospital number (of child)……. ☐☐-☐☐-☐☐

1.3 Date of birth (dd/mm/yyyy)…….. ☐☐/☐☐/☐☐☐☐

1.4 Date of admission (dd/mm/yyyy)…… ☐☐/☐☐/☐☐☐☐ Admission at time (24Hr) (tt:mm)… ☐☐:☐☐

1.5 Admission from…… ☐ 1 Labour ward
☐ 2 Home
☐ 3 Other hospital, specify: ……..
☐ 4 Labour during transport

1.5 Date of discharge (dd/mm/yyyy)…….. ☐☐/☐☐/☐☐☐☐

1.6 If newborn: Name of mother….. Hospital number (mother).. ☐☐-☐☐-☐☐

1.7 If admission from KCMC labour ward give Birth Registry ID ……. ☐☐☐☐

(2) Examinations

2.1		Results:	Comments
☐ 01	Hb		
☐ 02	Blood sugar		
☐ 03	Ph Acid/base ☐ 1		
	☐ 2		
	☐ 3		
	☐ 4		
☐ 04	Bilirubin		
☐ 05	X-ray		
☐ 06	Ultrasound		
☐ 07	Lumbar puncture		
☐ 08	Other:		

(3) Treatment

			Do	Duration
☐ 1	I.V. fluid			
☐ 2	Blood transfusion			
☐ 3	Incubation, ventilation	☐ 01 Incubator air		
		☐ 02 Incubation excess oxygen		
		☐ 03 CPAP		
☐ 3	Antibiotics			
☐ 08	Other:			

(4a) Neonatal diagnosis

4.4 Selected groups of neonatal diagnoses

☐ **P20** Hypoxia	☐ **P36** Bacterial sepsis	☐
☐ **P21** Asphyxia	☐ **P58** Jaundice	☐
☐ **P22** Respiratiory distress	☐ **P80** Hypotermia	☐
☐ **P24** Aspirational syndrome	☐ **P90** Convultion	☐

(4b) Congenital malformations

4.4 Selected groups of congenital malformations

☐ **Q00** Anenchefalus	☐ **Q20** Malformations of heart ventricle	☐ **Q69** Polydactily
☐ **Q01** Encefalocele	☐ **Q21** ?	☐ **Q70** Syndactyli
☐ **Q03** Encefalocele	☐ **Q22** Malformation of cardiac valve	☐ **Q72** Reduksjonsdeformitet
☐ **Q05** Spina bifida	☐ **Q25** Malformation of blood arteriy	☐ **Q90** Down syndrome
☐ **Q07** Other malfom of nervous system	☐ **Q35** Cleft palate	☐ **Q92** Trisomy
☐ **Q11** Anophtalmus	☐ **Q36** Cleft Lip	☐
☐ **Q18** Facial malformations	☐ **Q37** Cleft Lip and palate	☐

Discharge diagnosis (both neonatal diagnosis and congenital malformations:

Primary diagnosis ..... ICD-X:

Secondary diagnosis ..... ICD-X:

Tertiary diagnosis ..... ICD-X:

(5) Death status and diagnoses

5.1 If neonatal death..... ☐ 1 Died within first 24 hours

☐ 2 Died within first week

Date of death:

Hospital diagnosis of cause of death

Primary diagnosis..... ICD-X:

Secondary diagnosis..... ICD-X:

Tertiary diagnosis..... ICD-X:

5.2 Cause of death confirmed by post mortem..... ☐ 1 Died within first 24 hours

☐ 2 Died within first week

Date of death:

Post mortem report: Cause of death

Primary diagnosis ICD-X:

Secondary diagnosis ICD-X:

Tertiary diagnosis ICD-X:

Departemental clinical comments

Name Sign Date

10.4 Ethical clearance to conduct research in Tanzania

THE UNITED REPUBLIC OF TANZANIA

National Institute for Medical Research
P.O. Box 9653
Dar es Salaam
Tel: 255 22 2130770/2125185
Fax: 255 22 2130660/2131864
E-mail: headquarters@nimr.or.tz

Ministry of Health
P.O. Box 9083
Dar es Salaam
Tel: 255 22 2120262-7
Fax: 255 22 2110986

NIMR/HQ/R.8a/Vol. IX/126

5th May, 2003

Prof J Mlay.
KCMC,
P o Box 3010.
Moshi, Tanzania

CLEARANCE CERTIFICATE FOR CONDUCTING MEDICAL RESEARCH IN TANZANIA

This is to certify that the research entitled: "Registry based reproductive health research: Medical Birth registration at KCMC" Mlay J et al, Principal Investigator, has been granted clearance to be conducted in Tanzania. The PI of the study must ensure that the following conditions are fulfilled:

[v] Progress report is made available to MoH and NIMR every six months.
[v] Permission to publish the results is obtained from NIMR (manuscript being attached to the request) before any publication is made.
[v] Copies of final publications are made available to MoH and NIMR for action and records.

CHAIRMAN
NATIONAL MEDICAL RESEARCH COORDINATING COMMITTEE

This is to certify that Permission is hereby granted for the conduct of the study entitled: "Registry based reproductive health research: Medical Birth registration at KCMC" Mlay J et al Principal Investigator, within the health services and/or communities in Tanzania.

CHIEF MEDICAL OFFICER
MINISTRY OF HEALTH

10.5 Ethical clearance from KCM-College

CRERC FORM 07

TUMAINI UNIVERSITY

KILIMANJARO CHRISTIAN MEDICAL COLLEGE
P. O. Box 2240, MOSHI, Tanzania

RESEARCH ETHICAL CLEARANCE CERTIFICATE

No 333

Research Proposal No. 334

Study Title: PREGNANCY CONDITIONS AND NEONATAL HEALTH OUTCOMES OF NEWBORNS TRANSFERRED TO NEONATAL CARE UNIT AT KCMC HOSPITAL BASED REGISTRY STUDY IN NORTHERN TANZANIA.

Study Area: KCMC

P. I Name: DR.BLANDINA MMBAGA

Institution (s): KILIMANJARO CHRISTIAN MEDICAL CENTRE AND UNIVERSITY OF BERGEN.

The Proposal was approved by on: 15TH JULY, 2010.

Duration of Study: FROM 15TH JULY, 2010 TO 14TH JUNE, 2011.

Name: BEATRICE Z. TEMBA

Signature.....

Research Administrator – CRERC

Name PROF. FRANKLIN W. MOSHA

Signature.....

Chairman – CRERC

Errata for
Pregnancy and perinatal health outcomes in Northern Tanzania: a registry based study

Neonatal care admissions and recorded causes of neonatal and perinatal deaths

Blandina Theophil Mmbaga

Thesis for the degree philosophiae doctor (PhD)

at the University of Bergen

Bmbaga.

(signature of candidate)

(signature of faculty)

2013

Erratum

Paper 1

Page 9: Table 4 Body height <150 in model C ‘1.1 c(0.9-1.2)’ should read ‘1.1 (0.9-1.2)’

Page 9: Gestational age 34-36 in model C ‘1.3 1.3 (1.1-1.5)**’ should read ‘1.3 (1.1-1.5)**’

Page 10: under strength and limitation second paragraph, reference ‘[20]’ should read ‘[2]’

Thesis

Section 5.2: Page 60: sub-section; Antenatal care

First sentence: reference ‘[20]’ should read (and have been replaced with) ‘[23]’

Third sentence: reference ‘[20]’ should read (and have been replaced with) ‘[23]’

Fourth sentence: reference ‘[92,93]’ should read (and have been replaced with) ‘[96,97]’

Fifth sentence: reference ‘[115,167]’ should read (and have been replaced with) ‘[119,120]’

Sixth sentence: reference ‘[94]’ should read (and have been replaced with) ‘[98]’