CHARACTERISTICS AND CORRELATES OF STILLBIRTHS AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET-KENYA

BY

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MOI UNIVERSITY

DECLARATION

Declaration by the candidate

This is my original work and I confirm that it has not been presented to anyUniversity or any other institution of higher learning for the award of any degree or academic credit.

Signature……Date……..

James Munene Waweru

SM/PGRH/05/12

Declaration by the Supervisors

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DEDICATION

I dedicate this work to my family for their support and perseverance.

ABSTRACT

Background: Few obstetric complications are as emotionally devastating for patients and clinicians as stillbirths. There were 2.64 million stillbirths globally in 2009; the stillbirth rate in Kenya was estimated at 21.8 per 1000 births. The last study on this subject at this hospital was in 1994 when hospital incidence was 30.5 per 1000 births. The World Health Organisation (WHO) defines a stillbirth as a baby born dead at or after 22 weeks gestation. For international comparability the WHO allows a cut off at 28 weeks gestation. This study was based on a cut off gestation of 28 weeks because of the minimal chance of survival of a baby born earlier than 28 weeks in Kenya.**Objective**: 1.To describe characteristics of stillbirths delivered at MTRH. 2. To describe maternal and perinatal characteristics associated with stillbirths at MTRH.3.To explore the correlation between maternal/perinatal characteristics and the type of stillbirth. (macerated or fresh stillbirth) **Methods:** the study was carried out in maternity and pathology departments of MT&RH. The period of data collection was between May and October 2015. This was a cross-sectional descriptive study. The study involved evaluating the clinical circumstances, maternal records abstraction, and findings of laboratory investigations (blood/urine tests and placental histopathology). The target populationincluded mothers who delivered stillbirths at MT&RH at 28 weeks or later' gestation. Cases were recruited consecutively. Data was collected using interviewer-administered semi-structured questionnaires, medical records abstraction, and laboratory results. Data was entered into Microsoft Access software and analysed using R Core Team, 2015. Correlation between categorical outcome variables (type of stillbirth) and categorical independent variables (maternal and perinatal characteristics) was done using Fisher's exact test. Continuous variables were compared using independent samples t-test. The findings have been presented in form of tables.**Results**: During the study period 121 stillbirths were delivered at MTRH. There were 5250 deliveries in this unit in this period, translating to approximate hospital stillbirth rate of 23.03 per 1000 births. 113 mothers were recruited. Out of these, 104 placentae were examined histopathologically. A tenth (11.5%)of the mothers who delivered stillbirths were aged 35 years and over, while 5.3% were less than 18 years of age. A quarter (27.2%) of these mothers had attended at least four antenatal visits. Forty-five percent of the respondents were primigravidae. About a third (31.9%) of the stillbirths were fresh stillbirths(FSB). Majority of the stillbirths (58.4%) were male. Forty seven (41.6%) of the stillbirths were small-for-gestational age(SGA). The major maternal conditions among mothers with stillbirths were hypertensive disorders and urinary tract infections affecting 15.0% and 14.1% of the respondents respectively. Seventy-five percent of the examined placentae had pathological abnormalities. SGA was associated with FSB, OR: 2.32; 95% CI [1.04, 5.19; P=0.044]. No association between abnormal placentalpathology and type of stillbirth (P>0.999).**Conclusion:** The main maternal conditions associated with stillbirths were hypertensive disorders and UTI. Majority of the placentae had pathological findings. SGA was associated with increased risk of FSB. There was no association between abnormal placentae and type of stillbirth. **Recommendations:** 1. Stakeholders in obstetrics should explore cost-effective approaches to enhance diagnosis of SGA fetuses in early third trimester to reduce fresh stillbirth rates. 2. A case-control study should be carried out to help establish the clinical significance of placental pathological findings among stillbirths in our setup.

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DEFINITIONS OF TERMS

Fetal death-The World Health Organization (WHO), through, The International Classification of Diseases, 10th revision (ICD-10) defines a fetal death as "death prior to the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy; the death is indicated by the fact that after such separation the fetus does not breathe or show any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles" without specification of the duration of pregnancy (ICD 10,1993).

Stillbirth-The definition varies between countries. For example, in the USA it refers to a baby born without signs of life after22 weeks of gestation, while in United Kingdom the cutoff is 24 weeks gestation.For international comparability, the World Health Organization allows a cut off of 28 weeks gestation, or a baby born dead weighing at least 1000g (Lawn JE, et al.2010)

Fresh stillbirth- a stillbirth with intact skin i.e. no signs of degeneration.

Macerated stillbirth-is a stillbirth with signs of degeneration suggesting the death having occurred more than twelve hours before delivery.

Small-for-gestational age: used to describe a baby whose birth weight is less than 10th percentile of that expected at a particular gestation.

Perinatal characteristics of stillbirth: These include findings on the stillborn, the placenta and cord at birth; also includes histologic findings on the placenta and cord.

ABBREVIATIONS

CS Caesarean section

FSB Fresh stillbirth

ICD-10 International Classification of Diseases, 10th edition

IUGR: Intrauterine growth restriction

MSB Macerated stillbirth

MTRH: Moi Teaching and Referral Hospital

SGA Small for gestational age

TTTS: Twin-twin transfusion syndrome.

UTI Urinary Tract Infection

VDRL: Venereal disease research laboratory-screening test for syphilis.

WHO: World Health Organization

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CHAPTER ONE

INTRODUCTION

1.1 Background information

Few obstetric complications are as emotionally devastating for patients and clinicians as stillbirths (Silveret al., 2007). There were 2.64 million stillbirths globally in 2009, translating to an average of 18.9 stillbirths per 1000 total births (Cousenset al., 2011). Approximately 76·2% of stillbirths occurred in south Asia and sub-Saharan Africa. The stillbirth rate in sub-Saharan Africa is approximately 10 times that of developed countries (28 vs. 3 per 1 000 births) (McClure et al., 2006).

According to ICD 10, a stillbirth is a baby born without any sign of life at or after 22 weeks gestation or 500 grams birth weight. The World Health Organization (WHO)recommends a cutoff of 28 weeks gestation or 1000 grams birth weight; this takes into account the reality that in many low-income(e.g. Kenya) and middle-income countries, survival is limited for babies born before 28 weeks' gestation or weighing less than 1000 grams (Goldenberg et al., 2011; WHO, 2016). This WHO cutoff allows for international comparability. Most studies carried out in Kenya on the subject of stillbirths have applied 28 weeks' gestation (Njuguna, 2010; Khasakhala&Ndavi, 2007 ;). The baby may die antepartum or intrapartum. The baby may be born fresh or macerated.

Probable causes of stillbirths include intrauterine growth restriction and congenital anomalies (Fretts, 2005). Obstetric complications are important causes of stillbirths especially in the less developed world (Were, 1994;Onyiriuka, 2009;Getahun, Ananth& Kinzler,2007;Schmiegelow et al., 2012).

Placental and cord risk factors associated with stillbirths include placental insufficiency, placental abruption, placenta praevia, fetomaternal hemorrhage, cord prolapse, placental malformations (Hossain&Khan, 2009;Silveret al., 2007;).Other equally important causes of stillbirth include infections, severe fetal-maternal hemorrhage, and severe maternal illness (Reddy et al., 2009).

All these factors and probable causes may not be easily definable in specific cases, but may present as observable characteristics in the mother, during labor and delivery, in the baby and in the placenta. The observable characteristics are what this study has described among the mothers who suffered stillbirths. It is hoped that the recommendations arising from this study will be taken up and thereby lead to improving our understanding of the problem of stillbirths.

1.2 Problem statement

Stillbirth is a devastating outcome of pregnancy for the family and the clinician. In 2009, 2.64 million babies were born dead after 28 weeks gestation, 20% of whom were at or near term (Silveret al., 2007; Korteweg, Erwich & Timmer, 2012). The stillbirth rate in Africa is ten times higher than in the developed world. Between 1995 and 2009, the global decline in stillbirth rate was 14.5%; but the decline in Sub-Saharan Africa was 8.1%. Despite the magnitude of the problem, relatively little attention has been focused on stillbirths during the past decades (Silveret al., 2007). Improved data and improved use of data are crucial to ensure that stillbirths count in global and national policy (Cousenset al., 2011). In Kenya very few studies have been conducted on this subject of stillbirths.

1.3 Justification

Perinatal mortality and still births rates are important indicators of the quality of antenatal and obstetric care in the community. Evaluations for features of stillbirths are often incomplete or absent due to limited availability of services, concerns about cost, or difficulty in discussing death or postmortem examination (Parker et al, 2011). However, performing a thorough investigation can help in counseling patients about recurrence risk and, in some cases, guide medical interventions to improve outcomes in subsequent pregnancies (Parker et al., 2011; Korteweg et al., 2012). The Stillbirth Collaborative Research Network (SCRN) has reported that performing a systematic medical evaluation leads to a probable or possible cause of death in the majority of stillbirths (Parker et al., 2011). Moreover investigatingstillbirths would aid public health specialists and policy makers to prioritize health service resources and strategies for prevention (Gardosi et al., 2013).

At Moi Teaching and Referral Hospital, as is the case in most health facilities in Kenya, stillbirths are neglected; rarely is an attempt made to explain the cause of or characterize a stillbirth.The last study conducted on this subject at our institution, which was a retrospective study, was in 1994.The stillbirth prevalence rate at this hospital that year was 30.5 per 1000 births. Among these, 45.8% were due to intrapartum birth asphyxia (Were, 1994). My study aimed at adding placental histologyto this subject two decades later.

It was expected that the finding of this study would provide new evidence to guide intervention that will ultimately lead to a significant reduction in the rate of stillbirths.

1.4 Research Question

What are the characteristicsand correlates of stillbirths delivered at Moi Teaching and Referral Hospital maternity?

1.5 Objectives

1.5.1 Broad Objective

To determine the characteristicsand correlates of stillbirths delivered at Moi Teaching and Referral Hospital (MTRH),Kenya.

1.5.2 Specific Objectives

1. To describethe characteristics of stillbirths delivered at MTRH.
2. To describe maternal and perinatal characteristics associated with stillbirthsat MTRH
3. To explore thecorrelation between maternal and perinatal characteristics,and type of stillbirth

1.6 Significance of the study

The last study conducted at this hospital on stillbirths was in 1994. It was a retrospective study based on case series.No placental histology was carried out to attempt to describe further features of the stillbirths (Were, 1994). Moreover a lot of time has passed since this study was done. The study carried out at Kenyatta National Hospital by Njuguna et al in 2011 was during a period when maternity serviceswere paid for by patients; this study was carried out during an era of free maternity services.

Thisstudy was prospective thereby mitigating on lost or missed data. In addition, and significantly, this study included doing histological examinations of the placentae

1.7 Limitation of the study

This study did not assesscharacteristics of lives births and associated placental and maternal characteristics. The estimation of gestational age was mostly based on the last normal menstrual period, which is not always correct. This was because most mothers did not have early trimester obstetric ultrasound scans.

CHAPTER TWO

LITERATURE REVIEW

The global burden of stillbirths varies with regions. Sub-Saharan Africa is hard hit by the scourge of stillbirth, with a stillbirth rate of 31.0 per 1000 births as of 2009 estimates. South Asia had similar figures at 30.2 per 1000 births. North Africa, Europe and Russia had low stillbirth rates of 3.8, 1.6 and 2.2 per 1000 births respectively. Oceania had the lowest stillbirth rates 0.3 per 1000 births according to the 2009 stillbirth estimates (Cousenset al., 2011. Nigeria had the highest stillbirth rate in Africa at 41.7 per 1000 births. That year Kenya lost 34,130 babies through stillbirths at rate of 21.8 per 1000 births.

The majority of stillbirths are preventable, evidenced by the regional variation across the world. When we look at the changes in stillbirth rates between 1995 and 2009 there was a reduction of 14.5% in global stillbirth rates. Sub-Saharan Africa was the worst performer in that regard, with stillbirth rates declining by 8.7%; East Asia, North Africa and Europe declined by 47.5 %, 22.9%, and 17.6% respectively (Cousenset al., 2011).

Hospital based studies tend to yield higher stillbirth rates than community studies, but countries with high community-based rates tend to have high hospital-based rates. In a study conducted at Kenyatta National Hospital in Kenya, in 2011 by Njuguna the stillbirth rate was found to be 52 per 1000 births (Njuguna, 2011). Were conducted a retrospective study at Eldoret District Hospital (currently Moi Teaching and Referral Hospital) and established that the stillbirth rate then was 30.2 per 1000 births (Were,1994).

The maternal features in this study are what would be described as determinants in other studies designed differently. The World Health Organisation defines a risk factor

as any attribute, characteristic or exposure of an individual that increases the likelihood of an outcome .The risk factors for stillbirths can be categorized into, maternal, obstetrical, placental and fetal (Fretts,2005). Many context-dependent factors temper the impact of other risk factors.

A study by Khasakhala and Ndavi (2007)with regard to the main risk factors for perinatal mortality identified various variables that may impact on stillbirths. Among these are factors that exist before conception (parents' socioeconomic and cultural characteristics, mother's demographic characteristics and mother's habitat and environment); variables appearing during pregnancy (i.e., medical supervision during pregnancy, and delivery related variables (i.e., medical supervision during delivery, delivery complication and child's characteristics at birth).

Parents' socioeconomic characteristics include education (both maternal and paternal), work status, wealth, as well as the mother's habitat and environment (depicted by region of residence). The cultural characteristics include religion. All these are likely to impact on the mother's health through their effect on her nutritional status. Maternal demographic characteristics include age, parity, birth order, and pregnancy interval; these may directly influence pregnancy outcome.

Maternal morbidities include chronic and acute medical and surgical conditions that may directly impact on the pregnancy. These include diabetes mellitus, chronic hypertension, renal failure, syphilis, malaria, acute abdominal conditions, among others. Many obstetric complications may arise in the course of labour and delivery and have major impact on the outcome of a pregnancy. Examples include placental abruption, cord prolapse, shoulder dystocia.

In most geographic areas in developing countries, various socio-demographic factors, including rural residence, low socioeconomic status, lack of education, lack of a partner, and poor nutrition have been associated with increased stillbirth rates. Other risk factors include advanced maternal age, short inter-pregnancy interval, prior stillbirth, and history of adverse pregnancy outcomes (Fretts,2005; Onyiriuka,2009; Khasakhala& Ndavi2007;Di Mario, Say & Linchetto, 2007). Nulliparity and grand multiparity are also recognized risk factors for stillbirth (Hossain& Khan., 2009).

The leading maternal clinical risk factors for stillbirths include hypertensive disorders, antepartum hemorrhage, diabetes, anemia,prelabor rupture of membranes and urinary tract infections, and cholestasis of pregnancy (Schmiegelow et al., 2012).

In developed countries, between 10% and 25% of stillbirths may be caused by an **infection,** whereas in developing countries, which often have much higher stillbirth rates, the contribution of infection is much greater.(Goldenberget al.,2009; McClureet al., 2009).

Placental and fetal infections likely originate from two predominant pathways. The most common is an ascending infection to the fetal membranes and the fetus. This may manifest as inflammatory response in the chorioamnion (chorioamnionitis), in the amniotic fluid (amnionitis), in the umbilical cord (funisitis), or in the fetus (usually pneumonitis). Infections may also spread hematogenously from the woman to the fetus through the placental villi (villitis) (McClure et al., 2009).

Infection may lead to stillbirth through several pathways. First, through maternal infection resulting in systemic illness, for example, high maternal fever, severe maternal illness, or respiratory distress, the fetus may die, without the organisms

transmitted to the placenta or fetus; severe maternal infection is defined as an illness requiring hospital treatment, usually marked by high fever above 38^0C, and the need for treatment such as intravenous antibiotics, surgery, or ventilator support. Secondly, infection of the fetus may damage vital organs, such as heart or brain, resulting in stillbirth. Thirdly, infection may also result in an anomaly that later kills the fetus.Fourthly, the placenta may be directly infected without spread of the organisms to the fetus with reduced blood flow resulting in a stillbirth (Reddyet al., 2009; Goldenberg); this has been observed in cases of malaria and syphilis severe enough to affect placental function. A placental infection may be assumed if there is evidence of placental histologic changes compatible with that infection. In other important instances the infection may precipitate preterm labor with the fetus dying intrapartum. In this case there will be histologic evidence of chorioamnionitis(Reddy et al.2009).

Syphilis is prevalent in Sub-Saharan Africa; more than 10% of pregnant women are sero-positive in some geographic areas. In areas where this occurs, up to half of all stillbirths are in syphilis sero-positive women and estimates suggest that 25% of all stillbirths are attributable to syphilis alone (Goldenberg et al., 2010; Southwick et al., 2001). In Kenya the Venereal Disease Research Laboratory test is a routine antenatal test. Bacterial infection can be regarded as the cause of fetal death there is a positive culture of fetal blood or of maternal blood combined with signs of infection of the placenta, ie, chorioamnionitis or funisitis. Chorioamnionitis on itself should not be invoked as a cause of stillbirth except in cases whereby it causes preterm labor with the fetus dying in labor.

Globally, approximately half of all births occur in areas with endemic malaria, with high rates of stillbirth (Wort, Hastings, Mutabingwa & Brabin, 2006).Malaria is not

often associated with higher stillbirth rates in multigravidae. Stillbirth risk is increased during times of malaria peaks. Women infected for the first time in pregnancy are at higher risk for stillbirth (Wort et al., 2006). Placental damage is the likely cause for stillbirths associated with maternal malaria. Malaria parasites, particularly *Plasmodium falciparum*, tend to be sequestered in the placenta (Desai M et al., 2007). Although the primary catchment area of MTRH is not a malaria-endemic zone, the hospital receives referrals from the Western Kenya region, part of which is malaria-endemic. In addition travelling leads to exposure of mothers with low immunity to malaria.

Overall, about 10% of all fetal deaths are related to maternal medical illnesses such as hypertension, diabetes, obesity, systemic lupus erythematosus, chronic renal disease, thyroid disorders, and cholestasis of pregnancy (Simpson, 2002; Coletta& Simpson, 2010). The presence of any of these conditions is an important feature of the mother who suffers a stillbirth.

Hypertensive disorders in pregnancy include chronic hypertension, gestational hypertension, superimposed preeclampsia, preeclampsia, and eclampsia. Preeclampsia/eclampsia occurs in about 6% of pregnancies globally (McClure et al., 2009). Some studies have attributed more than a fifth of stillbirth to hypertensive disorders in pregnancy. Preeclampsia/eclampsia often is associated with placental insufficiency leading to intrauterine growth restriction which may terminate in stillbirth.Where blood pressure and urine protein screening are not routine, and where induction of labor or cesarean sections are unavailable, fetuses frequently die secondary to hypoxia associated with maternal preeclampsia or eclamptic seizures. The risk or stillbirth increases with multisystem disease. Preeclampsia may be considered a cause

of death if it progresses to eclampsia, or if it is associated with abruption or fetal growth restriction (Reddy, et al., 2009).

Diabetes mellitus leads to stillbirths through multiple pathways: congenital abnormality, placental insufficiency/IUGR, macrosomia and obstructed labor. Diabetes mellitus increases the risk of stillbirths fourfold to fivefold (Macintosh et al., 2006). Diabetes mellitusmay cause either intrauterine or intrapartum asphyxia, large forgestational age fetus, small for gestational age fetus, or severe malformation. Diabetes also lead to intrauterine or intrapartum asphyxia or the placenta can demonstrate characteristic histopathologic findings such as immature villi with stromal edema, enlarged villous diameters, and an increase in the prominence of cytotrophoblast (Reddy et al., 2009). Diabetes mellitus is screened using random blood sugar in routine antenatal clinic.

Thyroid disease refers to situations of hyperthyroidism or hypothyroidism. Treated thyroid disease carries low risk of stillbirth. The exception is Graves' disease, with thyroid stimulating immunoglobulin leading to fetal thyrotoxicosis which can rarely cause fetal death. There is an increased risk of stillbirth among women with untreated hyperthyroidism. Untreated hypothyroidism also is associated with higher risk of stillbirth when it is symptomatic and associated with abruption and pregnancy-induced hypertension (Reddy et al., 2009; Simpson, 2002). Thyroid disease is screened antenatally by thyroid stimulating hormone assay (TSH).

Liver disease in pregnancy includes hepatitis, liver cirrhosis, and cholestasis of pregnancy and acute fatty liver of pregnancy. Cholestasis of pregnancy and acute fatty liver of pregnancy are rare but accepted causes of stillbirth(Reddy et al., 2009).

In developing countries with high incidences of stillbirths due to the other causes, the proportional role of **congenital anomalie**s is significantly less than other causes of birth complications. In developing countries, recent studies have attributed less than 5% of stillbirths to congenital anomaliescompared to nearly a quarter due to anomalies in developed countries(Reddy et al., 2009).

Intrauterine growth restriction is defined as birth weight below the 10th percentile of the birth-weight-for-gestational age reference curve (WHO;Wollmann H.A, 1998). Customized growth curves adjust for physiologic variation such as maternal weight, parity and ethnic origin, thus help distinguish between normal small and pathologically small fetuses. However not all regionshavecustomized growth curves. The risk of stillbirth may be as high as sixfold in IUGR, with IUGR being identified in about 40-60 % of stillbirth(Flenady et al., 2011; Clausson,Gardosi,Francis & Cnattigius, 2001; Fretts, 2005).Intrauterine growth restriction is not an actual cause of stillbirths but a highly relevant condition that is found in a significant proportion of stillbirths and in the majority of cases that are sometimes classified as unexplained.Use of customized charts to detect IUGR in pregnancy has been associated with significant reduction in stillbirth rates (Gardosi et al., 2013). Pathologic associations with IUGR include fetal abnormalities (chromosomal and structural); multifetal gestation; maternal conditions such as infection, hypertensive disease, malnutrition, and smoking; placental disease; and cord abnormalities (Reddy et al., 2009).

Some authors have described the placenta as the ‘black box’ to help in investigating a stillbirth (Heazel, 2015). The placenta is a key component of the feto-placental unit. Placental dysfunction and abnormalities have a well-known association with poor pregnancy outcome. Placental causes can be classified into circulatory abnormalities,

infection/inflammation, genetic abnormalities, developmental abnormalities and migrational disorders. The main circulatory abnormality is abruption which may be concealed or apparent; it may also be acute or chronic. Genetic abnormalities of the placenta include confined placental mosaicism and vascular lesions. Developmental abnormalities of the placenta include placenta previa, and neoplasms. The main migrational disorder is vasa previa whereby submembranous fetal vessels cross the endocervical os where they may rupture during labor or following rupture of membranes.It is also understood that placental functiondiminishes as the pregnancy nears or goes over due (Hussain, Yakoob, Imdad &Bhutta, 2011). Post-term pregnancy is known to be associated with stillbirth, due to progressive uteroplacental insufficiency when the pregnancy progresses past term (Warland & Mitchell, 2011).

Placental abruption refers to prenatal separation of the placenta. It may be apparent in which case there is vaginal bleeding. Abruption may also be concealed. According to some studies placental abruption accounts for upto 7% of all perinatal deaths, 77% of which occurred in utero (Tikkanen et al., 2013). The risk factors for placental abruption include advanced maternal age, low birth weight, small for gestational age, maternal smoking, preeclampsia, major congenital anomalies, male fetal sex, anemia and low social economic status(Tikkanen et al., 2013; Raisanen S et al., 2013). Placental abruption may be considered the cause of stillbirth when there are clinical or histolological signs of placental detachment of 30% or more. In cases of chronic abruption there may be hemosiderin deposit in the placenta; it may also manifest as marginal fibrin deposition, decidual necrosis or even placental infarction (Reddy et al., 2009).

Umbilical cord abnormalities account for 3.4-15% of stillbirths depending on the preponderance of other causes of stillbirths (Reddy et al., 2009).Umbilical cord pathology includes velamentous and furcated cord insertions, umbilical cord prolapse, and umbilical cord occlusion. Velamentous cord insertion refers to abnormality where the vessels insert on the membranes rather than the placenta; they are therefore at risk of vasa previa. With furcated insertion of the umbilical cord, the umbilical cord vessels lose the protective cover of Wharton's jelly before entering the chorionic plate; they are thus exposed to external trauma or twisting leading to stillbirth (Collins, 2002).Umbilical cord prolapse is defined as presentation of the cord in advance of the presenting fetal part.

The aforementioned conditions will lead to either cord hemorrhage or cord occlusion. Cord occlusion can result from external compression, torsion, or cord hematoma. Nuchal cords are not associated with increased risk of stillbirth. True cord knots are also common among livebirths; they are only attributed as cause of death if associated with constriction of umbilical vessels in longstanding cases and edema, congestion, or thrombosis in more acute ones (Reddy, et al, 2009). However an otherwise innocuous cord compression may prove fatal in a vulnerable fetus, especially with IUGR (Warland et al.,2011).

According to Parast et al (2008), 'minimal criteria' suggestive of cord accident were defined as vascular ectasia and thrombosis within the umbilical cord, chorionic plate and/or stem villi. A definitive diagnosis of cord accident requires in addition regional distribution of avascular villi or villishowing stromal karyorrhexis. In a review by Parast et al, nonacute cord compression was implicated in over half of otherwise 'unexplained fetal deaths' (Parast et al., 2008). Corroborating evidence fetal hypoxia

will confirm the cord accident as the initiator of the pathophysiologic cascade leading to fetal death (Reddy UM et al., 2009).

There are specific placental abnormalities associated with multifetal gestation, the most common being twin-twin transfusion syndrome (TTTS)-occurs in about 9% of monochorionic diamniotic gestations as a result of arteriovenous anastomoses. In a prospective study by Lewi et al in 2008 involving 202 twin pairs, it was found that the mortality of TTTS was about 55%(Lewi et al., 2008);of the fetal losses in that study, 80% occurred before 24 weeks of gestation. The mechanism of death is through anemia in the donor twin leading to hypoxia manifest by IUGR and hydrops; the recipient twin may also succumb to the effect of polycythemia which can cause congestive cardiac failure.

Other important causes of fetal demise among monochorionic twins includeisolated severe discordant growth, anemia-polycythemia sequence, and congenital defects (Lewi et al., 2010).

Monochorionic monoamniotic twins occur in 5% of monochorionic twins. There is high stillbirth rate mainly due to cord entanglement. Other potential contributors to fetal death include preterm birth, growth impairment, malformation, genetic abnormalities, and vascular anastomoses.

Twin reverse arterial perfusion is a rare complication of monochorionic twins involving about 1% of such pregnancies. It results from artery-artery anastomoses with reverse transfusion in one of the twins. The reverse flow of deoxygenated blood leads to abnormal development of one so that the heart develops abnormally and cannot function. The dependent twin cannot develop. The pump twin is also at risk due to the

additional cardiac demands. Mortality has been reported to be as high as 12% to 50% of pump twin(Jellin et al., 2010; Sullivan, Varner, Ball, Jackson& Silver 2003).

Intrapartum stillbirth refers to death of a fetus during labor and delivery.While there are not good data available about the number of stillbirths occurring secondary to asphyxia/hypoxia, approximately 23% of stillbirths occur intrapartum. In developed countries because intrapartum stillbirth is reduced with adequate care, it is likely that stillbirths could be reduced significantly with adequate care in developing countries(Ngoc NT et al., 2006).

According to a study conducted by Weiner and colleagues, at Kilifi District Hospital, Kenya, in 2003, labor complications have a strong effect on perinatal mortality; 53 % of all perinatal deaths were attributable to labor complications in that study. The factors involved are many. Some of the important risk factors for intrapartum stillbirths include prolonged labor, malpresentation, antepartum hemorrhage, and premature labor(Weiner et al 2003).

Birth asphyxia is a common cause perinatal mortality especially in developing countries (Lawn et al., 2005). Cord accidents are a serious cause of fetal asphyxia and stillbirth. Other contributing factors include abruption and uterine rupture which are discussed elsewhere.

CHAPTER THREE

METHODOLOGY

3.1 Study Setting

The study was carried out at maternity wing and pathology department of Moi Teaching and Referral Hospital (MTRH). This is the second-largest public referral hospital in Kenya that caters to the western part of Kenya. The hospital handles referral cases from the western region of the republic. It also handles primary cases from the surrounding areas. Moi Teaching and Referral Hospitalhas a total bed capacity of 1000. The maternity wing comprisedthe antenatal ward, postnatal ward and labor ward with a bed capacity of 29, 35, and 17 respectively. This wing has two operating theatres.According to hospital records, the hospital handledapproximately 1100deliveries per month in 2015, with an average caesarean delivery rate of approximately 19%.

3.2 Study Design

This wasa descriptive cross-sectionalstudy, It involved description of maternal features and perinatal features of the stillbirths, including assessment of the placentae. Maternal demographic and obstetric characteristics categorized were described based on records clinical findings and laboratory test results. In addition all placentae were submitted for histopathological examination by the hospital pathologist. Stillbirths that were delivered were categorized and described based on gestation, weight, sex and external physical findings. Eventually, the correlation between maternal and placental characteristics (independent variables), and the type of stillbirth i.e. whether FSB or MSB, (dependent variable) was calculated, based on a P value of 0.05. Factors that were found to be associated with type of stillbirth were submitted to multivariate analysis within 95% confidence interval, upon which adjusted odds ratios were derived.

3.3 Study population

The study population comprised all mothers who delivered stillbirths at the antenatal and labor wards.

3.4 Sample size

The sample size calculation was based on a similarstudy conducted by Njuguna in Kenyatta National Hospital. In that study, the major conditions found in the mothers were hypertensive disorders, antepartum hemorrhage and anemia. The main condition found on the stillborns was congenital malformations. In Njuguna's study 26.7% of the mothers who had stillbirths had hypertensive disorders (Njuguna, 2011). Estimation of the sample size that answers the proportion of still births with these disorders required that we use one of the disorders as a group of interest and the rest as a compliment. Here we used the proportion of still births whose mothers had hypertensive disorders. Thus, in order to be 95% sure that the proportion of still births associated with hypertensive disorders was within plus or minus 5% of the population proportion of 26.7%, a sample size was computed (Cochran, 1963).

$$
\begin{aligned}
n &= \left(\frac{Z^2_{1-\alpha/2}}{\delta^2} \right) P(1-P) \\
&= \left(\frac{1.96^2}{0.05^2} \right) 0.267 \times 0.733 \\
&= 301
\end{aligned}
$$

Whereby:

P, the proportion of still births due to hypertensive disorder, was obtained from Njuguna (2011).

$Z_{1-\alpha/2}$ is the quantile from the standard normal distribution under a type 1 error of 5%,

δ is the margin of error, assumed to be 5%.

During the first six months of year 2014 up to 180 cases of still births were reported in Moi Teaching and Referral Hospital (MTRH). Therefore, given the fact that our target group was mothers who hadstillbirthsthat formed our population. This is a finite population hence we needed to do a finite population correction within this period. The sample size therefore is

$$\left(\frac{n}{1+n/N}\right)=\left(\frac{301}{1+301/180}\right)=113$$

Where N was the population size.

3.5 Sampling Technique

Consecutive sampling technique was used in this study to pick the mothers. This was mainly due to the fact that stillbirth is relatively uncommon (Njuguna, 2011; Onyiriuka, 2009; Hossain, 2009; Mmbaga, 2012).Selection of eligible mothers was done as soon as it was established that the mother had intrauterine fetal death, or delivered a stillbirth at or after 28 weeks gestation, or where the gestation was not clear, at least 1000 grams in weight. After the interview additional consent was sought from the parents for postmortem examination of the placenta.

3.6 Eligibility criteria

3.6.1 Inclusion criteria:

1. Stillborn babies at least at 28 weeks gestation, or at least 1000 grams in weight.
2. Stillborn babies of mothers who could consent or accompanied by an adult who could consent.
3. Stillborn babies in cases of pregnancy terminated due to severe fetal compromise and severe fetal malformations meeting the above criteria, irrespective of whether the fetus died during termination of pregnancy or before.

4. Stillbirths who met criteria number 1 and 2, in cases of pregnancies terminated due to severe maternal illness.

3.6.2 Exclusion criteria

1. Babies whose gestation was less the 28 weeks, or if gestation was unknown, weighed less than 1000grams.
2. Stillborn babies of mothers who declined interview, or who could not legally consent and not accompanied by next-of-kin relatives who could consent.
3. Stillborn babies delivered before arrival at the hospital.

3.7 Data Collection and management

A small team of four research assistants recruited from among clinical officer internists, was trained on how to seek consent from the parent(s) and how to conduct maternal interviews. They were also trained on how to handle the specimens particularly the stillborn and the placenta.

The chief investigator informed all the health workers particularly nurses and residents in labor and antenatal wards on the need to notify any of the research assistants when an intrauterine fetal death is diagnosed, or a stillbirth was delivered. In addition the health care workers were sensitized on the need to preserve the placenta of a stillbirth in formalin.My role as the chief investigator was to handle logistics as well as address unexpected issues that arose.

3.7.1 Data collection

Semi-structured interviewer-administered questionnaires were used to collect data from the mothers. The data collected included the demographics, medical, obstetric and social history; the questionnaires were also used to capturerelevant data in medical records.

Additional investigations were also requested if not already done as per the list below. The stillborn baby was examined and weighed after birth. The placentae were then taken for histologic examination.

3.7.1.1Maternal interview

Maternal interviews were conducted to help elucidate factors, behaviors and events that may have contributed to incident of stillbirth. Maternal interview captured: socioeconomic characteristic (i.e., marital status, living situation, income, level of education(maternal and paternal), use of alcohol, smoking); demographics (i.e., age, parity, birth order); reproductive history (including outcome of all previous pregnancies, previous history of stillbirths);complications of the index pregnancy (including specific conditions, medications, and infectious symptoms); and early indications of problems with the pregnancy such as abdominal pain, bleeding, drainage of liquor or hotness of body(Parker, et al., 2011;). Inquiry on history of domestic violence in the index pregnancy was also made. Enquiry on relevant family medical history including family history of stillbirth, birth defects, hypertension, and diabetes mellitus shall be asked.

3.7.1.2 Medical records abstraction

Review of medical records was done .by the research team. The medical records used included antenatal cards/recordsand inpatient files. Besides the physical findings on the mother, these records contained recorded treatments during the antenatal period, laboratory results and imaging studies. The delivery notes provided information on any complications that developed peripartum, the state of the baby, whether fresh stillbirth or macerated, and the gross findings on the cord and placenta.

3.7.1.3 Laboratory Investigations

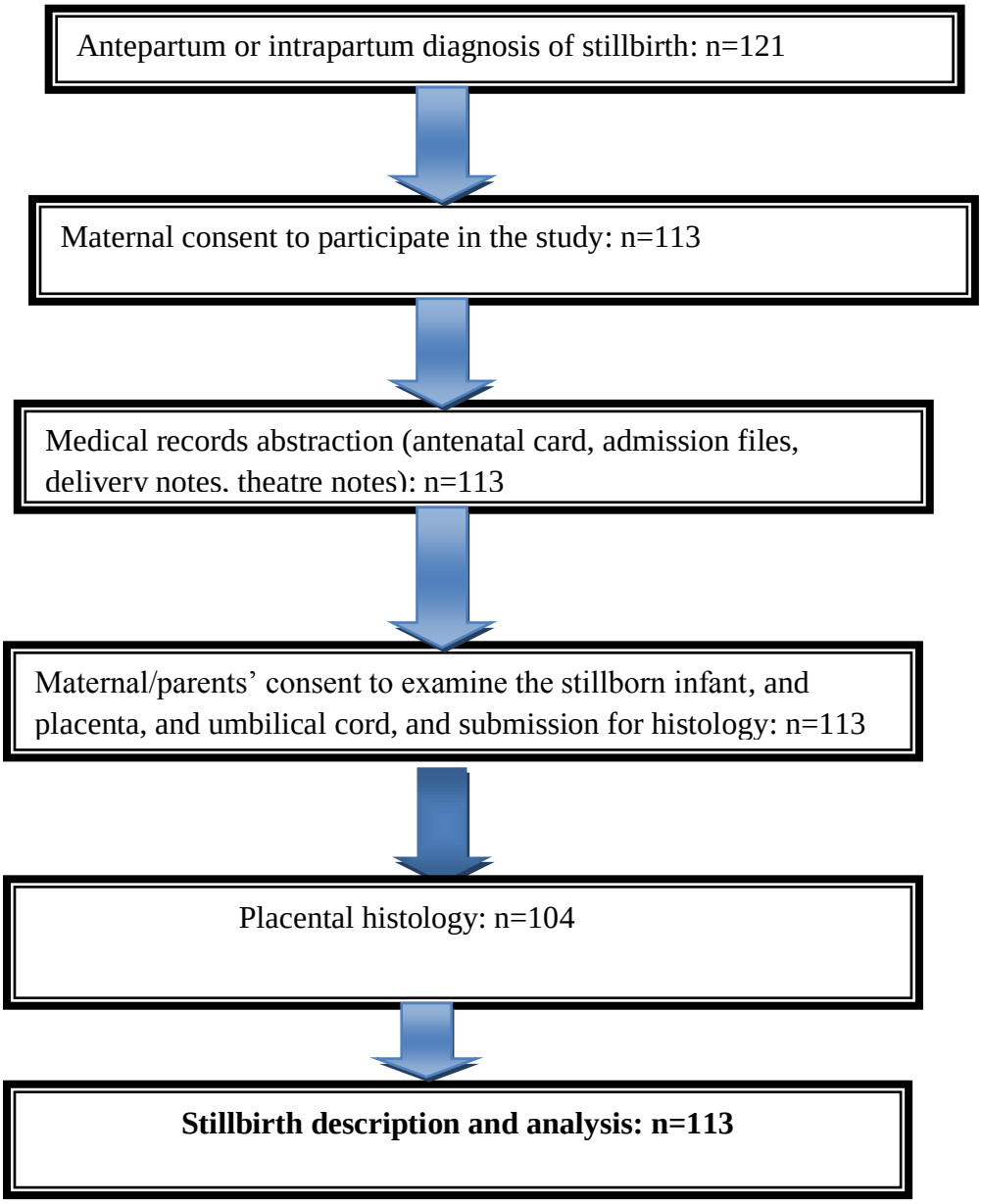
Routine laboratory investigations were requested if these had not already done. These were based mainly on hospital protocol on investigation of stillbirths. The laboratory investigations included the following:

- blood group
- Rhesus antigen
- Indirect Coombs Test in rhesus negative mothers
- Random blood sugar
- complete blood count and hematocrit
- urea and electrolytes, where indicated
- Venereal Disease Research Laboratory (VDRL)test for syphilis
- Human Immune Deficiency Virus (HIV) rapid test
- thyroid stimulating hormone (TSH)

3.7.1.4 Pathology Examination and biospecimen

Examination of the stillborn baby was done at delivery by the midwife or the clinician conducting the delivery. All findings noted were recorded as observed. These included findings of cord prolapse, length of the cord, nuchal cord, retroplacental clot, and any other significant findings. The placentaewere then preserved in formalin and transferred to the pathology laboratory for histologic examination. Only one surgical pathologist was involved in histological examination of all the placentas.Sampling of placental tissues included four full thickness placental tissues, two specimen from the cord (proximal and distal), and two pieces of the membranes.

Summary of the investigation protocol:



3.7.2 Data Management

Data collected during this study was managed confidentially. Each client's data was coded and only the chief researcher was able to link the different aspects of the data.The data was entered into a computer Microsoft Access database and later exported for analysis. Data cleaning was done by verifying incongruous data with available original patient records.Diagnoses were re-evaluated afresh based on clinical logic.

3.7.3 Data Analysis and presentation

Data analysis was done using software for statistical computation known as R (R Core Team, 2015). Categorical variables were summarized as frequencies and the corresponding percentage. Continuous variables were assessed for Gaussian assumptions using Shapiro Wilk test for normality. The continuous variables that assumed Gaussian assumptions were summarized as mean and the corresponding standard deviation (SD) while those that violated the assumptions were summarized as median and the corresponding inter quartile range. Results have been presented in form of tables.

Association between categorical outcome variables and categorical independent variables was done using Fisher's exact test. The outcome variables were defined as type of stillbirth, i.e. whether the stillbirth was fresh or macerated; the independent variables were defined as maternal and perinatal characteristics. Continuous variables were compared using independent samples t-test. The P value was set at 0.05.

Factors that were statistically significant in the bivariate analysis were included in a multivariate logistic regression model assessing the predictors that jointly explain the

type of stillbirth. Odds ratios (OR) and the corresponding 95% confidence interval (95% CI) were derived.

3.8 Ethical Issues

Approval for this study wasobtainedfrom the Institutional Research and Ethics Committee of Moi University and Moi Teaching and Referral Hospital (IREC).Informed written consent was obtained from the participants for interview and investigations. No inducement was used to encourage patients to participate in the study. Failure to participate in the study did not affect care for the patients. All study related materialswere locked up in a private secure cabinet and wereavailable only to the principal investigator.Interviews were conducted in privacy.Placental tissues were not used for any other purpose outside the aspects of the study. All placental and other tissues were disposed of through the hospital system on disposal of hazardous waste. Data was made available to the MTRH for policy issues.The findings of each investigation were posted in the patient's file. No conflict of interest has been declared for this study.

CHAPTER FOUR

RESULTS

The total number of deliveries conducted at MTRH during the study period was 5051. Out of these, 121 stillbirths were reported, translating to a stillbirth rate of 23.9% per 1000 births. Those who were recruited were 113. Out of these 104 placentae were examined.

4.1 Characteristics of stillbirths

Table 4.1: Characteristics of stillbirths and delivery events

Variable		**n (%) or Median (IQR) or Mean ±SD**
Mode of delivery	Spontaneous vertex	96 (85.0%)
	Caesarean	13 (11.5%)
	Breech	3 (2.7%)
	Vacuum assisted	1 (0.9%)
Gestation	Mean	34.9-=
	28-34	45 (39.8%)
	34-37	21 (18.6%)
	37-42	44 (38.9%)
	>42	3 (2.7%)
Baby's sex	Male	66 (58.4%)
	Female	47 (41.6%)
Type of stillbirth	Fresh stillbirth	36 (31.9%)
	Macerated stillbirth	77 (68.1%)
Weight of stillbirth	Babies' mean weight (grams)	2229 ± 877.2 grams
	Low birth weight (<2500g)	66 (58.4%)
	Normal weight 2500-4000g	46
	Macrosomic >4000g	1
Weight vs gestational age	Small for gestational age	47(41.6%)

The mode of delivery was spontaneous vertex delivery (SVD) for 85.0%.The mean gestation period was 34.9 weeks.

Fresh stillbirths comprised 31.9 % of the stillbirths. Of the total stillbirths, 58.4% were male while the rest were female. The baby's mean weight ±SD was 2229 ± 877.2

grams. Forty seven (41.6%) of the stillbirths were small for gestational age (SGA) based on WHO fetal weight chart.

Seven of the stillbirths had cord round the neck (**nuchal cord**) at least twice. Six of the seven were male. Five (4.4%) of the stillbirths were found to have umbilical cord round at least one extremity. Four were female. None of the stillbirths with cord entanglement had histological evidence of strangulation in the form of vascular thrombosis.

Seven mothers delivered stillbirths with major **congenital malformation**. These included two with spina bifida cycstica, two with hydrocephalus, one anencephaly, one gastroschisis, and one with phocomelia. This translated to a rate of 6.2% among the stillbirths.

4.2 Maternal and placental characteristics

4.2.1 Maternal demographic and obstetric characteristics

Table 4.2: Maternal demographic and obstetric features

Variable	Description	n (%)

Age (years)	<18	6 (5.3%)
	18-34	94 (83.2%)
	≥35	13 (11.5%)
Marital status	Married	80 (70.8%)
	Single	31 (27.4%)
	Divorced/widowed	2 (1.8%)
Education level	None	2 (1.8%)
	Primary	45 (39.8%)
	Secondary	41 (36.3%)
	College	25 (22.1%)
Place of residence	Urban	62 (54.9%)
	Rural	51 (45.1%)
Gravidity	Primigravida	51 (45.1%)
	2	41 (36.3%)
	3-4	16(14.1%)
	>4	5 (4.4%)
ANC attendance of at least 4 visits (N=113)	28-<34 wks (n=45)	10 (8.85 %)
	34-<37 wks (n=21)	5 (4.42%)
	37-<42wks (n=44)	14(12.39%)
	≥42 wks (n=3)	2 (1.8%)
	Rural (n=51)	14 (12.39%)
	Urban (n=62)	17 (15.04%)
ANC profile	HIV positive	7 (6.2%)
	Rhesus negative	2 (1.8%)
	VDRL positive	0
	Diabetes Mellitus	4(3.5%)
	Hypothyroid	1
	Hyperthyroid	0
	Hb	Mean 13 g/dl IQR (11.0,14.0)
Maternal obstetric conditions/complications	Anemia	20(17.6%)
	Hypertensive disorder	17(15.0%)
	Urinary tract infection	16(14.1%)
	Antepartum hemorrhage	8(7.1%)
	Ruptured uterus	3 (2.6%)
	Cord prolapse	2(1.8%)

The respondents comprised of 83.2% aged 18-34 years, 11.5% aged 35 years and over and 5.3% aged below 18 years. Almost half of the respondents (45.2%) were primigravidae.

More than two thirds (70.8%).were married. Forty five (39.8%), 41 (36.3%), and 25 (22.1%) had primary, secondary and college education respectively.

Close to three quarter (76.1%) of the participants were resident in Uasin Gishu County.Virtually all participants (99.1%) had at least one ANC visit. On average only about a quarter of the participants (27.4%) made at least four ANC visits.

None of the respondents had a history of having delivered a baby with congenital malformations. Six (5.3%) of the mothers had a history of miscarriage, while 6 (5.3%) gave a history of having had a preterm delivery.

One respondent was a **smoker,** while 13(11.5%), reported having been exposed to tobacco smoke at home or at work almost on a daily basis

Use of **insecticide-treated** mosquito nets was reported among 101(89.4%) of the mothers. Among these 9 (8.9%) contracted malaria, compared to 2 (16.7%) among those who did not use the nets.

Seven (6.2%) of the participants had **HIV**; all of them were on antiretroviral medication. Four mothers (3.5%) were found to have diabetes mellitus (**DM)**. One mother was found to be **hypothyroid**(i.e. TSH level>4.2 mU/L). No mother had positive **VDRL** test.

Two of the mothers had **rhesus** negative blood group. One of these stillbirths was term. The indirect coomb's tests were negative for these cases.

Twelve mothers (10.6%) experienced significant blunt trauma during the pregnancy leading to hospital consultation; two of them being domestic assault. Seven of these stillbirths were FSB. Six were term.

With regard to maternal **obstetric conditions/complications**, more than half of the respondents had various conditions either antenatally or during labor that would

adversely affect pregnancy outcome. Almost a fifth (17.6%) had anemia, i.e. hemoglobin of less that 11g/dl. Fifteen percent(n=17) had a hypertensive disorder complicating pregnancy, while 14.1% and 7.1% had urinary tract infection and antepartum hemorrhage complicating their pregnancy/delivery respectively. Ruptured uterus and cord prolapse complicated 3(2.6%) and 2(1.8%) pregnancies each resulting in fresh stillbirths.

4.2.2 Placental histology findings

Table 4.3: Placental Histology (N=104)

Histology	**n (%)**
No abnormalities reported	26 (25.0%)
Infection/inflammation (*Placentitis, chorioamnionitis, funisitis*)	23 (22.1%)
Calcifications	22 (21.1%)
Syncytial knots	11 (10.6%)
Perivillous fibrin deposition	9 (8.7%)
Abruptions	8 (7.7%)
Malformations	2 (1.9%)
Others (*edema, peudostratification, arterial thrombosis*)	3 (2.9%)
Total	**104**

*Nine placentae out of the 113 were excluded due to poor preservation

Out of the 113 placentae submitted for histology, 9 were rejected due to poor preservation. Among the 104 placentae examined, majority (75%) had pathologic findings. The findings were as follows: 26 (25.0%) had no apparent abnormalities, 23 (22.1%) had features of infection/inflammation, 22 (21.1%) had calcifications and 11 (10.6%) had syncytial knots. Perivillous fibrin was reported in 9.0%.

Table 4.4: Cross-tabulation between maternal conditions and placental histopathology findings

Maternal condition	**Placental Pathologic finding**					
	Normal	**Calcification**	**Inflammatio**	**Syncytial**	**Perivillous**	**Abruption**

			n/infection	**knots**	**fibrin**	
Hypertension	2	3	3	3	4	1
Urinary tract infection	3	4	5	3	1	-
Diabetes mellitus	2	1	-	-	1	-
Anaemia	4	3	3	3	4	-
Malaria	-	2	1	2	-	-
Smoking	2	2	2	1	4	3
Trauma	4	2	4	1	-	2

Due to the small numbers involved, and the fact that some cells would be empty, statistical association between the maternal and conditions and placental pathologic findings was not explored.

4.3 Maternal and placental correlates of type of stillbirth

Maternal and placental characteristics were evaluated for correlation with the type of stillbirth in the bivariate analysis based on a P value of 0.05. Those factors found to be associated with type of stillbirth were submitted to multivariate analysis.

Table 4.5: Placental histopathological findings in relation to type of still births

Placental pathology	**FSB**	**MSB**
Infection/inflammation (*Placentitis, chorioamnionitis, funisitis*)	7	16
Calcifications	10	12
Syncytial knots	1	10
Perivillous fibrin deposition	5	4
Abruptions	4	4
Malformations	0	2
Others (*edema, peudostratification, arterial thrombosis*)	0	3
Sub-total	*27 (25.9%)*	*51(49.1%)*
No abnormalities reported	9(8.6%)	17 (16.3%)
Total	**36**	**68**

*Nine placentae were not included due to poor preservation.

Association between placental pathologic findings and type of stillbirths was not explored because of the small numbers involved, including some empty cells. Therefore all abnormal placentae with lumped together as one composite (abnormal placentae), while normal placentae were handled as one composite; these were submitted for bivariate analysis in relation to the type ofstillbirth as depicted in table 4.6.

Statistical correlation between some of the maternal characteristics and type of stillbirths was determined. The findings are presented in table 4.6.

Table 4.6: Maternal, placental and stillbirth correlates of MSB/FSB outcome

	Type of stillbirth			Fisher's Exact test
	MSB (N=77)	**FSB N=36)**	**OR;(95% CI)**	**P-value**
Mother's age (Years)				
<18	1 (1.3%)	5 (13.9%)		
≥ 18	76 (98.7%)	31 (86.1%)	12.26(1.38,109.2	0.012
Marital status:				
Married	57(81.4%)	23(53.5%)		
Not married	13(18.6%)	20(46.5%)	0.62(0.27,1.45)	0.276
Personal education:				
<Secondary	28(36.4%)	19(52.8%)		
≥Secondary	49(63.6%)	17(47.2%)	0.51(0.23,1.14)	0.11
Experienced trauma during pregnancy	8 (10.4%)	5 (13.95)	1.39 (0.42, 4.59)	0.753
Small for gestational age	27 (35.1%)	20 (55.6%)	2.31 (1.03, 5.19)	0.044
The time at which babies movement ceased:				
Not sure	13 (16.9%)	3 (8.3%)	0.45 (0.12, 1.68)	0.263
On the admission day	5 (6.5%)	4 (11.1%)	1.8 (0.45, 7.15)	0.463
While admitted	10 (13.0%)	19 (52.8%)	7.49 (2.9, 19.03)	<0.001
>1 day before admission	49 (63.6%)	10 (27.8%)	0.22 (0.09,0.52)	<0.001
Baby's sex: Male	44 (57.1%)	22 (61.1%)	1.17 (0.53, 2.64)	0.838
Female	33 (42.9%)	14 (38.9%)		
Placenta Histology: Normal	17 (65.4%)	9(34.6%)	1 (0.39,2.54)	>0.999
Abnormal	51 (65.4%)	27(34.6%)		

There was evidence of association between the mother's age and pregnancy outcome of stillbirth. Mothers aged < 18 years were more likely to end with fresh stillbirths, p = 0.031.

There was no evidence linking marital status, personal education and partner's education level to type of stillbirth (P values=0.26, 0.11 and >0.999, respectively.

Babies who were small for gestational age were more likely to have been delivered as fresh stillbirths, 55.6% vs. 35.1%, p = 0.044.

Results show that the participants who reported having lost fetal movement more than a day prior to admission were more likely to end up with macerated stillbirth, p <0.001. Loss of fetal movement while admitted was significantly associated with fresh stillbirth, P<0.001.

There was no evidence of association between the sexof the baby and the typeof the stillbirth, p= 0.838.No association was found between abnormal placentaeand type of stillbirth, P>0.999.

Factors that were found to associated with type of stillbirth i.e. *P*<0.05 were submitted to multivariate analysis as depicted in table were derived from what was found to be significantly associated with type of stillbirth in univariate analysis in tables 4.4 and 4.6 above.

Table 4.7:Logistic regression model assessing the factors that jointly explain the type of stillbirth

Variable	Unadjusted OR (95% CI)	P Value	Adjusted OR (95% CI)	P value
Age (Years) (<18 vs. >=18)	12.26 (1.38, 109.23)	0.025	-	
Small for gestational age	2.32 (1.04, 5.19)	0.042	2.24 (0.91, 5.50)	0.079
Baby ceased moving while admitted	7.49 (2.94, 19.03)	<0.001	4.40 (1.35, 14.36)	0.014
Baby ceased moving > 1 day before admission	0.22 (0.09, 0.52)	0.001	0.48 (0.16, 1.48)	0.201

OR: Odds Ratio, CI: Confidence Interval

The results show that SGA babies had more than twice increased odds of being fresh stillbirths but statistically not significant, OR: 2.34 (95% CI: 0.91, 5.50); the babies who ceased to demonstrate activity while the mother was already admitted were more than four times likely to have been fresh stillbirths, OR: 4.40 (95% CI: 1.35, 14.36), and babies who ceased to move more than a day before admission had up to 52% reduced odds of being fresh stillbirths, but non-significant, OR: 0.48 (95% CI: 0.16, 1.48).

CHAPTER FIVE

DISCUSSION

5.2 Characteristics of the Stillbirths

Most of the stillbirths (85.0%) were **delivered by** spontaneous vertex delivery **(SVD)**, while 11.5% were delivered by caesarean section (CS). This is consistent with many studies. In Were's study of 1994, most stillbirths were delivered by SVD. In the study by Jamme in The Gambia in 2010, 8% of the stillbirths were delivered by caesarean section. However in the Gambian study the stillbirth rate was much higher at 156 per 1000 births, and the fresh stillbirth fraction comprised 57.8%; this would imply that the timing of caesarean delivery is important in prevention of stillbirths (Archana S. et al., 2009; Jamme A.et al.2010).The indications for the CS's were fetal distress, prolonged labor or amother having had a previous scar, with an IUFD but not in labor. According to the hospital records, the average CS rate is 19%. Majority of the indications for the cs are non-reassuring fetal status. Any delay in doing surgery may have been occasioned by poor judgement. Some unforeseen complications including cord prolapse and ruptured uterus may have ended up in theatre but with inevitable poor fetal outcome.

Regarding**sex**, 58.4 of the stillbirths were male, 41.6% female. This was consistent with a meta-analysis of 30 million births by Debapriya and colleagues in 2014 in which they found male stillbirths to be 10% higher than females (Debapriya et al., 2014). The reason for this difference was not apparent from thisstudy. Based on the hospital records the overall newborn sex ratio is approximately 1.15 to the males. This implies that there are more male fetuses in the third trimester of pregnancy. My statistical analysis indicated that being male was not necessarily associated with any type of stillbirth.

The mean **gestational age** was 34.9 weeks. This was similar to findings of a study by Were in 1994 in the same institution in which the average gestation of stillbirths was found to be 35.4 weeks. This implies the underlying mechanism of stillbirth causation are generally the same, and the key to stillbirth reduction may lie in identifying pregnancies at risk.

The mean **birth weight** was 2229±877.2 grams. Sixty-six (58.4%) of all the stillbirths evaluated were of low birth weight (less than 2500 grams). This proportion is significantly higher than the underweight rate available in hospital records of 8.8% among all births in the same period. However, this was higher than in the study by Were in 1994 in the same institution in which 43.9% of stillbirths were of low birth weight. This difference may, partly, be due to the fact that a higher proportion of the stillbirths in my study were macerated.Low birth weight has been associated with adverse pregnancy outcomes including stillbirths.

Fresh stillbirths comprised 31.9% (n=36), which was a decline compared to the study by Were (1994) in which proportion of fresh stillbirths was 72.2%. This finding also contrasts with findings by Onyiriuka (2009) in a study in a Nigerian hospital in which the proportion of fresh stillbirths was 48.1%.Of note is that these other studies had stillbirth rate higher than the findings in my study. This may be a sign of improvements in many aspects of patient care over time in our set up. The hospital CS rate of 19% is protective from avoidable intrapartum fetal death except for late referrals. A significant portion of the fresh stillbirths arose from unforeseen complications including ruptured uterus, cord prolapse and massive placental abruption.

Small-for-gestational age (SGA) stillbirths comprised 41.6% (n=47) of all stillbirths studied. No local study has looked at this aspect of stillbirths. In comparison to studies

in other countries, rates of SGA among stillbirths ranging from15.5% to 49% have been reported (Poon LC, et al., 2016; Gardosi J et al., 1998; Lee et al., 2013) .With regard to SGA stillbirths, there is paucity of local stillbirth data to compare with. One weakness of this study is that it did not categorize SGA stillbirths into symmetric and asymmetric; this would provide further insight into whether the cause of the SGA state was in early pregnancy or late pregnancy. The explanation for this high proportion of SGA stillbirths would be the observation that most of the placentae had pathological findings, leading to fetal demise especially during labor. In addition congenital malformation, which would predispose to poor intrauterine growth, washigher than in the general population.

Among all the stillbirths who had nuchal cords or cord around extremities, none had placental histologic features suggestive of strangulation, including vascular obstruction in the cord or thrombosis in the placental bed. Therefore, there was no evidence to attribute the stillbirths to cord accident in these situations (Peesay M, 2012; Ghosh S et al., 2008). Nuchal cord has been reported in as high as 37% of livebirths. Studies indicate that the incidence of nuchal cord increases with increasing gestation (Clapp JF, 2003). Out of the 7 stillbirths who had nuchal cord, 6 were male. Studies have made similar findings of more nuchal cords among males (Di Renzo GC et al., 2007; Wang L et al., 2016).

The proportion of stillbirths with major congenital malformation was 6.1%. This figure does not include internal malformations. This is similar to finding of 6.7% by Njuguna et al (2011) at Kenyatta National Hospital. Except for anencephaly, these malformations are not essentially considered lethal and, therefore, their contribution to fetal demise is difficult to assess. A congenital malformation rate of 6.1% is almost

thrice the rate among live birth according to a study in Eastern India (Sarkar S et al., 2013). This implies that congenital malformation may partly have contributed to the incidence of stillbirths.

5.2 Maternal Demographic and Obstetric Characteristics

The number of stillbirths was equivalent to a rate of 23.91 per 1000 births. This was less than findings by Were in this Hospital in 1994 when the stillbirth rate was found to be 30.5 per 1000 births. This may be due to improved maternity services over time.The finding also contrasts with that of a study in Kenyatta National Hospital (KNH) by Njuguna in 2011 in which the hospital stillbirth rate found to be 50.1 per 1000 births. This difference may be attributed to improved access to maternity services with provision of free maternity services during my study; free maternity program in Kenya was started in the year 2013.According to the Kenya demographic and Health Survey (2014) the proportion of mothers who had skilled birth attendance had increased from 43.8% in 2008 to 61.8% in 2014. Before implementation of the free maternity program by the national government in Kenya in 2013, MTRH attended to approximately 600 deliveries monthly. This had increased to an average of 1100 deliveries per month during the period of free maternity services within which this study was carried out.This is a sign of increased utilization of skilled birth attendance. Moreover, as noted from the data, attendance of antenatal clinics was high.

Three quarters of the respondents were resident in Uasin Gishu County. This may be as expected given that the hospital serves as a primary care centre for a lot of patient; moreover the county does not have other hospitals with consultant or even theater services. Slightly over half (54.9%) of the respondents lived in urban set up. The possible explanation may be the fact that MTRH is located in Eldoret Town, a town

that hosts 32.4% of the county population (Kenya Interagency Rapid Assessment (KIRA) report of 2015).In addition MTRH is the only public level 4 hospital in Uasin Gishu County.

Mothers under 18 years of age comprised 5.3% of the respondent, lower than that reported in Were's of 2004 of 24.5%. This difference may partly be explained by a general decline in teenage pregnancy rate in Rift Valley from 30.5% to 21.2% in 2003 and 2014 respectively (KDHS 2003; KDHS 2014).The reduction in teenage pregnancy may partly be attributed to increased school retention given that primary and day secondary education is free of charge.

Maternal age: the proportion of those aged 35 years or more among respondents, who delivered stillbirths, is similar to findings in KDHS 2014 among mothers who had live births i.e. 11.5% versus 13.4% respectively. My study design may not attribute or rule out association between advanced maternal age and stillbirth. The similarity with KDHS may imply that advanced maternal age above 35 years is not associated with increased stillbirth rate, which is against findings in studies in other localities (Waldestrom et al., 2015; Huang et al., 2008). This study may not be able to explain this but majority of these mothers did not have any predisposing medical or surgical conditions. It therefore seems that age by itselfmay not increase the risk of stillbirth.

Primiparas comprised 44.2% of the respondents. This is more or less similar to the findings in Were's study of 1994 conducted in the same institution in which 37.7% of the respondents were primiparas. The findings are also comparable to findings in a study by Jamme (2010) in which 46% of the mothers who delivered stillbirths were primigravidae.

Marital status: among the respondents 70.8% (n==80) were married, while 27.4% were single. This proportion of single mothers is similar to their proportion amongthose who delivered live births as reported in KDHS 2014 at 28.9%. Studies have had inconsistent findings on the contribution of single status to risk of stillbirth and other adverse pregnancy outcomes. A study by Cheptum (2009) concluded that single status was not significantly associated with poor pregnancy outcome including stillbirths.

Antenatal care (ANC) attendance: having at least one ANC visit was 99.1%. This was comparable to other studies that looked at stillbirths and live births including KDHS 2014 at96%(KDHS 2014; Jammeh A., 2010). This high attendance of antenatal clinic may imply adequate access to antenatal care services.

The proportion of respondent who made at least four antenatal visits during their pregnancy was 27.4% (n=31). When analysis of advanced gestations was done, it was found that among the category of at least 34-37 weeks' gestation, 29% made four ANC visits; while among those who were, only ≥37 weeks, 31% (n=18) had made at least four ANC visits during the index pregnancy. This was lower than the findings reported in KDHS 2014 whereby mothers who had a live birth who had made at least 4 ANC visit comprised 58%. This may imply association of stillbirth with inadequate ANC visits, (Jammeh, et al., 2010). There was no difference between rural and urban respondents in making four antenatal visits at, 27.4% respectively. This contrasts with KDHS 2014 which showed significant difference between rural and urban respondents with live births at 68% and 51% respectively. This may imply that access to health facilities may not be the only reason for the respondents suffering stillbirths among the respondents in my study. Antenatal follow-up is important to help detect adverse indicators in pregnancy, and also provide opportunity for education of the mother on

danger signs to look out for in pregnancy.Some mothers may attend ANC to get ITN's and also acquire an antenatal card which is demanded for during admission for delivery.

Use of insecticide-treated mosquito nets (ITN) was reported among 89.4% of the mothers. In KDHS 2014, use of ITN in general population was recorded among 72% of the household. The Ministry of Health in Kenya issues ITN's to all pregnant women attending ANC. This explains the increase in coverage. Among those who used nets, 9 (8.9%) reported having suffered from malaria during the pregnancy; among those who did not use the ITN, 2 (16.7%) reported having suffered from malaria during the pregnancy. The catchment area of MTRH is a low malaria zone; moreover this study could not account for malaria infection attributable to travel to malaria-endemic areas.

The participants who had HIV comprised 6.2%. All the mothers were on antiretroviral therapy and were generally healthy. This is less than prevalence of 10 % among mothers with stillbirths at KNH (Njuguna, 2011) and 6.9% among pregnant women (Ndege et al., 2016). Studies have shown a trend of declining HIV prevalence among pregnant women (Eaton, J.W., et al., 2014).All the stillbirths among these mothers were not SGA. Four were macerated while 3 were FSB. No association between HIV infection and stillbirths is apparent. Studies on this subject have given conflicting results, (Shapiro R et al., 2016; Habib NA, et al., 2008; Chi BH et al., 2007). None of the mothers had positive VDRL test. This may be due to low prevalence of syphilis in the general population in Kenya, ranging between 1.8% and 3% (Lawi JD et al., 2015; Otieno-Nyunya et al., 2011; Nyamwamu LD et al., 2009). Moreover, with the high access to ANC services, any positive cases may have been detected early because ANC profile is usually done in the first visit.

Only one respondent had abnormal TSH level (above 4.2mU/L). She could be described as hypothyroid. However the lab does not pregnancy-specific cut-offs. Finding is lower than that in a hospital-based study among antenatal mothers in first trimester in India at 7.5%-however the TSH range used in this study was 0.3-3.0mU/L (Singh A. et al., 2015). Hypothetically, if I had lowered the reference range the prevalence among the respondents would have been 5%). Moreover hypothyroidism is associated with high pregnancy wastage particularly in the first trimester. This, in addition to the high TSH cut-off may partly explain the low rate of thyroid disorders among the respondents.

Anemia, referring to blood hemoglobin concentration of less than 11g/dl, was detected in 17.6% (n=20) of the respondents. Nineteen of these mothers had mild or moderate anemia. This was higher than in a similar study by Njuguna in 2010 in which the proportion of mothers who had delivered stillbirths with anemia was 11.1%. The reason behind the difference is not clear. Significantly, in a study at Mbagathi District Hospital, Nairobi, Kenya, the proportion of mothers with anemia among antenatal mothers was 36.2% (Nduhiu-Githinji, 2012). According to WHO data for 2011, anemia is common among pregnant women in Kenya at 36%. Studies have not associated mild and, moderate anemia with increased risk of stillbirths (Abdelaziem, Duria, Tajeldin, Mustafa &Ishag, 2011). While it has been reported in studies that hemoglobin kevels above 14g/dl are associated with increased risk of stillbirths, above findings would seem to indicate that anemia may not be associated with stillbirths.

Hypertensive disorders were present in 15% of the mothers who delivered stillbirths. The hospital records indicated that among all mothers who delivered during the same period 4.08% had hypertensive disorders. This would imply that, locally, hypertension

is associated with increased risk of stillbirths. In a similar study by Njuguna in Kenyatta national Hospital, 26.7% of the mothers who had stillbirths had hypertension. This difference is unexplained. However the proportion in my study is similar to findings in a study by Gibbins and associates (Gibbins et al., 2016), in which15% of the mothers who delivered stillbirths had hypertensive disorders.A study in Pakistan attributed 24% of stillbirths to hypertensive disorders (Korejo,Butta, Noorani & Butta, 2007).

Urinary tract infection was diagnosed among 14.1% of the mother who suffered stillbirths. This was similar to findings in the study in Kenyatta National Hospital in 2011 in which 11.1% of affected mothers had urinary tract infection (Njuguna, 2011).It is important to note that the urine tests mainly involved use of dip stick and wet preparation urine tests. The WHO recommends use of grams stain of mid stream urine culture. Hence the estimates may not be true figures. The causal relationship between urinary tract infection and stillbirths is unclear.

Antepartum hemorrhage (APH) was a complication that affected 8 (7.1%) of the deliveries that had stillbirths outcome; only one case had placenta previa. This was lower than that in the study in Kenyatta National Hospital in Kenya (Njuguna, 2011) in which 34.1% of the cases had APH. This may be partly explained by the higher proportion of hypertension in the latter study; otherwise most of the difference remains unexplained.

5.3Placental histopathology findings

Kenya and Africa do not have many studies on the subject of stillbirths that have included placental histology findings as part of their protocol. In addition, many studies globally that include histology tend to have various findings, probably due to the study designs (Hargitai et al., 2016). Moreover, the placental histology findings in my study

may be limited by the fact that the examination was done by a surgical pathologist rather than a perinatal pathologist.

Approximately 22.1% of the placentae examined had features of infection/inflammation. This proportion is similar to the findings in the study by Njuguna in Kenyatta National Hospital in 2010 in which these findings accounted for 21.1%. In a study by Pinar et al, in 2014, inflammation/infection accounted for 30.4% of the findings among the placentae. It should be noted that in the study by Pinar and others, the stillbirths were included from 24 weeks' gestation; infections tend to be more among earlier stillbirths (Pinar et al., 2014; McClure et al., 2010*)*). Placental inflammation may have infectious or non-infectious etiology. Infection may cause fetal death through damage to vital fetal organs or by impairing placental function. Placental inflammation has also been found to adversely affect placental function (Reddy et al., 2009).No blood or urine cultures were done. It was therefore difficult to relate placental inflammatory features to maternal or fetal infection. Cross-tabulation between maternal medical conditions and placental findings did not seem to suggest a relationship between UTI and placental inflammation.

Placental calcification was documented in 21.1% of the placentae in this study. This is lower than that documented in the study by Njuguna in which 78% of placentae were found to have calcification. Most studies do not document calcification findings (Pinar et al., 2014). The most sensitive method for assessing calcification is by radiological analysis (Tindall et al., 1965).

Syncytial knots are aggregates of syncytial nuclei at the surface of terminal villi. Syncytial knots have been noted to increase with increasing gestation. However syncytial knots are increased in conditions associated with malperfusion (pre-

eclampsia, pregnancy-induced hypertension) (Loukeris K, et al., 2010; Fogarty NM, et al., 2013). A review by Jerzy (2013) associated syncytial knots with hypertensive diseases of pregnancy and poor placental perfusion. According to these researchers, syncytial knots involving more than 30% of the placenta are a sign of placental hypermaturity and are associated with poor outcome. In my study, syncytial knots were demonstrated in 9(8.6%) of the placentae examined. However the histopathology reposts did not quantify the extent of placental involvement. Studies have reported rates of syncytial knots among live births of 10% at 26 weeks to 28% at term (Loukeris K et al., 2010). The difference may be attributed to inter-observer differences occasioned by the fact that my placental examinations were carried out by surgical pathologists.

Perivillous fibrin deposition is a pregnancy complication of unknown etiology characterized by extensive deposition of fibrin either within the intervillous space or primarily within and around the basal plate. Significant areas of chorionic villi become entrapped by fibrin, with obliteration of intervillous space, with resultant secondary villous atrophy (Sebirea NJ et al., 2002). This finding has been described in studies as pathological placental findings associated with adverse fetal outcome including intrauterine growth restriction, intrauterine fetal death, and poor neonatal outcome. Perivillous fibrin deposit has been described as part of the spectrum that includes maternal floor infarcts (Feist H et al., 2015). Perivillous fibrin was found in 8.7% of the placentae examined. This was almost similar to findings by Pinar and others (2014), in which they found perivillous fibrin deposit among 9.2% of the stillbirths. In my study 9 placentae had perivillous fibrin deposit. A third had been exposed to tobacco smoke, while 3 (33.3%) had hypertension in pregnancy. There was no preponderant maternal condition that was would be associated with this placental finding. Due to the low numbers, statistical association was not calculated.

Abruption was documented histologically in 7.7% of the specimen examined. This differs from the study by Njuguna in which this finding was found in 13.3% of an almost similar sample. In the study by Pinar in 2014 retroplacental hematoma were documented in 23.8% of the stillbirths. Syncytial knots and intervillous fibrin deposition indicate impaired placental perfusion and therefore, reduced placental reserve; similarly abruption impairs placental function. All these may be related tohypertensive disorders.

5.4 Maternal and placental correlates of type of stillbirth

Univariate analysis revealed that being under 18 years of age is associated with delivery of FSB (P=0.012). This is consistent with some studies that have established that teenagers are at increased risk of stillbirth, particularly intrapartum stillbirths (Wilson RE et al., 2008).

Similarly, the analysis indicated that SGA fetuses are more likely to die during labor and be delivered as FSB (P=0.044). No published data was found exploring association SGA state and fresh stillbirth. However guidelines advocate proper triaging, and continuous fetal heart rate monitoring during labor involving SGA fetuses due to the risk of perinatal mortality and morbidity (NICE guidelines, Dec 2014). This may result from the diminished placental reserve that is compromised further by uterine contraction as evidenced by the high proportion of placentas with pathologic findings.

Mothers'reports on fetal movement seems to be a reliable indicator of fetal wellbeing. Mothers who reported having lost fetal movement while already admitted in the ward were significantly more likely to deliver FSB (P=0.001). Conversely, mothers who reported no fetal movement before admission to hospital were more likely to deliver

MSB (P=0.001). It is also important to note that mothers who delayed coming to hospital after perception of reduced fetal movement delivered MSB. This reliability of maternal perception of fetal movement in predicting risk of adverse perinatal outcome is consistent with findings in other studies (Stacey T et al., 2011; Koshida S et al., 2017). However, with poor antenatal follow-up the mothers may not have been educated on the significance of reduced fetal movements.

Neither male nor female fetuses are more likely to be FSB or MSB (p=0.838). The sex of the stillbirths seems to be proportionately represented in both types of stillbirths. This finding is similar to other studies (Debapriya et al., 2015).

There was no association between abnormal placentae and the type of stillbirth (P=.0.99). This is in contrast to a retrospective study by Stanek et al in 2014 that found that fresh stillbirths were associated with ascending infection and placental abruption (Stanek J et al., 2014). The difference may, partly, be attributed to the fact that my study may not have had adequate numbers to bring out the differences.

No studies were found that looked at relationship between mother's level of education, partner's level of education, marital status and type of stillbirth. Majority of the mothers had at least secondary education. This mostly likely equipped them with almost equal capacity to understand basic requirements such as need for antenatal care.

CHAPTER SIX

CONCLUSION AND RECOMMENDATION

6.1 Conclusions

1. A significant proportion of the stillbirths were small-for-gestational age.
2. The main maternal conditions among mothers who suffered stillbirths were hypertension and urinary tract infections.
3. Most of the placentae had abnormal pathology findings.
4. There was association between small-for-gestational age finding and fresh stillbirths.
5. There was no association between abnormal placentae and type of stillbirth.

6.2 Recommendations

1. Obstetric stakeholders should explore cost-effective approaches to enhance diagnosis of SGA fetuses in early third trimester to reduce fresh stillbirth rates.
2. A case-control study should be carried out to help establish the clinical significance of placental pathological findings among stillbirths in our setup.The weakness with my study was that it addressed itself to different aspects of the same outcome; it does not bring out why some mothers had stillbirths while others did not. The distinction between FSB and MSB may be due to timing of delivery and not to do with underlying causes.

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APPENDICES

Appendix 1: Questionnaire (English)
CAUSES OF STILLBIRTHS AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET-KENYA

SERIAL NO…….. PT IP NO:……
DATE……..

Mother's Name: …… Phone no ……

Interviewer's name: ……..

SECTION A: Mother's Socio-Demographic Characteristics

1. Age group: [ ] below 18 years [ ] 18 – 34 years [ ] 35 years and above

2. Marital status: [ ] married [ ] single [ ] divorced [ ] widowed

[ ] cohabitation

3. Your highest level of education: [ ] no education [ ] primary school [ ] secondary school [ ] college

4. Your partner's highest level of education. [ ]No education [ ] primary school [ ] secondary school [ ] college [ ] N/A

5. County of residence……..

6. Places of residence: [ ] within an urban community [ ] within a rural community

7. Source of water: [ ] borehole [ ] well [ ] stream [ ] pipe-borne

8. Are you gainfully employed? [ ] yes [ ] no

9. In your estimation, how much do you earn in a month? [ ] KShs.6, 000 or less [ ] more

than KShs.6000

10. Is your partner gainfully employed? [ ] yes [ ] no [ ] N/A

11. How many children do you already have? [ ] None [ ] 1-2 [ ] 3-4 [ ]> 4

12. What type of fuel do you use for cooking? [ ] firewood [ ] charcoal [ ] gas

[ ] Other, specify……..

13. Is your partner polygamous? [ ] yes [ ] no [ ] not sure [ ] N/A

SECTION B: Mother's Reproductive-Obstetrical information (on the current delivery)

14. Date of delivery…….

15. First visit for antenatal care: [ ] first trimester [ ] second trimester [ ] third trimester

16. How many times did you visit the hospital for antenatal care? [ ] one [ ] two [ ] three [ ] four [ ] more than four

17. Mother's weight at first trimester……..

18. Mother's weight at last trimester……

19. Current weight after delivery…….

20. Height of the mother ……..

21. BMI: in kg/M^2

22. Diastolic BP: 1^{st} trimester …… 2nd Trimester……. #rd trimester ……

23. Hb: first trimester…… Second trimester …… third trimester ……

24. Mode of delivery: [ ] caesarean [ ] spontaneous vertex delivery [ ] breech delivery [ ] vacuum assisted delivery

25. Gestation at delivery (in weeks)

26. Weight of baby at birth (grams) …… Length of baby (cm)…… Head circumference (cm)….

27. Outcome of pregnancy: [ ] fresh stillbirth [ ] macerated stillbirth

28. Sex of baby: [ ] male [ ] female

29. When did you stop feeling the baby's movement? [ ] more than 1 day before admission [ ] on the day of admission [ ] while admitted in the hospital [ ] Not sure

30. How long was the labor, in hours? ..... [ ].N/A

31. During the course of your pregnancy, did you experience any kind of obstetric anomalies?

[ ] yes [ ] no

32. If yes, what obstetric problem was it? [ ] bleeding [ ] drainage of fluid [ ] urinary tract infection [ ] Lower abdominal pains [ ] malaria [ ] other infection

33. During the course of your pregnancy, did you experience any form of trauma? [ ] yes

[ ] no

34. If yes, what was it? [ ] accidental physical injury/fall.[ ] physical assault

[ ] psychological stress. [ ] other, specify…….

35. What was your general state of health during the course of pregnancy? [ ] sickly

[ ] healthy

36. If sick, specify what sickness…….

37. Did you use treated mosquito net during the pregnancy? [ ] yes [ ] no

SECTION C: Past obstetric history

38. When was your previous delivery? [ ] less than 2 years ago [ ] 2-3years ago [ ] more than 3 years ago

39. Do you have previous history of stillbirth? [ ] no [ ] once [ ] more than once

40. Do you have previous history of miscarriage? [ ] no [ ] once [ ] more than once

41. Do you have history of a baby dying within two weeks of birth? [ ] No [ ] Once [ ] More than once.

42. Do you have history of a baby born with malformation? [ ] No [ ] Once [ ] More than once

43. Do you have history of baby born before due date? [ ] No [ ] Once [ ] more than once

SECTION D: MOTHER'S PAST MEDICAL HISTORY

44. Do you history of any of the following conditions:

a) Diabetes mellitus [ ] Yes [ ] No
b) Hypertension [ ] Yes [ ]No
c) Clot in the leg [ ] Yes [ ] No
d) Hypothyroidism [ ] Yes [ ]No
e) Hyperthyroidism [ ] Yes [ ] No
f) Renal failure [ ] yes [ ]No
g) Systemic lupus erythematosus [ ] Yes [ ] No
h) Hepatitis [ ] Yes [ ] No
i) Other, specify……..

SECTION E: Maternal behaviours

45. Did you take any medication during pregnancy? [ ] yes [ ] no

46. If yes, what was the name(s) of the medication?

1st trimester medication…….

2nd trimester medication……..

3rd trimester medication …….

47. What is the nature of your occupation? [ ] light manual work [ ] Heavy manual [ ] Field work [ ] management [ ] N/A [ ] other, specify.....

48. How long do you work a day? [ ] less than 8 hrs [ ] more than 8 hrs [ ] N/A

49. How many meals do you eat in a day? [ ] one [ ] two [ ] three or more meals

50. In your opinion, do you think you eat balanced diets? [ ] yes [ ] no

51. Do you smoke cigarettes or use other tobacco products? [ ] yes [ ] no

52. Does anyone in your household/workplace smoke? [ ] yes [ ] no

53. Do you drink alcoholic beverages? [ ] yes [ ] no

54. If yes, how often? [ ] daily [ ] once a week [ ] Less frequently

SECTION F: Family History

55. Do you a family history of;

a) Recurrent abortions [ ] Yes [ ] No
b) Stillbirths [ ] Yes [ ] No
c) Babies dying within two weeks of birth [ ] Yes [ ] no
d) Babies born with malformations [ ] Yes [ ] No
e) Venous thrombosis [ ] Yes [ ] No
f) Developmental delay [ ] yes [ ]No

SECTION G: Perinatal findings (*FOR THE MID WIFE*)

56. Did the mid wife find:

a) Congenital anomalies in the baby [ ] NO [ ] Yes……

b) Small for gestational age baby [ ] No [ ] Yes

c) Post mature baby [ ] No [ ] Yes

d) Cord round the neck [ ] No [ ] Yes x2 x3 >x3

e) Cord round an extremity [ ] No [ ] Yes

f) True knot [ ] No [ ] Yes

g) Cord prolapse [ ] No [ ] Yes

h) Abnormal cord [ ] No [ ] Yes ....describe……..

i) Bleeding before baby was delivered [ ] No [ ] Yes

j) Retroplacental clot [ ] No [ ] Yes …amount……..

k) Calcified placenta [ ] No [ ] Yes

l) Placental tumors [ ] No [ ] Yes

m)Weight of placenta in grams …….. Proportion to baby weight …….

Other finding…….

Thank you for your cooperation.

Checklist for investigations:

Urinalysis [ ] Not done [ ] done- prot … Gluc…. Leucocytes ……. Blood……

CBC [ ] not done [ ] done –Hb (g/dl) ……. Plt ($x10^9$/L) …. WBC ($x10^3$)……

TSH [ ] not done [ ] done –N, [ ] hypothyroid, [ ] hyperthyroid

LFT: [ ] Not done [ ] Done – normal, abnormal …AST……Alb……..

Creatinine: [ ] not done [ ] done – normal, abnormal ……umol/L……

RBS: [ ] not done [ ] done- Normal, Abnormal … Mmol/L……

Bs for mps: [ ] Not done [ ] done, result

Conclusion on type of stillbirth: [ ] Antepartum stillbirth [ ] Intrapartum stillbirth

Histology results

[ ] chorioamnionitis [ ] placentitis [ ] malaria [ ] infarction [ ] Placental thrombosis

[ ] placental malformation [ ] abruption [ ] placental insufficiency [ ] cord accident

:

Other……
……

Comments……
……

Probable direct cause of fetal death:

[ ] Abruption [ ] cord accident [ ] placental insufficiency [ ] infection [ ] Perinatal asphyxia [ ] Prematurity [] Congenital malformations [ ] Unknown

Other…….

Underlying cause of fetal death:

[ ] Hypertensive disease [ ] Malaria [ ] Infection [ ] Cord accident [ ] placental insufficiency [ ] Congenital malformations [ ] Placental insufficiency [ ] unknown

Other, ……

APPENDIX 1B: Questionnaire (Kiswahili)
DODOSO (KISWAHILI)
NAMBARI…….. **TAREHE…**

SEHEMU YA A: Tabia ya kijamii na idadi ya watu ya Mama

1. Rika: [ ] chini ya miaka 18 [ ] katiya miaka 18 – 34 [ ] miaka 35 na zaidi

2. Hali ya ndoa [ ] Nimeoleka [ ] sijaoleka [ ] Talaka [ ] mjane [ ] naishi na mchumba

3. Kiwango cha juu cha elimu: [ ] sijasoma [ ] shule ya msingi [ ] shule ya upili

[ ] chuo [ ] nyingine (taja)……..

4. Kiwango cha juu cha elimu ya mchumba wako [ ] sijasoma [ ] shule ya msingi [ ] shule ya upili [ ] chuo [ ] nyingine (taja)……..

5. Unapoishi: [ ] mjini [ ] kijijini

6. Aina ya makao: [ ] nyumba ya boma [ ] nyumba kamilifu [ ] nyumba iliyowachana kiasi na zingine [ ] nyingine (taja)……..

7. Chanzo cha maji: [ ] kisima [ ] chemi chemi [ ] mkondo [ ] mfereje

8 Unacchukua dakika ngapi kufika kwenye chanzo cha maji kutoka kwa nyumba yako...

9. Umeajiriwa? [ ] ndio [ ] la

10 Kwa makadirio yako, nikiasi kipicha mapato unapata kwa mwezi? [ ] Chini Elfu sita [ ] zaidi ya shilingi elfu sita

11. Unafanya kazi aina gani? .....

12. Je, mchumba wako ameajiriwa? [ ] ndio [ ] la

13. Una watoto wangapi? .....

14. Mnaishi wangapi katika familia? .....

15. Je, chanzo cha nishati unatumia kupika niupi? [ ] kuni [ ] makaa [ ] gesi

[ ] nyingine, taja……..

16 Je, mchumba wako ana mke zaidi ya mmoja? [ ] ndio [ ] la [ ] sina uhakika

SEHEMU B: habari ya mama kuhusu uzazi na ujaa uzito (kulingana na kujifungua hivi majuzi)

17. Tarehe ya kujifungua…….

18. Ziara ya kwanza kwa huduma za kliniki: [ ] miezi mitatu ya kwanza [ ] miezi mitatu ya pili [ ] miezi mitatu ya tatu

19. Ziara ya mwisho katika kliniki kabla ya kujifungua: [ ] miezi mitatu ya kwanza [ ] miezi mitatu ya pili [ ] miezi mitatu ya tatu

20. Ulitembelea hospitali kwa huduma za ujaa uzito? [ ] moja [ ] mbili [ ] tatu [ ] nne [ ] zaidi ya mara nne

21. Umri wa ujaa uzito kabla ya kujifungua?
.....

22. Uzito wamama miezi mitatu ya kwanza ya ujaa uzito……..

23. Uzito wa mama miezi mitatu ya mwisho ya ujaa uzito ……

24. Uzito kwa sasa baada ya kujifungua…….

25. Urefu wa mama ……..

26. BMI: [ ]<20 kg/m^2 [ ] 20-24.9 [ ]25-29.9 [ ]30-34.9 [ ]31-34.9 [ ] > or =35

27. Kiwango cha damu (Hb) miezi mitatu ya kwanza …… miezi mitatu ya pili …… miezi mitatu ya tatu……

28. Mbinu ya kujifungua: [ ] kupasuliwa [ ] kupitia kwa uke [ ] mtoto kutoka na miguu [ ] mtoto kuvutwa na chombo

29. Uzani wa mtoto wakati wa kuzaliwa (kwa gramu)…….

30. Matokeo ya kujifungua: [ ] uzazimfu safi [ ] uzazimfu aliyeharibika

31. jinsia ya mtoto: [ ] kiume [ ] kike

32. Ni lini siku ya mwisho ulihisi mtoto akisonga? [ ] zaidi ya siku moja kabla ya kulazwa hospitalini [ ] siku ya kulazwa hospitalini [ ] nikiwa nimelazwa hospitalini [ ] sina uhakika

33. Urefu wa machungu ya kujifungua? .....

34. Je ulikuwa na hisia yoyote ya ujaa uzito usio wa kawaida wakati wa ujaa uzito?

[ ] Ndio [ ] la

35 Kama ndiyo, ni tatizo lipi la uzazi ulihisi? [ ] Kutokwa na damu [ ] mifereji ya maji

[]ya maambukizi ya njia mkojo [ ] maambukizi ya maji [ ] malaria [ ] maambukizi mengine

36. Wakati wa ujauzito wako, je, ulipata jeraha la aina lolote? [ ] ndio [ ] la

37. Kama ndio, aina gani? [ ] ajali ya kugongwa na kitu / kuanguka [ ] kupigwa [ ] maumivu ya mawazo [ ] nyingine, taja……

38. Hali ya afya wakati wa ujaa uzito? [ ] mgonjwa [ ] mwenye afya

39. Ikiwa ulikuwa mgonjwa, taja ugonjwa …….

40. Ulitumia tiba aina gani? .....

41. Je, ulitumia neti ya kuzuia mbu? [ ] ndio [ ] la

SEHEMU YA C: Historia ya Uzazi

42. Ulijifungua awali lini? [ ] chini ya miaka miwili iliyopita

[ ] miaka 2-3 iliyopita [ ] zaidi ya miaka mitatu iliyopita

43. Je, una historia ya uzazimfu? [ ] la [ ] mara moja [ ] zaidi ya mara moja

44. Je, una historia ya mtoto kutoka? [ ] la [ ] mara moja [ ] zaidi ya mara moja

SEHEMU C: mama wa zamani historia ya matibabu

45 Je, una historia ya hali hizi?:

a. ugonjwa wa kisukari

b) Shinikizo la damu

c) Hipothairoidi

d) Haipatharoidi

e) Kufeli kwa figo

f) Utaratibu lupus erythematosus

g) Ugonjwa la ini

h) Nyingine, taja .....

SEHEMU D: Tabia ya uzazi

46. Je, ulitumia madawa yoyote wakati wa ujaa uzito? [ ] ndio [ ] la

47. Kama ndio, taja majina ya madawa

Miezi mitatu ya kwanza…….

Miezi mitatu ya pili……..

Miezi mitatu ya tatu …….

48. Kwa siku, unafanya kazi kwa muda gani? [ ] Chini ya masaa 8 [ ] zaidi ya masaa 8

49. Ulikuwa unafanya kazi ya aina gani wakati mtoto aliaga? [ ] kazi ya nyumba [ ] kazi ya kutumia nguvu [ ] kazi ya ofisi [ ] kazi uwanjani

50. Unapata mlo mara ngapi kwa siku? [ ] moja [ ] mbili [ ] tatu au zaidi

51. Kwa fikira zako, je unafikiri unapata lishe bora? [ ] ndio [ ] la

52. Je, unavuta sigara? [ ] ndio [ ] la

53. Je, unatumia bidhaa zifuatazo za tumbaku? [ ] ugoro [ ] kutafuna tumbaku

[ ] biri [ ] hakuna

54. Je, kuna yeyote kwako au unakofanya kazi anayevuta sigara? [ ] ndio [ ] la

55. Je, unatumia vinywaji vya kulevya? [ ] ndio [ ] la

56. Kama ndio, mara ngapi? [ ] kila siku [ ] mara moja kwa wiki

[ ] nyingine, taja …….

Ahsante kwa ushirikiano wako

APPENDIX 2A: CONSENT FOR MATERNAL INTERVIEW

My name is James Munene Waweru. I am a qualified doctor, registered by the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a Masters degree in Reproductive Health at Moi University. I would like to recruit you into my research which is to study the likely causes of still birth.

ABOUT STILLBIRTH

Stillbirths are caused by maternal, obstetric and fetal related factors. These factors interact and can result in stillbirth. For us to know the likely causes, we will request to interview you on your socio-demographic and obstetric history. I will take upto 15 minutes to complete the interview.

Benefits

This is a research project and the findings will be beneficial to doctors involved in management of mothers who experience stillbirths.

Risks

This is a minimal risk study and the psychological risks that may arise among relatives will be addressed through counseling.

We will keep all your information in confidence. Treatment and any assistance does not depend on your participation in this study. We will offer appropriate treatment for any condition that we find from assessing you.

This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

May we proceed? Verbal consent: Yes……No……..

Proxy consent: Signature …….

Date **…**……..

Thank you

Contacts for the research team,

Dr. James Waweru Munene

MOI UNIVERSITY, ELDORET P.O BOX 4606 -0100 Eldoret, Kenya

Phone; 0721945203**, E- Mail address**; wawerumunene@yahoo.com

APPENDIX 2B: CONSENT FOR MATERNAL INTERVIEW (KISWAHILI)
IDHINI YA MAHOJIANO YA UZAZI

Jina langu ni James Munene Waweru. Mimi ni daktari aliyehitimu na nimesajiliwa na Bodi la madaktari ya Kenya. Kwa sasa ninatafuta shahada ya uzamili katika afya ya uzazi katika Chuo Kikuu cha Moi. Ningependa kukusajili katika utafiti wangu inanuia kujifunza sababu ya uwezekano wa bado kuzaliwa.

KUHUSU UZAZIMFU

Uzazimfu unasababishwa na uzazi, kujifungua na sababu za kuhusiana na mtoto aliye tumboni. Mambo haya kuingiliana na inaweza kusababisha uzazimfu. Ili kujua sababu za uwezekano, tunaomba kukuhoji kuhusu tabia ya kijamii na idadi ya watu na historia ya uzazi. Nitatumia dakika 15 kumaliza mahojiano.

Manufaa

Mradi huu ni wa utafiti wa utafiti na matokeo yake yatafaidi jamii kuelewa sababu ya uwezekano wa uzazimfu katika mazingira yetu.

Hatari

Utafiti huu una hatari kidogo sana na hatari ya kisaikolojia ambayo yanaweza tokea yatashughulikiwa kupitia ushauri nasaha.

Tutaweka habari yako yote kwa siri. Matibabu na msaada wowote utakaopata hautategemea kushiriki kwako katika utafiti huu. Tutatoa tiba sahihi kwa hali yoyote tutakayopata kutokana na kukutathmini.

Utafiti huu umeidhinishwa na Taasisi ya utafiti na Kamati ya Maadili (IREC) katika Chuo Kikuu cha Moi.

Je, tunaweza kuendelea? Ridhaa ya domo: Ndiyo..... La.....

Ridhaa Wakala:
Sahihi..... Tarehe.....

Asante

Anwani ya timu ya utafiti,

Dkt James Waweru Munene

MOI UNIVERSITY, ELDORET PO BOX 4606 -0100 Eldoret, Kenya

Simu; 0721945203, barua pepe: wawerumunene@yahoo.com

APPENDIX 3A: CONSENT FORM (for histology of placenta and cord)

PROBABLE CAUSES OF STILLBIRTHS AND ACCEPTABILITY OF AUTOPSY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET-KENYA

Good morning/afternoon, Madam/Sir. My name is Dr. James MuneneWaweru. I am here today from Moi University, Eldoret to collect information and data for the study on causes of stillbirth at MTRH.

I will be asking you permission to dissect your placenta and umbilical cord for histological examination. I plan to sample 42 stillbirth at MTRH/MU. All information obtained will be confidential.

The Institutional Research and Ethics Committee (IREC) of Moi University have approved this research

Benefits

This is a research project and the findings will be beneficial in understanding the probable causes of stillbirth in our setting.

Risks

This is a minimal risk study and the psychological risks that may arise will be addressed through counseling.

May we proceed? Verbal consent: Yes……No……..

Proxy consent: Signature …….

Date **…**……..

Thank you

Contacts for the research team,Dr. James Waweru Munene,0721945203

MOI UNIVERSITY, ELDORET P.O BOX 4606 -0100 Eldoret, Kenya

APPENDIX 3BConsent form for histology(Kiswahili)
KIAMBATISHO CHA TATU B: FOMU YA RIDHAA (KWA KIPIMO CHA KONDO LA NYUMA (PLACENTA) NA KITOVU)

SABABU ZA UWEZEKANO WA UZAZIMFU NA KUKUBALIKA KWA UKAGUZI WA WAFU KATIKA HOSPITALI YA MAFUNZO NA RUFAA YA MOI (MTRH), ELDORET-KENYA

Habari za asubuhi / mchana, Bibi /Bwana. Jina langu ni Daktari Waweru. Niko hapa leo kutoka Chuo Kikuu cha Moi (MU), Eldoret kukusanya taarifa na ujumbe kwa ajili ya utafiti juu ya chanzo uzazimfu katika MTRH.

Nitakuomba ruhusa ya kupasua kondo la nyuma (placenta) chako na kamba ya kitovu ili niweze kupima. Niko na mpango wa kusampuli watoto wachanga wafu 42 katika MTRH / MU. Habari zote zitakazopatikana zitakuwa siri.

Utafiti huu umeidhinishwa na Taasisi ya utafiti na Kamati ya Maadili (IREC) katika Chuo Kikuu cha Moi.

Manufaa

Mradi huu ni wa utafiti wa utafiti na matokeo yake yatafaidi jamii kuelewa sababu ya uwezekano wa uzazimfu katika mazingira yetu.

Hatari

Utafiti huu una hatari kidogo sana na hatari ya kisaikolojia ambayo yanaweza tokea yatashughulikiwa kupitia ushauri nasaha.

Je, tunaweza kuendelea? Ridhaa ya domo: Ndiyo..... La.....

Ridhaa Wakala:

Sahihi..... Tarehe.....

Asante

Anwani ya timu ya utafiti,

Dkt James Waweru Munene ; Simu; 0721945203, barua pepe: wawerumunene@yahoo.com

APPENDIX 7: TIMELINES

	March 14		June-14	July-14	Sept-14	April 2015	Sept 2015	Sept-Dec-15	Dec-15	Dec- 15	Feb-16
Developing proposal											
Presenting proposal to supervisors											
Proposal Submission to IREC											
Piloting data collection tools											
Finalisation of data collection tools											
Data collection											
Data entry, coding and cleaning											
Interim analysis											
Final Analysis											
Thesis write up(results, discussion)											
Notice of intent to submit											
Mock defence											
Submission of Thesis for Examination											
Thesis defence											
Graduation											

APPENDIX 8: BUDGET

Items	**Quantity**	**Unit Price (Kshs)**	**Total (Kshs)**
Stationery & Equipment			
Printing Papers	5 reams	500.00	2,500.00
Black Cartridges	2	2,000.00	4,000.00
Writing Pens	1 packet	500.00	500.00
Flash Discs	1	2,000.00	2,000.00
Box Files	2	200.00	400.00
Document Wallets	2	50.00	100.00
Sub total			**9,500.00**
Research Proposal Development			
Printing drafts & final proposal	10 copies	500.00	5,000.00
Photocopies of final proposal	6 copies	100.00	600.00
Binding of copies of Proposal	5 copies	100.00	500.00
Subtotal			**6,100.00**
Data collection			
Histology of placenta and cord Specimen collection and submission	113	0	20000
Sub total			**20000**
Personnel			
Biostatistician	1	21000.00	21,000.00
Sub total			**21,000.00**
Thesis Development			
Printing of drafts and final thesis	10 copies	800.00	8,000.00
Photocopy of final thesis	6 copies	200.00	1,200.00
Binding of thesis	6 copies	300.00	1,800.00
Sub total			**11,000.00**
Total			**67,600.00**
Miscellaneous Expenditure (10% of Total)			**6760.000**
Grand Total			**74,360.00**

Appendix 9: MTRH Approval

MOI TEACHING AND REFERRAL HOSPITAL

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

Ref: ELD/MTRH/R.6/VOL.II/2008

12th January, 2015

Dr. James Waweru,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
12 JAN 2015
APPROVED
P. O. Box 4606-30100 ELDORET

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

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

"Causes of Stillbirths at Moi Teaching and Referral Hospital, Eldoret, Kenya".

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

for 12/1/2015

DR. JOHN KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

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

Appendix 10: IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2014/225
Approval Number: 0001322

12th January, 2015

Dr. James Waweru,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
12 JAN 2015
APPROVED
P. O. Box 4606-30100 ELDORET

Dear Dr. Waweru & Team,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Causes of Stillbirths at Moi Teaching and Referral Hospital, Eldoret, Kenya"

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1322*** on 12th January, 2015. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 11th January, 2016. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc Director - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix 11: Growth chart for estimated fetal weight regardless of fetal sex

Gestational Age (Weeks)	Estimated Fetal Weight (g) by Percentile								
	2.5	5	10	25	50	75	90	95	97.5
14	70	73	78	83	90	98	104	109	113
15	89	93	99	106	114	124	132	138	144
16	113	117	124	133	144	155	166	174	181
17	141	146	155	166	179	193	207	217	225
18	174	181	192	206	222	239	255	268	278
19	214	223	235	252	272	292	313	328	340
20	260	271	286	307	330	355	380	399	413
21	314	327	345	370	398	428	458	481	497
22	375	392	412	443	476	512	548	575	595
23	445	465	489	525	565	608	650	682	705
24	523	548	576	618	665	715	765	803	830
25	611	641	673	723	778	836	894	938	970
26	707	743	780	838	902	971	1,038	1,087	1,125
27	813	855	898	964	1,039	1,118	1,196	1,251	1,295
28	929	977	1,026	1,102	1,189	1,279	1,368	1,429	1,481
29	1,053	1,108	1,165	1,251	1,350	1,453	1,554	1,622	1,682
30	1,185	1,247	1,313	1,410	1,523	1,640	1,753	1,828	1,897
31	1,326	1,394	1,470	1,579	1,707	1,838	1,964	2,046	2,126
32	1,473	1,548	1,635	1,757	1,901	2,047	2,187	2,276	2,367
33	1,626	1,708	1,807	1,942	2,103	2,266	2,419	2,516	2,619
34	1,785	1,872	1,985	2,134	2,312	2,492	2,659	2,764	2,880
35	1,948	2,038	2,167	2,330	2,527	2,723	2,904	3,018	3,148
36	2,113	2,205	2,352	2,531	2,745	2,959	3,153	3,277	3,422
37	2,280	2,372	2,537	2,733	2,966	3,195	3,403	3,538	3,697
38	2,446	2,536	2,723	2,935	3,186	3,432	3,652	3,799	3,973
39	2,612	2,696	2,905	3,135	3,403	3,664	3,897	4,058	4,247
40	2,775	2,849	3,084	3,333	3,617	3,892	4,135	4,312	4,515

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