STUDY TITLE: PLACENTA STRUCTURE OF PATIENT WITH FRESH STILLBIRTH AT PUMWANI MATERNITY HOSPITAL IN 2021: AN UNMATCHED CASE CONTROL STUDY

PRINCIPAL INVESTIGATOR:
DR. PAUL OGANDA OMAGWA,
H58/11135/2018
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY,

A research dissertation submitted in partial fulfilment of the requirements for the award of the degree of Master of Medicine, in Department of Obstetrics and Gynaecology, Faculty of Health Sciences, University of Nairobi.

2023

DECLARATION

I confirm that the proposal hereby presented is original in content and has never been presented for an academic award in my university or any other university. This complies with the requirements for Masters of Medicine degree, Department of Obstetrics and Gynaecology at the University of Nairobi

Signature:  **Date:** 10/06/23

CERTIFICATION OF SUPERVISION

This dissertation has been under the guidance and blessings of the following supervisors from the Department of Obstetrics & Gynecology, University of Nairobi

Professor Eunice Cheserem

Associate professor, Department of Obstetrics and gynecology and

Chairperson of the Department, Faculty of Health Sciences, University of

Nairobi.

Signature: ..... **Date:** 10. 06.2023

Professor Omondi Ogutu.

Associate Professor and Consultant Obstetrician and Gynecologist, Department of Obstetrics and Gynecology, Faculty of Health Sciences, University of Nairobi.

Signature: **Date:** 10th June, 2023

Professor. Obimbo Moses,

Consultant Obstetrician and Gynecologist and Chaiman, Departments of Human Anatomy, Faculty of Health Sciences, University of Nairobi.

Signature: **Date:** 10th June, 2023

Dr. George Gwako Nyakundi,

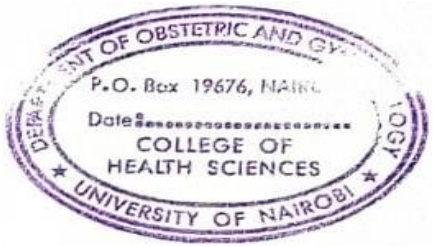
***Lecturer and Consultant, Obstetrician and Gynaecologist, Department of Obstetrics and gynaecology Faculty of Health Sciences, University of Nairobi*.**

Signature: Date:10/06/2023

DEPARTMENTAL APPROVAL

This is to certify that this research proposal is an original work and is being submitted by Dr Paul **Oganda Omagwa,** a Master of Medicine Student in the department of obstetrics and gynecology. It was presented at the departmental level and approved for submission to the Kenyatta National Hospital – University of Nairobi Ethics and Research Committee (KNH-UON ER

Signature:  **Date:**10th June 2023



Professor, Eunice J. Cheserem,

Chairperson, Department of Obstetrics and Gynaecology, Faculty of Health Sciences, University of Nairobi.

LIST OF ABBREVIATIONS AND ACRONYMS

ANC - Antenatal care

BCT- Basic Clinical and Translational lab

CHAMPS – Child Health and Mortality Surveillance

EDTA- Ethylenediaminetetraacetic acid

FSB - Fresh stillbirth

HIC-High income countries

HIV- Human Immunodeficiency Virus

IUFD - an intrauterine foetal demise

IUGR - Intrauterine growth restriction

KAVI- Kenya Aids Vaccine Institute

LMIC – low middle income countries

MSB - Macerated stillbirth

SPSS - statistical package for social science

TBST- Tris-buffered saline **(TBS)** and Polysorbate 20

WHO - world health organization

OPERATIONAL DEFINITION

Abortion – Loss or termination of pregnancy before 20 weeks' gestation.

Early neonatal death – Death of neonates within the first week of life

Live Births – refers to successful extraction or expulsion of a foetus showing signs of life such as breathing

Preterm births – Births below 37 weeks' gestation

Stillbirth – New-born delivered at or past 28 weeks' gestation with no signs of life

Fresh stillbirth- delivery of a baby with no signs of life and no skin disintegration where the duration of death is assumed to be less than last 12 hours before delivery

LIST OF TABLES AND FIGURES

Tables

Figures

TABLE OF CONTENTS

ABSTRACT

Background: Globally approximately 2.65 million stillbirths occur annually. This gives an estimate of over 7100 deaths per day. Most (98%) of these stillbirth cases occur in low and middle-income countries including sub-Saharan Africa. Fresh stillbirth is defined as death that has occurred in the last 12 hours before the expulsion of the product of conception at or above 20 weeks of gestation. The fresh stillbirth rate in Kenya was noted to be 19.7 per 1000 births as of 2019. It is estimated that 50% of stillbirths occur intrapartum. Around 8-20% of intrapartum deaths are classified as unknown causes without conclusive examination of the placenta. Examination of placenta in cases of stillbirth is not routinely practiced in sub-Saharan Africa despite placenta being vital organ which can elucidate on cause of stillbirth. Our aim is to assess placental pathology in cases of fresh stillbirth.

Objective: To compare the differences of gross morphology and histology of placentae of patients with fresh stillbirth and patients with livebirth.at Pumwani maternity hospital.

Methodology: This was a case-control study involving a total of 88 placentae of which 44 placentae were FSB (cases) versus 44 live births placentae (controls) at Pumwani Maternity hospitals. Informed consent was signed by the participants. A structured questionnaire was administered to collect socio-demographic and reproductive health information. Placentae were collected, refrigerated between 2°- 4° Celsius. Photographs were taken of the maternal and fetal surfaces of the placentae. The gross morphology of both cases and controls were simultaneously recorded. Afterwards we made cut sections from placenta disc: 3 from central location and 3 from peripheral location. After the completion of placentae collection, blocks and later slides were made for microscopic histological examination. The socio-demographic and clinical characteristics of the study participants such as age, gestation age, and parity were calculated and presented as tables of frequencies. The proportion of women presenting with FSB and those with abnormal placental histology were estimated using simple frequencies. Pearson's correlation was used to assess the correlation between the maternal demographic and clinical characteristics and the placental changes with FSB Data was analysed using SPSS v.21 for both descriptive and inferential analysis.

Results: A total of 88 placentae were analysed. (44 FSB and 44 live birth). The mean age of cases and control were 29.2 (±6) and 26.2(±5). In assessing gross morphology of the placenta disc; mean placental mean weight was lower in cases (398.4g) than controls (440.65g) p (value=0.041). Retro-placental hematoma were more in cases OR 4.19(1.24,14.13) p=0.002. There were no statistically significant findings in other gross morphology of placental disc (shape length and width calcification, and infarction). There was no statistical difference in gross morphology of umbilical cord between the two groups. In Assessing gross morphology of the membranes; Green colour was statistically significantly associated with fresh stillbirth OR 5.92(1.1, 330.65) p-value =0.04. In the histology of placenta disc, villitis AOR-5.7(1.82-25.2) p=0.004, fetal thrombotic vasculopathy 6.4(1.73, 26.03) 0.016, villous vascularity AOR 6.94(2.4, 20.84) p<0.001 were significant. In our secondary objective, assessing socio-demographic, medical and obstetric risk factors older maternal age >35(p=0.043), lower maternal education (primary education p=0.013), lower birth of weight <2500g (p=0.0046) referral from other facility (p=0.036) were identified.

Conclusion: Lower placental weight retro- placental hematoma green colour membrane was associated with fresh stillbirth**.** In histology villitis, villous vascularity, and fetal vasculopathy were significantly associated with fresh stillbirth.

Utility: The study findings will play critical roles towards preventing fresh stillbirth; thereby, reducing the stillbirth rate. Also, placental examination can identify the cause of stillbirth can yield recommendations for the management of future pregnancies, provide a risk of recurrence, and give families a sense of closure.

CHAPTER 1: INTRODUCTION

1.1. Background

Stillbirth is defined by the World Health Organization (WHO) as a new-born with no signs of life at or above the gestation age of 28 weeks (1). A fresh stillbirth is a baby born dead, assumed to have died within the past 12 hours, but has no signs of skin desquamation or maceration(2). Over half of stillbirths occur during labour and birth and are mostly preventable(3).

We have 2.6 million annual stillbirths globally which is approximately 7,800 deaths per day. Global stillbirth rate is 13.9 per 1000, equating to 1 in 72 total births. Close to 98% of this occurs in middle income and low-income countries with south Asia and sub-Saharan Africa recording high numbers about half of the stillbirth occurs in intrapartum and also called a fresh stillbirth(4)

The most useful investigation towards a diagnosis after stillbirth is pathological examination of the placenta. Some studies have attributed abnormal placental pathology in stillbirths ranged from 20.7% to 39.6% depending on the classification system used.(5) The importance of identifying gross morphology of this placentae of patient with stillbirth cannot be ignored. Placenta lesions or pathologies could be associated with adverse neonatal outcome, in our case stillbirth, in patients with unidentifiable risk of stillbirths. We will identify gross morphology of these placentae to determine if difference indeed exist in such patients.

Given the high rates of stillbirth in Africa and Kenya in particular, understanding the mechanistic pathway of how it occurs could shed more light on how possible interventions can be fashioned. In addition, this would enable us to know the proportion of still birth attributable to placenta ageing and which ones are due to asphyxia and other obstetrical and medical conditions in pregnancy.

1.2. Problem statement

Despite advancement in antenatal and intrapartum care stillbirth rate is still high in LMIC.98% of stillbirth globally occur in LMIC.

Stillbirth is a burden to our society. Apart from it having effect in subsequent pregnancy it is associated with psychological stress of involved family.

There is considerable percentage of stillbirth that are classified as unknown cause in LMIC. This is percentage might be reduced if fetal autopsy and placenta (both Gross and histology) assessment could be done to shed light on causation of stillbirth in our society. We aimed in identifying the cause of stillbirth and identify any changes in placenta structure.

CHAPTER 2: LITERATURE REVIEW

2.1. Definition and prevalence of stillbirth

According to WHO Stillbirth is defined as the death of a fetus at or beyond 28 weeks or >1000g.(1) It also describes it as the death of a fetus before the expulsion of the product of conception with no signs of life that include cardiac activity spontaneous breathing and movements and no pulsation of the cord. Rates of stillbirth have shown a downward trend over the last decade but not to a level that is expected. Stillbirth is a burden in Africa. Prevalence of stillbirth varies greatly between countries and continents. We have 2.6 million annual stillbirths globally which is approximately 7,800 deaths per day. Global stillbirth rate is 13.9 per 1000, equating to 1 in 72 total births. Close to 98% of this occurs in middle income and low-income countries with south Asia and sub-Saharan Africa recording high numbers about half of the stillbirth occurs in intrapartum and also called a fresh stillbirth. Kenya had the lowest stillbirth rate (per 1000 stillbirths) in the region [13] compared to Rwanda [15], Uganda [16], Tanzania [18] and Burundi [23]. Low maternal education, high maternal age, smoking and consumption of water from unimproved sources were the major risk factors of stillbirths(6)

Stillbirth was not accounted for in millennium development goals and was not amongst sustainable growth despite high numbers of the same being recorded. Its exclusion in MDG and SDG has led to a lack of funds due to inexistence policies and programs to deal with it. (7)

A study by Morten Bjerregaard-Andersen et al a retrospective study conducted in Guinea Bissau from October 2007 to April 2013. The findings were stillbirth rates OF 81/1000 live births. Fresh stillbirths were noted to be 51/1000 births which is approximate 70.3 % of stillbirth during that period of study. The hospital FSB was highest between 4 pm to midnight. Stillbirth rates were

Also shown to have reduced if the mother attended antenatal care >7 consultations. The authors concluded that the fresh stillbirth rates were unexpectedly high and attribute it to a low level of antenatal care and maternal education (8).In study conducted by Madhi et al which was a prospective hospital-based observational study in Soweto South Africa between October 9 2014 to November 8 2015, (9), 36% (n = 106) of the total 354 stillbirths involved in the study were considered as intrapartum fetal losses (fresh stillbirths). Overall stillbirths were attributed to four major causes; a maternal medical condition, placental, and foetal infection, pathological placental pathology, and clinical obstetrics complications. In a study by Aminu et al 'understanding cause of stillbirth multi-country prospective observational study in 2019 conducted in four major countries' (12 hospitals in total);1563 stillbirth were studied among 43,979 total births stillbirth rates were 20.3/1000 in Malawi,34.7/1000 in Zimbabwe 38.8/1000 in Kenya and 118.1 in Sierra Leone. There were a total of 1563 stillbirths recorded of which 35.9% were recorded as FSB. The researcher also attributes the cause to asphyxia (18.5-37.4), placenta disorder (8.4-18.1%), maternal hypertension (5.1-15.6%), infection (4.5-9.0%) cord problems(3.3-6.8%),and ruptured uterus (2.6-6.1%).In conclusion, they suggested that despite the majority of stillbirth have a known cause, other diagnostic parameters should be used to identify the specific cause of death of the fetuses.(10) A cross-sectional descriptive study by Njuguna et al in Kenya at Kenyatta national hospital looked at the factors associated with intrauterine fetal death in 2010 findings were as follows; Total deliveries were 10744stillbirth rate was noted to be 51 per 1000 live birth. Similar study by Wako et al in Marsabit in 2019 cross-sectional descriptive study found out the stillbirth rate was 5.9 %.(4)

2.2. Socio demographic, obstetrics, medical risk factors and stillbirth

Some studies have revealed the association between socio-demographic obstetrics and medical risk factors in causation of stillbirth.

2.2.1. Socio demographic factors

In a study by Ongesa et al, institutional based cross- sectional descriptive study at Mbagathi hospital Kenya in 2017 looked at factors influencing high prevalence of fresh stillbirth in Mbagathi hospital. Lower maternal age, low socioeconomic and lower level of education was associated with fresh stillbirth. Total number of fresh stillbirth was 40,of which 55% were below age of 20,25% of respondents were aged between 21-30 and 12.5% were ages above 40.In investigating level of education,57.5% had attended only primary education compared to only 23 % that had attended tertiary education.62.5% of respondents were unemployed compared to 10% of cases that were employed.(11)

Similar findings were noted in Gwako et al in Kenya case control study conducted in four hospital in Nairobi, between August 2018 and April 2019; Mothers with a stillbirth were likely to have primary-level education 76(34.6%) vs. 99(23.1%), P = 0.002); those who had a stillbirth were likely to be older (mean age 28 vs 26 years, P = .006), an obstetric complication 78(36.4%) vs. 37(8.9%) P = 0.001(12)

In a study by Zhum et al in China between 2012-2014 cross-sectional study, stillbirth rate was 8.8.However the stillbirth was noted to be high in ages below 15 (59/1000 live births OR 9.25 CI7.4 -11.82 p= 0.04).Stillbirth was also associated with unmarried 32.5/1000(OR 3.94 CI-2.3 – 5.9), and no educational level OR 4.4 CI 3.51-5.51(13). Jacob et al retrospective study done in Nigeria focused on the period between 2009 and 2014 assessing the prevalence and modifiable socio-demographic risk factors for antepartum foetal death. In that study, 9319 deliveries

occurred were evaluated, there were 270 stillbirths. The findings translated to 29 stillbirths for every 1000 deliveries, which was quite high. Associated factors identified with antepartum fetal death included being ≤ 20 years old, been in unskilled occupation, not married, Muslim and with no formal education. In addition, mothers who reported to have no antenatal visit, with five or more children, and with history of SB were associated with high occurrences of SB. Antenatal services were pivotal in reducing SB as well as having the mothers educated. Both these strategies increases access for information and health promotion strategies (14)

2.2.2. Medical and obstetric risk factors

Gwako et al case control research from four tertiary hospitals based in Nairobi evaluated how medical and obstetrics risk factors influenced the occurrence of stillbirth in LIMC between 2018 and 2019. The cases comprised of 214 mothers who had delivered stillbirths while the control group comprised of 428 mothers with live births past 28 weeks gestation. Main factors that were reported to have statistical significance difference (association) included mothers with a medical complication (P = 0.001), and early gestation (37 vs. 39 weeks, P = 0.001). The risk of stillbirth was increased by two folds in mothers with a medical condition (OR = 2.1, 95% CI 1.3– 3.2, P < 0.001), and increased eleven times for those with gestational diabetes mellitus (OR= 11.5, 95% CI 2.5–52.6, p= 0.001). Also, mothers with gravidity of over 4 were more likely to have a stillbirth (12).

In a case control study conducted in Nepal India by Ashish et al between July 2012 and September 2013 looking at incidence of intrapartum stillbirth and associated risk factors the following were associated with risk of intrapartum stillbirth; Antepartum hemorrhage (AOR 32.1 95% CI 1.8-5.5p,0.001),obstetric complication(AOR 4.5 95% CI 2.9-6.9 p<0.001) preterm birth(AOR 5.4 95% CI 3.5-8.2 p<0.001(15).In a retrospective cohort study between 2000 and 2014 conducted in Northern Tanzania by Chuwa et al they enrolled 47,681 singleton pregnancies. The following were associated with risk of stillbirth, pre-eclampsia AOR 3.99 CI

3.3-4.81, Placenta abruption AOR 2.02, low birth weight AOR 9.66 95% CI 8.66-10.77(16) In a cross-sectional study by Chuwa et al in Malawi between may to November 2017 the following was associated with stillbirth uterine rupture-15%placenta abruption 14.3 hypertensive disease 10.3% obstructed labor/prolonged labor 5.8% syphilis 7.1% congenital anomalies-2.4% diabetes5% (17).

2.2.3. Antenatal clinic attendance and still birth

A case-control study by Gwako et al evaluating 644 births that happened between August 2018 and April 2019 in four tertiary facilities in Nairobi indicated the significance of ANC services in averting the risk of stillbirths. Mothers who did not make even a single ANC visit were four times more likely to deliver stillbirths (OR = 4.1, 95% CI: 1.6-10, P < .003). The number of ANC visits made was also vital, with higher odds reported compared to those with at least three visits (OR = 2.96, 95% CI: 1.4-6.1, P = 0.003). Based on the mothers perception, those who indicated having satisfactory ANC care had lower odds of stillbirths. Having undergone for ANC profile services reduced the risk stillbirths, haemoglobin testing by 40% (P = 0.03), blood group test by 60% (p < 0.001), HIV test by 70 % (P = 0.001), VDRL by 80 % (P = 0.001), weight measurement by 30% (p = 0.047) (18). A population based survey in Ghana by Afulani et al in 2007inluded 4868 mothers who had a stillbirth rate of 15/1000.In bivariate analysis, stillbirth rate was higher in small group of women 5.6% who did not attend ANC visit compared to those that attended at least one antenatal clinic (19).

2.3. Gross placenta and histopathology and still birth

Placenta is a fetal organ that begins to develop from blastocyst soon after implantation. It plays very important role in exchange of gas waste and nutrients from mother to the fetus. It is also an endocrine organ producing hormones that regulate maternal and fetal physiology during pregnancy. Placenta has been associated with causation of death in some studies. In Aminu et al,

multinational observational study including Kenya in placental causes attributed to 8-15%.17.9-26% of cases had cause of stillbirth being unknown, which might be as a result of not examining placentas in most hospitals (10).

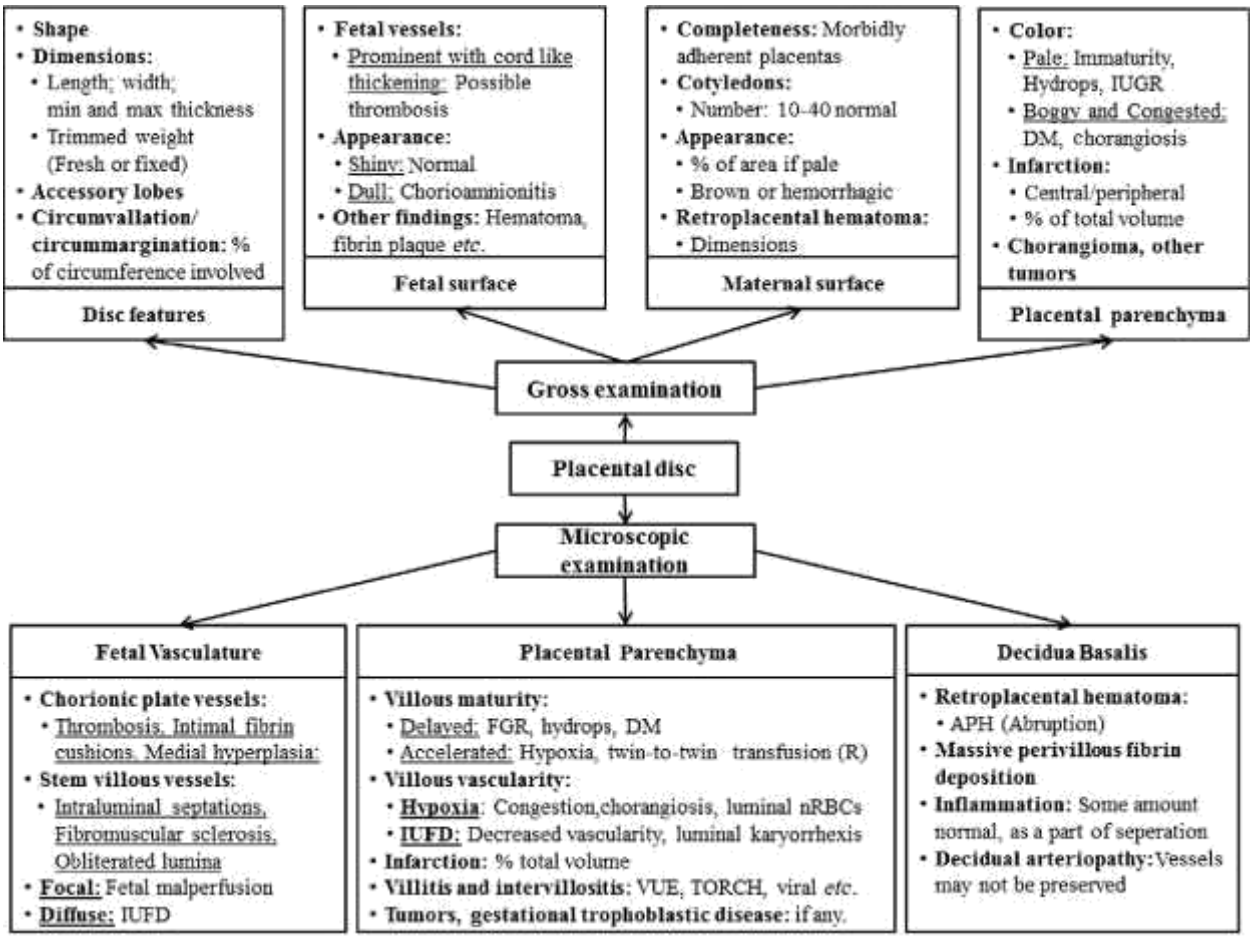


Figure 1: Gross and placental examination(Kulkarni et al)(20)

Examination of both gross and microscopic characteristics of placenta is of great importance. In sub–Saharan Africa including Kenya this kind of examination is rarely done especially in LMIC hospital. His examination can shed light on the cause of stillbirth in our hospital. A greater number of stillbirth (both FSB and MSB) are classified as unknown cause despite no fetal autopsy and placenta examination being done. This study will shed light on placenta lesions found in cases of stillbirth and will elaborate the significance of examination of placenta. This examination is recommended by international guidelines (21).

In a case control study Omollo et al,2011 Gross and the histopathological difference between placenta of mothers with intrauterine fetal death and live birth at Kenyatta National hospital in 2010 The results of his study were that there is no statistical difference in gross morphology of stillbirth and live birth in the cord attachment ,umbilical knots umbilical cord veins and arteries.(22). There was however statistically significant difference in mean placental weight (p 0.0001) and diameter (p=0.004) of the live birth group compared to the stillbirth group. Reduction of mass of functioning villi was found to be 11.9% in stillbirth compared to 2% in live births (P value=0.02). There were also statistically significant changes in histological chorioamnionitis. Stillbirth chorioamnionitis was noted to be around 51% versus those in live births 29.4% from this study done in Kenyatta national hospital we can allude that there was associated gross and histomorphological difference both placentae in both groups and that would have contributed to adverse outcome of those foetus.

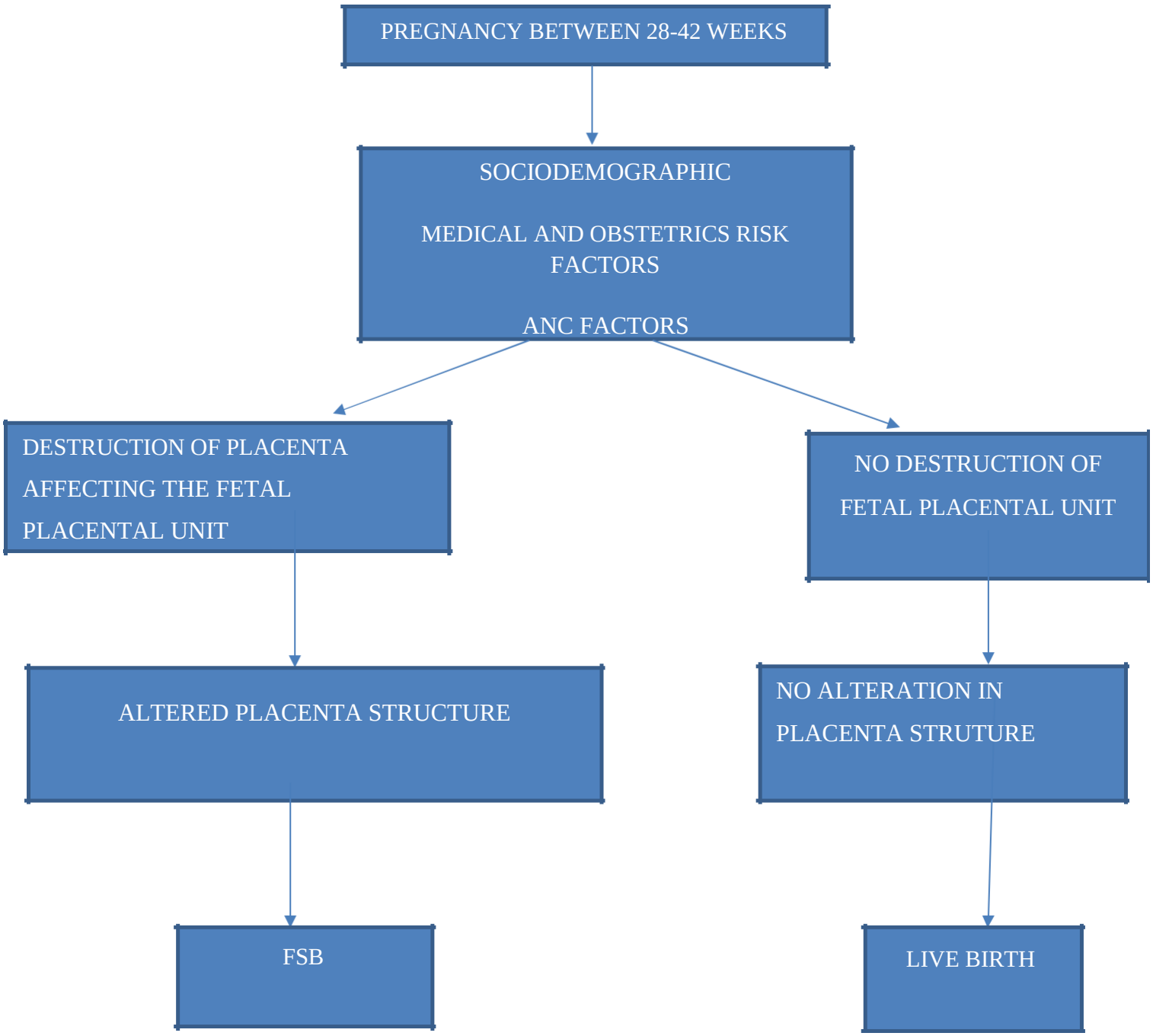
There was a study conducted by G..A Machin et al looking at abnormal umbilical cord coiling and associated adverse outcome in 2000.The normal umbilical cord is noted to be 1 coil /5cm, which is 0.1-0.2 coil per cm. In this study he looked at presence of hyper coiled and under coiled cord and associated outcome. The results were as follows, in hyper coiled group there was significant adverse effect that include fetal demise (29%), fetal intolerance to labour (14%), intrauterine growth restriction (10%) and chorioamnionitis (10%). In under coiled group, 29% was associated with fetal demise, fetal intolerance to labour (21%), intrauterine growth retardation (10%) and chorioamnionitis (10%.). Their conclusion was that abnormal cord coiling is a chronic state, established in early gestation, that may have chronic (growth retardation) and acute (fetal intolerance to labor and fetal demise) effects on fetal well-being (23).

In case control study by Anantha et al Mumbai India in 2019 looking at placenta changes in singleton placentae found that there were no statistical significance findings in gross placentae of patient with stillbirth versus live birth. However there was statistical significant findings in delayed villous maturity (p=0.02), chronic diffuse villitis (p=0.02), acute villous villitis (p=0.02), avascular villi-=P=0.02 (24). Similar findings were found in case control study in Meccaci et al in Italy in 2016 looked at stillbirth in singleton term pregnancy; stillbirth placenta had more pathologic changes compared to live birth (p=001) disruptive changes (p=0.01),obstructive changes p<0.01,adaptive changes p=0.01 (25). Similar case control study in India in 2021 by Purnima et al. The placental findings associated with stillborn placentas with highest odds at 95% confidence interval were placental hypoplasia (OR = 9.77; 5.46–17.46), necrotizing

chorioamnionitis (OR= 9.30; 1.17–73.96) and avascular villi (OR = 8.45; 3.53– 20.25). In addition, there were higher odds and statistical significance for all the broad categorization of gross placental findings in stillbirth cases. Gross placental morphological defects were higher by close to 8 times, cord gross with odds of close to five, gross membrane problems with almost double risks, while maternal vascular malformations had four times likelihood to be in stillbirth category. More so, fetal vascular malformations were higher by close to 8 times while inflammatory findings were twice higher in stillbirths (26).

A case control study by Halit et al evaluated data for the period March 2006 through September 2008 evaluating the stillbirths and placental defects in the regions of Georgia, Texas, and Utah. Among those with stillbirths, 7.7% had single umbilical artery compared to 1.7% from the livebirths category. Stillbirth cases had higher frequencies of velamentous cord insertion 5% compared to 1.1% for the livebirths. After 24 weeks gestation, fetal vascular thrombosis recorded higher rates in stillbirth category compared to livebirths. Diffuse placental infarction was far more common in stillbirths than live births. The overall prevalence in stillbirths and live births across gestation was 2.8 and 0.1 percent, respectively (odds ratio [OR] 43, 95% CI 5.6-328) (27).

2.4. Conceptual framework



Conceptual Framework Narrative

Stillbirth is a burden to our society.98% of stillbirth occurs in LMIC. There are many factors affecting/ associated with stillbirth.

Socio-demographic factors like age economic status level of education may affect outcome of pregnancy. These factors assist the patient in understanding the pregnancy process, access the availability services and adhere to required schedules in pregnancy. Lack of them might reduce the chances of benefiting from such services and might adversely affect the outcome of pregnancy.

Medical and obstetric risk factors is another risk factor that might affect pregnancy outcome. From literature hypertensive diseases, APH, IUGR anemia and HIV have been associated in causation of stillbirth. These medical and obstetrics factors can directly affect the fetal placental circulation and cause stillbirth in affected pregnancy.

Destruction of fetal placental tissue is associated with altered placenta structure. Placenta cause of stillbirth is estimated to be around 17-30% in our literature review. Placenta structure changes can occur independently or as result of obstetrics or medical risk factors. This is very important in cases where there is no known cause of stillbirth.

3.3 Justification

Stillbirth is burden to our society. The global stillbirth rate is 13.9/1000 livebirth.98% of these stillbirth occurs in low and middle income countries (ranges from 177.1-22/1000live birth) (28). A recent study in Kenya put the stillbirth rate at 38/1000(10).Half of stillbirth in our society are associated to be intrapartum death which are preventable.

Determination of cause of FSB has not received much attention in this part of the world. Examination /assessment of placenta and foetal autopsy as the cause of stillbirth has not been extensively done in sub-Saharan Africa. About 65% of the stillbirth is classified as an unexplained. This could be related to placental (Sultani et al)(29). In literature, increased gestation and medical conditions in pregnancy have

been associated with placental aging, and subsequent adverse neonatal and maternal outcomes. Our main aim was to identify risk factors of these stillbirth and asses if there was associated placenta structure difference between live birth and fresh stillbirth.

The association between these stillbirths and any medical condition will help us identify high-risk pregnancies and several measures will be put to decrease incidences of adverse neonatal and maternal outcomes. This includes 1) increased Antenatal visits for such patients with foetal monitoring 2) supplementation of antioxidants 3) may also benefit from early admission and early delivery.

This study will also help in risk screening of subsequent pregnancy. Linking between socio-demographic factors and stillbirth will also help us identify risk groups for still birth in our society.

This study will also help make us understand the importance of examination of placenta (Both gross and histology) to diagnose cases of unexplained foetal death and help practitioners in cases of litigation.

2.6. Study Question and Hypothesis

2.6.1. Study Question

Are there differences in placental structure in fresh stillbirth placentas versus placentas of those with live births at Pumwani Maternity Hospital?

2.6.2. Null Hypothesis

There are no differences in placenta structure in fresh stillbirth placentas versus placentas those with live births at Pumwani maternity Hospital

2.7. Study Objectives

2.7.1. Broad Objectives

To compare gross morphology and histology of placenta of patients with fresh stillbirth versus with live birth at Pumwani Maternity Hospital.

2.7.2. Specific Objectives

Among placentae of mothers with fresh stillbirth versus those of mothers with live birth

1. To compare Gross morphology.

2. To compare histology and histomorphometry.

3. Secondary Objective

To compare the socio-demographic, obstetrics and medical risk factors.

CHAPTER 3: METHODOLOGY

3.1. Study Design

This will be unmatched case-control study. The cases will comprise of 42 mothers with FSB deliveries while the control group will comprise of an equal number of mothers with livebirths. The unmatched criterion was arrived after assessing the nature of the targeted population and the limited duration of the study, which would challenge having matched cases. However, to reduce confounding variables, a case and a control will be picked concurrently and within 24 hours of delivery.

3.2. Study Area Description and setting

The study site was at Pumwani Maternity hospital. Pumwani maternity hospital is an obstetrics and referral hospital for Nairobi and its adjoining counties. Founded in 1976, it's the largest maternity hospital in Kenya and sub-Saharan Africa. It has 354 bed capacity, 144 baby cots, 3 theatres and High Dependency Unit. Pumwani maternity has approximately 15000 annual deliveries. In the last one year it recorded 244 fresh stillbirths.

Gross morphology and histopathology were done at Basic clinical and translational research laboratory at Chiromo, Department of Human Anatomy, University of Nairobi. The BCT laboratory is a new laboratory in the Department of Human Anatomy run by one of my mentors on this study. It was set up with support of a grant from Grand Challenges Africa and has a bio-repository with placenta specimens collected for the purpose of future research. The laboratory focuses on Human and Murine placenta, endometrial and other reproductive structures biology. The laboratory has a capacity of 10 scientists.

3.3. Factors that make the site suitable

1.Pumwani is a maternity hospital that specializes on Obstetrics maternity care both antenatal intrapartum and postpartum care. It deals with routine antenatal care and visits, and assessment

of high-risk pregnancy and Neonatal care services. It serves low- and middle-income area description of Nairobi County Kenya.

2. Pumwani boasts of 2,000 deliveries per month 77% vaginal deliveries and 33 % normal deliveries.

3. Pumwani has accessibility to different specialist doctors including obstetricians and pediatricians.

3.4. Study Population

Mothers admitted and delivered at pumwani maternity hospital.

3.5. Eligibility Criteria

Inclusion Criteria

Singleton pregnancy

Gestational age between 28-42

Mothers with stillbirth

Age > 18 years

Exclusion Criteria

- Mothers with macerated still birth
- Abdominal pregnancy

3.6. Samples Size Determination

The sample size will be calculated using the formula for comparing means as below:

$$n1 = \frac{(r+1)}{r} \frac{\sigma^2 (Z_\beta + Z_{\alpha/2})^2}{\text{difference}^2}$$

Based on a similar study conducted by A Owino et al titled ‘Gross presentation and histomorphology changes of placentae in patients presenting with intrauterine fetal death at the Kenyatta National Hospital' where there was a statistically significant difference between the placental weight for mothers who had a fresh stillbirth (mean placental weight 390.90, SD 155.6) compared to those who had live births (mean placental weight 486.27, SD 119.114) (22)
Applying this in the formula for difference in means gives a sample size of 42 per arm as shown:

Substituting the above values into the equation gives the sample size n_1

$$=$$

n_1	= Size of each group	
r	= ratio of cases to control group	= 1
σ	= standard deviation of the control group	= 155.6
difference	= clinically meaningful difference in means of the outcome: 486.27-390.9	= 95.37
z_β	= corresponds to the power of the study	= 80%
$n_{\alpha/2}$	= corresponds to two-tailed significance level	= 1.96 for $\alpha = 0.05$

$$\frac{155.6^2(0.84 + 1.96)^2}{1 \qquad 95.37^2}$$

$$= 21*2=42$$

3.7. Sampling Procedure

A non-probabilistic consecutive sampling procedure was used to identify 44 placentas eligible for inclusion into the study in each group for assessment of the morphometric changes for the cases

A probabilistic systematic sampling of 2nd delivery after case has been identified was used. Patients in control group were recruited within 24 hrs of delivery of fresh stillbirth.

3.8. Data Variables

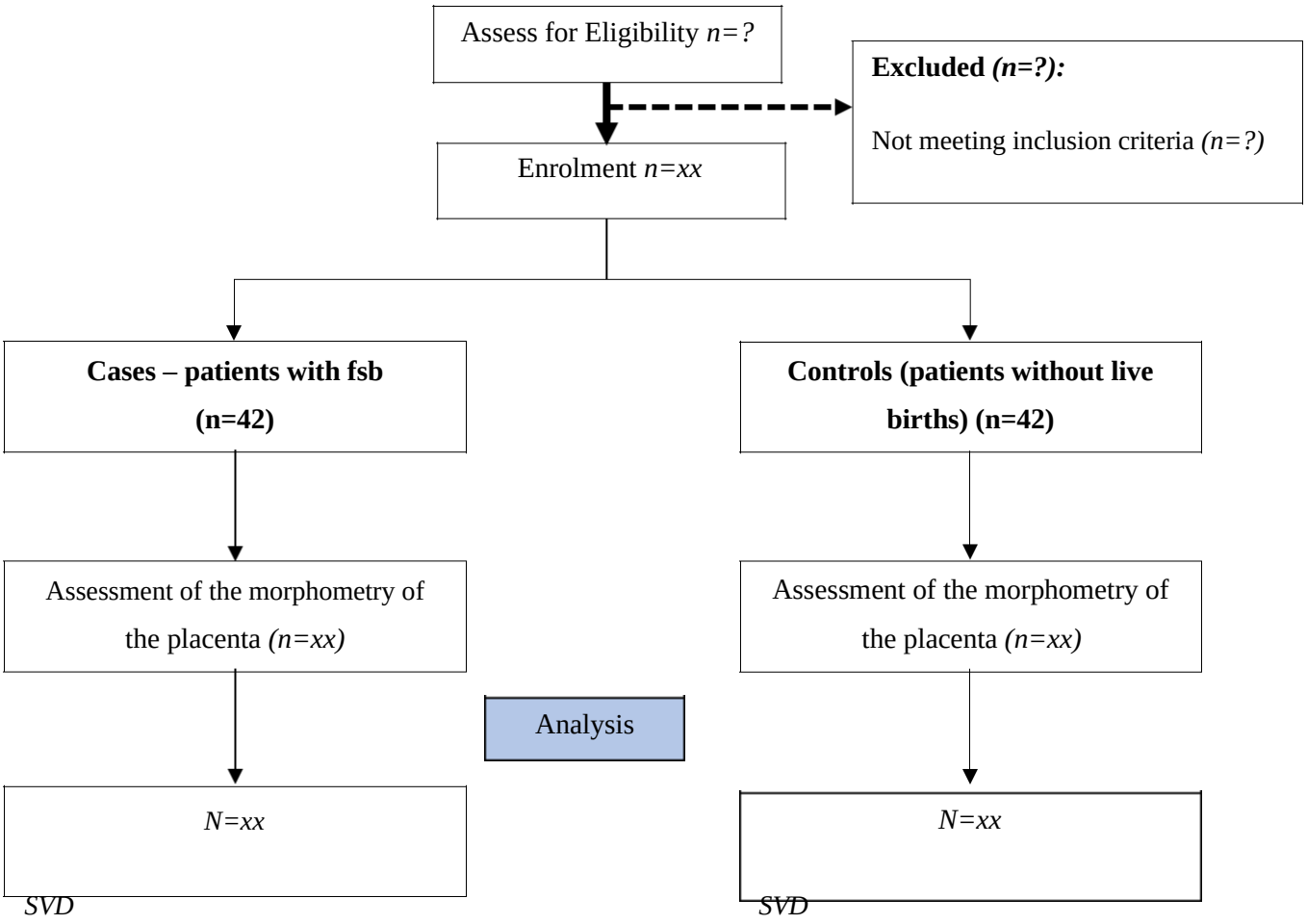
objective	Exposure variable	Outcome variable	Source of data
Gross morphology of placenta	Placenta of patient with fsb and live birth	Placenta weight infarction thrombosis hematoma umbilical cord and membrane	Placenta pathology report
Histology of placenta	Placenta of patient with FSB and live birth	Distal villous hypoplasia villous edema vilitis villous vascularity fetal vascular thrombosis	Placenta pathology report
Secondary objective socio-demographic obstetric medical factors	Placenta of patient with FSB and live birth	Age parity gestation marital status educational level occupation medical diseases and obstetric risk factors	Patient files

Dependent variable

1. Mothers with fresh stillbirth

2. Mothers with live birth

3.9. Study flow Diagram



3.10. Data Collection Procedure

Eligible participants were recruited in labor ward after delivery given that the primary inclusion criteria are based on fetal outcomes – stillbirth or live birth. Once identified, the potential participant was approached by either the principal assistant or my assistant. The potential participant will then be given the information, purpose, objectives, benefits, risks involved and voluntary nature of being involved in the study. Those who met the inclusion criteria and were willing to participate were then given a written consent form to sign. Then, the patient was interviewed using a questionnaire to acquire the bio data medical risk factors and obstetrics history. The placenta was then collected immediately after delivery from the patient who satisfies the exclusion and inclusion criteria, transported to Chromo BCT lab in a cool box. Pictures of the placenta (both fetal and maternal side) were taken.

Gross morphology

Using CHAMPS PROTOCOOL ;(30)The following placental characteristics were measured

i. Weight of the placenta using a Dual Display-Camry Scale
ii. ii. Gestational age
iii. iii. Presence of areas of infarction or thrombosis.
iv. iv. Shape of the placental specimen.
v. v. The colour of the placental membranes and the chorionic plate.
vi. vi. The length of the umbilical cord in centimetres using a flexible tape measure.
vii. vii. The mean diameter of the cord in 3 regions using a digital Vernier calliper

HISTOLOGY AND MORPHOMETRY

Using the CHAMPS PROTOCOL (child health and Mortality Surveillance) For (minimally invasive tissue sampling MITS).

Light microscopy

Consecutive sections of placental specimens measuring seven micrometers in thickness were prepared using a Leitz Wetzlar sledge microtome. These were floated in warm water and fixed on glass slides. Drying in an oven at 40°C was then done overnight. The serial sections were

stained with Masson's trichrome; or haematoxylin and eosin (H&E). H&E was used for demonstrating the general histomorphometry and Masson's trichrome was used to exhibit the connective tissue constituents. The slides were then analysed using a Richter Optica Plan Achromatic UX-1T digital light microscope interphase with Moticam BTU10 Camera system then connected to a computer and monitor. Our team of examiners comprised of a placental biologist, an anatomist, and a pathologist. The examiners were blinded to the status of disease of the mothers. Characteristics that were graded are degeneration of villi, delamination of the syncytiotrophoblast, villous vascularity, adhesion of red blood cells to the terminal villi, maturity of villi, syncytial knotting, villitis, and deciduitis

3.11. Data Management

The collected data was saved in a password protected computer software, only accessible to the principal investigator and the data manager. Managements of access rights was enforced and regulated by the researcher. Regular updating of electronic antivirus was also crucial. Backup to multiple sources with above security standards was encouraged as well. Data was cleaned, coded and uploaded to the SPSS software for analysis.

3.12. Data Analysis

The socio demographic and clinical characteristics of the study participants such as age, gestation age and parity were calculated and presented as tables of frequencies.

The proportion of women presenting with FSB and those with abnormal placental histology was estimated using simple frequencies.

Mean values and standard deviations were used for continuous variables, frequencies and percentages were used for categorical variables

Pearson’s correlation was used to assess the correlation between the maternal demographic and clinical characteristics and the placental changes with FSB. This was presented as tables and a correlation coefficient calculated. A p value of 0.05 was taken to be statistically significant.

3.13. Research Materials

Research materials include;

- Journal articles
- Recordings
- Files
- Badges of identification for my research assistant
- Calculators
- Laptops
- cryovials for storing placenta specimen
- Coolbox to store placenta specimen

3.14. Quality Assurance

A number of strategies was be adopted to ascertain the quality of the study. To begin with, a manual of operation was developed to guide in rolling-out the study step-wise. The study instrument was pre-tested and appraised to ensure they meet the study objectives. In effort to reduce confounding factor related to competency of research assistants, they underwent adequate training on the protocol and data collection process. The research assistants were either holders of a diploma or degree qualification in nursing, midwifery or clinical medicine, and had a valid practicing license from their respective regulating body. We were able to use expertise of professor Obimbo and Dr inyangala (pathologist)in histopathology. The researcher maintained a quality control system for data collection throughout the study by a) checking questionnaire for completeness, b) counterchecked 10% of the data sources to ascertain authenticity, and c) ensuring double data entry before analysis is be done.

3.15. Ethical Consideration

We s to sought permission to collect and analyse data and any other requirements from KNH-ERC. The researcher also got administrative approval from Pumwani maternity hospital. Informed consent will be sought for this study participants

Some of the ethical issues with study include

1. Patient with fresh stillbirth will not be in right psychological state to answer questions provided in the questionnaire. These women were linked to counselling services

2. Some questions were very sensitive and could have risk of causing psychological distress. The participants were identified and only interviewed at their convenience but before they are discharged home

3.16. Study Results Dissemination Plan

The results are planned to be published in a reputable journal and the manuscript will be accessible to the University of Nairobi library plus also shared in the Kenyatta National Hospital Resource and Program Centre. Furthermore, the researcher will seek to share the findings with Pumwani hospital, University of Nairobi through the department-organized results presentation Webinars. We also plan to share the results in local and international scientific conferences including Kenya obstetrics and gynecology society (KOGS), Ministry of health international Federation of obstetrics and gynecology.

3.17. Study Limitations

Study limitation	**Mitigation**
Expensive	Solicit for funding
Misclassification of FSB/MSB	Create manual of operation and train my research assistants on difference between the two groups Use of photos and charts
Placenta storage	Purchase a refrigerator /cool box and keep it in maternity unit before transporting to Histopathology lab.

CHAPTER 4: RESULTS

4.1. Introduction

The study compared the Gross morphology and histology of patients with fresh stillbirth and patients with live birth at Pumwani Maternity Hospital. The specific objectives that were included in the study were to compare stillbirth and live birth based on gross morphology histology as well as socio-demographic, obstetric and medical factors. A total of 44 cases and 44 controls were included in the study as shown in Figure 2.

Study flow chart

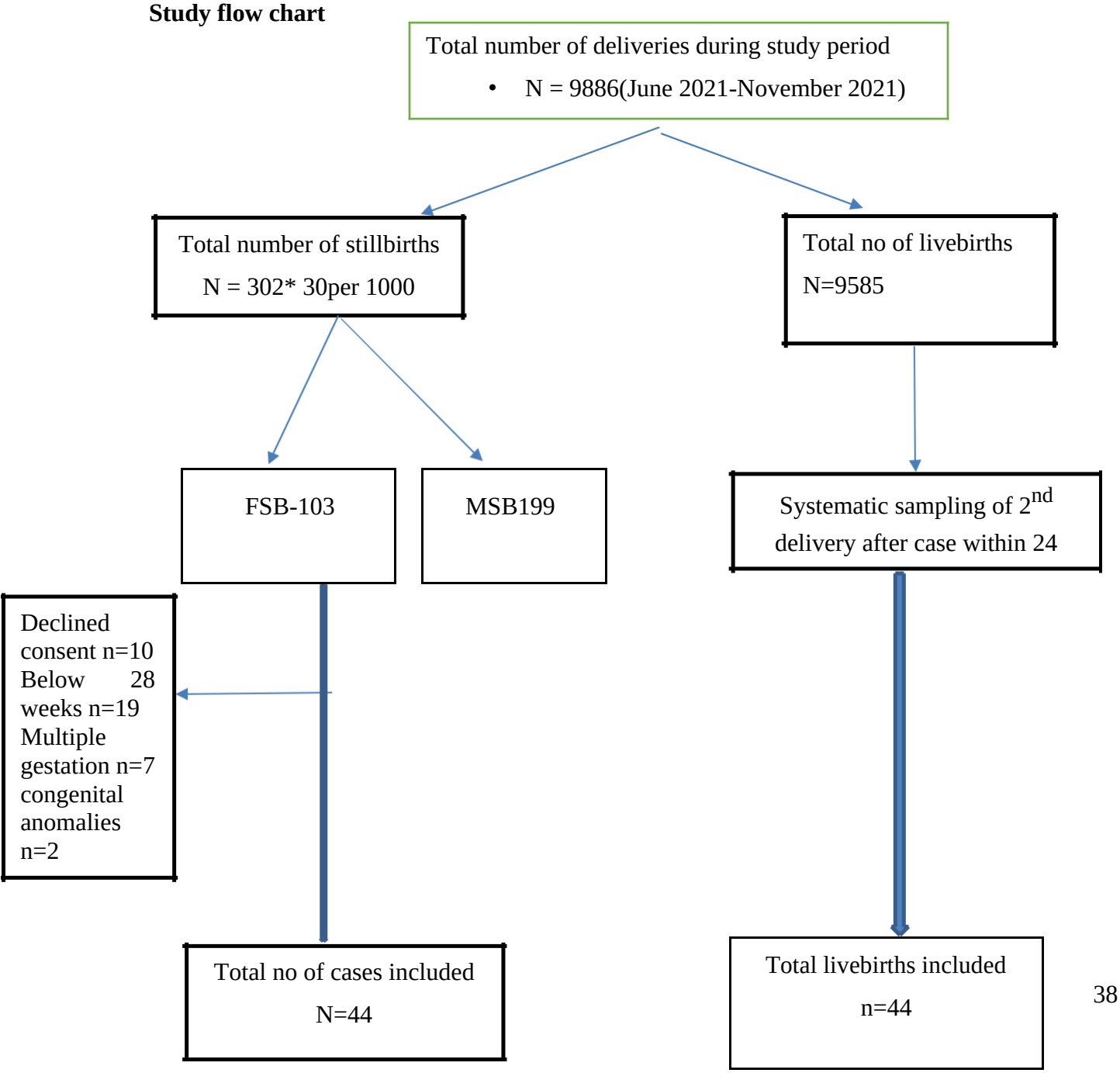


Table 1: Socio-demographic characteristics of FSB and live birth

SOCIODEMOGRAPHIC CHARACTERISTICS	**CASE n=44(%)**	**Control n=44(%)**
Maternal age (mean ±SD)	29.2±6	26.2±5
<20	4(9.1)	2(4.5)
20-34	29(65.9)	40(90)
≥35	11(25)	2(4.5)
Marital status		
Single	6(13.6)	4(9.1)
Married	38(86.4)	40(90.9)
Educational level		
Primary education	14(31.8)	9(20.5)
Secondary education	27(61.4)	22(50)
Tertiary education	3(6.8)	13(29.5)
Occupation		
Unemployed	25(56.8)	20(45.5)
Informal employment	13(29.5)	22(50)
Formal employment	6(13.6)	2(4.5

4.1. Objective 1: Gross morphological difference of placenta between fresh stillbirth and live birth

Table 2: Gross morphology difference of placenta disc

Placenta disc description	Case N=44	Control N=44	OR(CI)	P value	AOR(CI)	P value
Weight (mean ±SD)	**398.4(106)**	**440(91)**	**-**	**0.012**		**0.041**
Linear length(cm±SD)	18.4(2)	19.4(2.3)		0.08		0.09
Linear Width (±SD)	15.74(2.5)	16.44(1.8)	-	0.136		0.24
Hematoma on maternal surface						
>50%	**14**	**5**	**3.6(1.18,11.23)**	**0.020**	**3.9(1.22,12.83)**	**0.022**
<50%	30	39	ref			
Masses						
Yes	0	1(2.3)	-	-	-	-
No	44(100)	43(97.7)				
Other gross findings						
Yes	19	15	1,42(0.6,3.37)	0.283	1.2(0.5,4.5)	0.232
No	25	29	ref			

Table 3: Comparison of umbilical cord between FSB and live birth

Umbilical cord	**Cases**	**Controls**	**OR(95%CI)**	**P-value**	**AOR**	**P value**
Diameter of umbilical cord	1.5(0.3)	1.3(0.3)	1.8(1.23,2.41)	0.004		0.99
Length of Umbilical cord	44.3(18)	48.22(12)	1.02(0.99, 1.05)	0.252		0.34
Distance between insertion and nearest placental margin	4.58(2)	5.46(1.6)	0.61(0.22, 0.98)	0.034		0.957
Insertion of umbilical cord			-	-		
Lateral insertion(velamentous)	2(4.5)	0				
Central insertion	42(95.5)	44(100)				-
Presence of knots						
Yes	1(2.3)	0	-	-		
No	43(97.7)	44(100)				-
Appearance of umbilical cord						
Hyper coiled	1(2.3)	0				
Normal	39(88.6)	44(100)	-	-		
Hypo coiled	4(9.1)	0				
Presence of strictures						
No	44(100)	44 (100)	-	-		
Presence of discoloration						
Yes	25(56.8)	10(23.7)	4.3(1.7,10.9)	0.002	1.36(0.4,6.4)	0.06
No	19(43.2)	34(77.3)	1			
Number of vessels (Mean)	3	3	-	-	-	-

Table 4: Membranes difference between FSB and live birth

Membranes	**Case n=44(%)**	Control n=44(%)	**OR (95%)**	**P value**	**AOR**	**Pvalue**
Colour of membranes						
Green	**9(20.5)**	**2(4.5)**	**5.92(1.13,30.65)**	**0.04**	**6.92(1.28,38.08)**	**0.025**
Grey	16(36.3)	17(38.)	0.41(0.76,0.211)	0.871	0.51(0.86,2.15)	0.9
Red/ maroon	19(43.2)	25(56.8)	ref	-	-	-
Opacity						
Clear	1(2.3)	0	-	-	-	-
Opaque	5(11.3)	4(9.1)	1.32(0.33,5.27)	0.085	1,2(0.26,4.99)	0.08
Slightly opaque	38(86.4)	40(90.9)	ref			
Membranes complete						
Yes	43(97.7)	44(100)	-	-	-	-
No	1	0	ref			
Types of membranes						
Marginal	40(90.9)	38	ref			
Circummarginate/circumvallate	4(9.1)	6(13.6)	0.6(0.17,2.42)	0.369	1.4(0.32,5.90)	0.25

Gross Morphology pictures

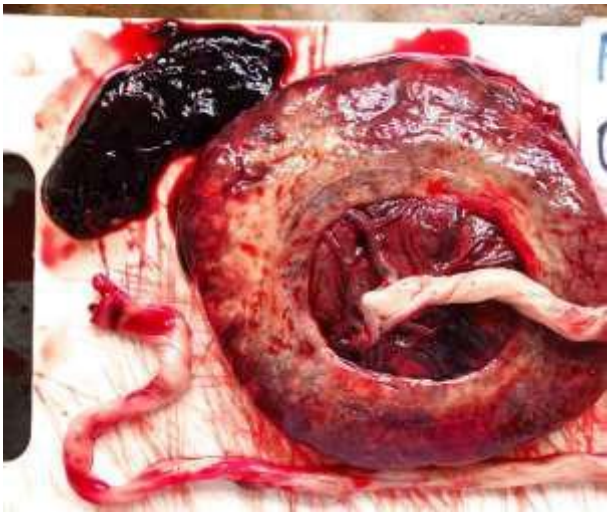


Figure 2: Circumvallate insertion

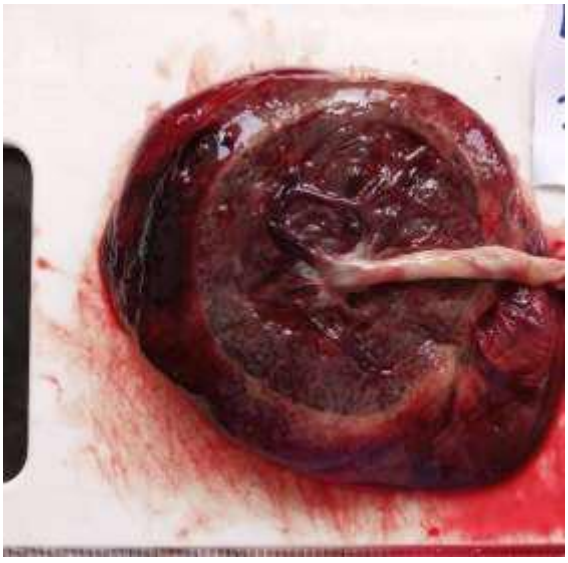


Figure 3: Circummarinate insertion

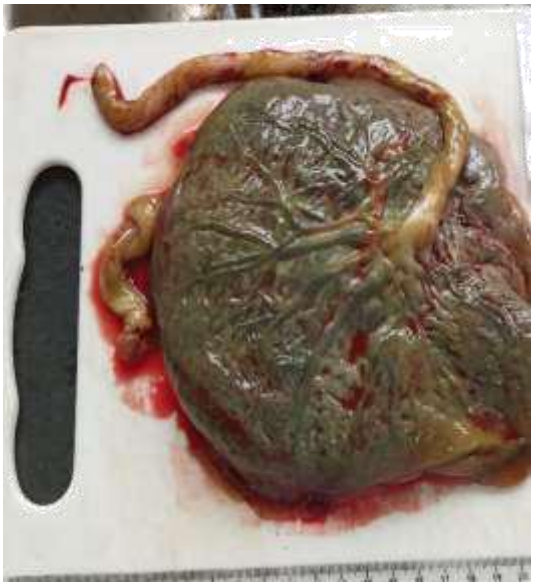


Figure 4: Green colour membranes

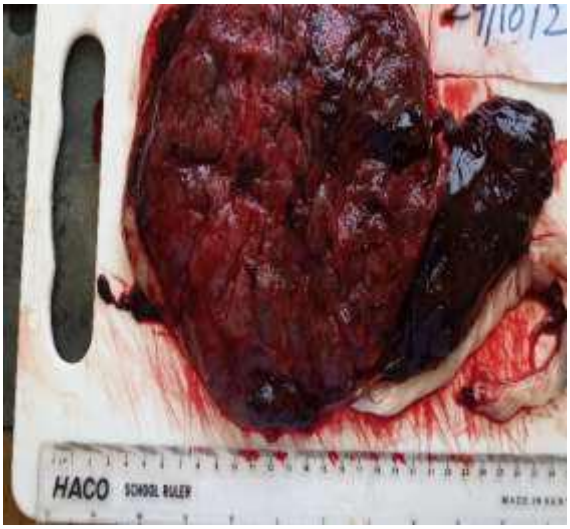


Figure 5: Retro-placenta hematoma

Figure 6: Succenturiate lobe

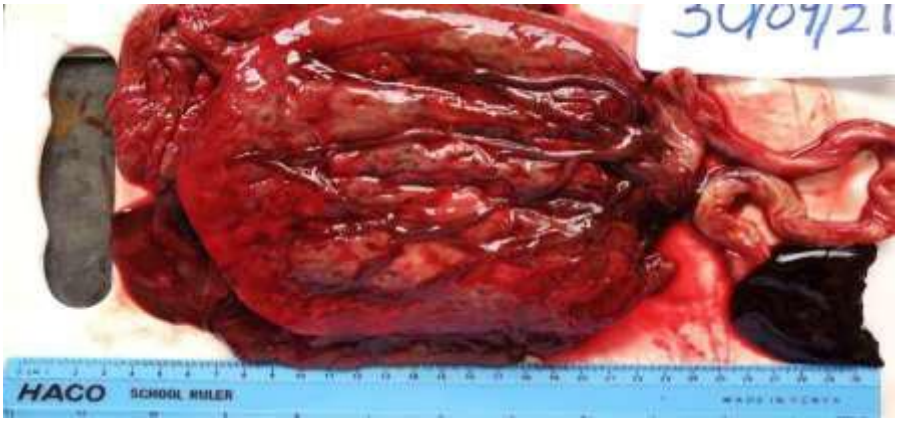


Figure 7: Lateral cord insertion in case of battledore placenta

4.3. Objective 2: Histological comparison of placenta between fresh stillbirth and live birth

Table 5: Showing histology difference between FSB and Live birth

	Cases N=44 (%)	**Controls N=44 (%)**	**Odds Ratio (95%CI)**	**P-Value**	**AOR-**	**PVALUE**
Delayed villous maturity Yes No	4(9.1) 35(79.5)	0(4.5) 42(95.5)	-	-	-	-
Accelerated villous maturity Yes No	4(9.1) 40(90.9)	0 (0.0) 44(100)	-	-	-	-
Distal villous hypoplasia Yes No	1(22.7) 34(77.3)	0(0.0) 44(100)	-	-	-	-
Villous Edema Yes No	16(36.4) 28(63.6)	4(9.1) 40(90.9)	2.83(1.73 – 18.92)	0.025	2.35(0.86-6.43)	0.097
Percentage Affected by Villous Edema >30% < 30%	5(29.4) 12(70.6)	4(80.0) 1(10.0)	0.1(0.009-1.18)	0.048		
Villous Necrosis Yes No	0(0) 44(95.5)	0(0.0) 44(100)	-	-	-	
Syncytial Knots Yes No	33(75.0) 11(25.0)	30(68.2) 14(31.8)	0.8(0.21 – 2.76)	0.680		
Percentage affected by syncytial knots >30% <30%	14(42.4) 19(57.6)	18(60.0) 12(40.0)	0.49(0.18 – 1.34)	0.167		

Table 6: Histology between fresh stillbirth and livebirth

	Cases N=44(%)	Controls N=44(%)	Odds ratio (CI)	P-Value	AOR	P value
Villitis						
Yes	**15(34.1)**	**4(9.1)**	**5.1(1.56 – 17.2)**	**0.005**	**5.7(1.82-25.2)**	**0.004**
No	29(65.9)	40(90.9)				
Intervillositis					3.4(0.85-18.23	0.290
Yes	6(13.6)	2(4.5)	3.32(0.63	0.322		
No	38(86.4)	42(95.5)	– 17.43)			
Fetal Inflammatory Response					-	-
Yes	2(4.5)	0	-	-		
No	42(95.5)	44(100.0)				
Calcification					-	-
Yes	2 (4.5)	0	-	_		
No	42(95.5)	44(100.0)				
Foetal thrombotic vasculopathy						
Yes	**10(22.7)**	**2(4.5)**	**6.1(1.27-30.11)**	**0.013**	**6.4(1.73,26.03)**	**0.016**
No	34(77.3)	42(95.5)				
Villous vascularity						
Yes	**25(56.8)**	**6(13.6)**	**7.6(2.92 – 23.7)**	**<0.0001**	**6.94(2.420.08)**	**<0.0001**
No	19(43.2)	38(86.4)				
Fibrin deposits					-	-
Yes	10(22.7)	0 (0.0)	-	-		
No	34((77.3)	44(100)				

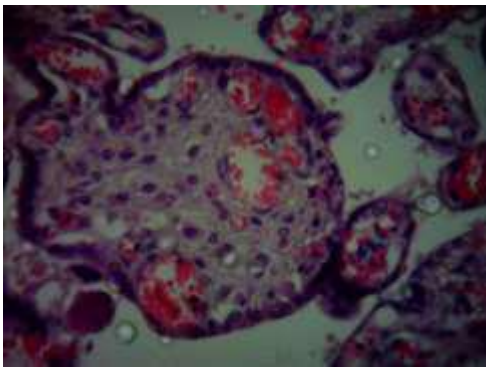


fig 7: ×400 polymorph nuclear cells infiltrating terminal villi in a case of villitis

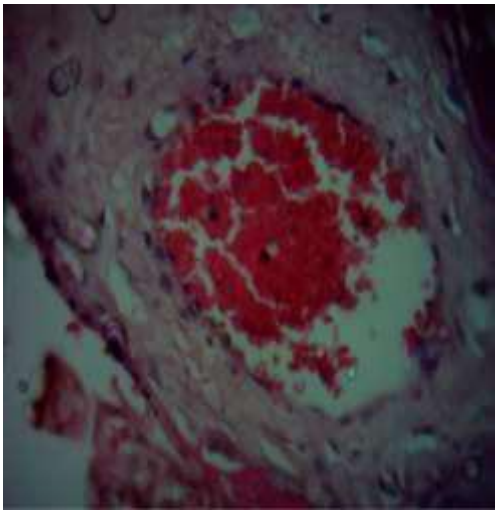


fig 8: ×400 fetal thrombotic vasculopathy

4.4. Objective 3: Socio-demographic, medical and obstetrics factors

Table 9: Socio-demographic characteristics between cases and controls

Socio-demographic characteristics	**Case N=44**	**Control N=44**	**OR(CI)**	**P-value**
Maternal age (Mean± SD)	29.2 (±6)	26.2(±5)		
<20	4(9.1)	2(4.5)	2.76(0.12-2.78)	0.07
20-34	29(65.9)	40(90.0)		ref
>35	**11(25)**	**2(4.54)**	**6.5(1.32-31.91)**	**0.043**
Education level				
Primary education	**14(31.8)**	**9(20.5)**	**6.74(1.49,30.48)**	**0.013**
Secondary	**27(61.4)**	**22(50.0)**	**5.32(1.34,21.05)**	**0.017**
Tertiary education	3(6.8)	13(29.5)		ref
Occupation				
Unemployed	25(56.8)	20(45.5)	2.4(0.44, 13.2)	0.314
Informal employment	13(29.5)	22(50)	5.1(0.89,28.9)	0.232
Formal employment	6(13.6)	2(4.5)	ref	
Religion				
Christian	43(97.7)	42(95.5)	2.1(0.18, 23.4)	0.5
Muslim	1(2.3)	2(4.5)		ref
Residence				
Nairobi	40(90.9)	43(97.7)	0.55(0.24,1.67)	0.131
Kiambu	2(4.5)	1(2.3)	0.87(0.06,1.41)	0.341
Kajiado	2(4.5)	0		ref

Table 10: Obstetrics and medical factors

	Cases n=44(%)	Controls n=44(%)	OR(CI)	P value
Parity				
≤1	31(70.5)	34(77.3)	0.7(0.27,1.83)	0.468
>1	13(29.5)	10(22.7)	ref	1
No of ANC Visits				
Less than 4	20(45.5)	16(36.4)	1.46(0.62, 3.43)	
4 and above	24(54.5)	28(63.6)	ref	
HIV	3(6.8)	3(6.8)		1.000
Anemia	4(9.0)	1(2.3)	4.3(0.46,40.12)	0.360
Pre-eclampsia (sf +wsf)	6(11.4)	2(4.5)	3.32(0.63,17.43)	0.433
Gestational diabetes	-	-		-
Chronic hypertension	1	0	-	-
Gender of child				
Male	33(75)	25(56.8)	2.2(0.92,5.6)	0.057
Female	11(25)	19(43.2)	ref	
Birth weight				
Less than 2500g	**16(36.4)**	**8(18.2)**	**2.5(1.56,6.87)**	**0.046**
2500g and above	28(63.6)	36(81.8)	ref	
Gestational age Mean	37.0(4)	37.3(3)		
<37 weeks	14(29.5)	10(27.3)	1.12(0.44,2.83)	0.510
≥37 weeks	30(70.5)	34(72.7)	ref	
Mode of delivery				
SVD	31(70.5)	37(84.1)	ref	ref
CS	11(25)	4(9.1)	3.28(0.95,11.34)	0.224
Breech	2(4.5)	3(6.8)	0.8(0.12,5.07)	0.33
Placenta abruption	5(11.6)	0	-	-
Obstructed labor	4	1	3.91(0.42 36.4)	0.170
No ½ fhr monitoring	**17**	**6**	**3.3(1.21,9.14)**	**0.04**
Referred from other facilities	13(29.5)	5(11.4)	3.27(1.05, 10.17)	0.036

CHAPTER 5: DISCUSSION

5.1. Objective 1: Gross morphology differnce between fresh stillbirth And livebirth

Placenta examination in cases of stillbirth can provide insight on causative/associated factors with fetal demise. There was a statistically significant difference in placental weight in cases compared to controls (.P=0.041.)Similar findings were shown in Omolo et al Kenya (22) Purnima Et al (26) where their findings were lower placental weight was significantly associated with stillbirth .Similar findings were also elaborated in Leftwich et al 2018 (USA)Placentas of (31) stillbirths were more likely to have decreased placental weight (44% vs. 20%).Determination of placental weights during gross examination is very important. Different gestational age has different placenta weights. Small placenta is associated with low reserve/capacity to support foetal needs. Small placental weights might also be a sign of IUGR that was not recognised during routine antenatal visits.

Retro placenta hematoma of ≥ 50% (maternal surface of placenta disc) was noted to be more in cases compared to the controls AOR 3.9(1.22, 12.83) P=0.022.This findings were similar to Pinar et al(27) 2014The prevalence of retro placental hematoma among stillbirths was significantly greater than in controls, 23.8% v 4.2% (OR 7.08, 95% CI 4.83-10.38). Weida et al in 2015 found that retro placental hematoma of > 50 was significantly associated with stillbirth. Retroplacental hematoma of more than 50% in gross pathology examination might attribute to presence of acute abruption that was not picked during intrapartum period and lead to fetal loss

Green colour of the membrane of placenta was significantly associated with fresh stillbirth AOR5.92 (1.13-30.65) p value 0.04. This green colour could have been an indicator of fetal distress or non-reassuring foetal status. A study done in in Ethiopia by Tasew et al(2019)

Ethiopia meconium stained liquor was associated with 13 times likelihood of stillbirth AOR 7.8 95% CI 1.73-8.18(32).In contrast lee et al in China (33) found poor Apgar score and admission into new-born unit was associated with meconium stained liquor as opposed to fresh stillbirth.

5.2. Objective 2: Histological difference between fresh stillbirth and live birth

In this study we found out that villitis, fetal thrombotic vasculopathy and villous vascularity to be associated with fresh stillbirth.

Villitis is defined as an inflammatory reaction on the terminal villi as seen by either presence of polymorph nuclear or lymphocyte/macrophage cells. This shows that there would have been an acute infection or chronic inflammation during intrapartum care. This was noted to be significant in cases compared to controls.(AOR 4.9(1.82-25.52) p=0.005).Similar findings in Anantha et al (acute villitis p 0.04, and chronic villitis p=0.02) and Varli et al (Sweden) (AOR 3.87 ci 1.38-10.83) (34) villitis was significantly associated with stillbirth.

Villous vascularity entails increased no of blood vessels in the terminal villi. The normal number of vessels per terminal villi is noted to be 2-6. In cases where we have more than 6 per terminal villi it will indicate hypervascularity. This is seen in cases of hypoxia where it is a compensatory mechanism to increase number of vessels in terminal villi. We found statistically significant findings in between cases and controls. Villous vascularity AOR6.94 (2.4-20.88) p<0.001. Sung et al in USA (35) and Atshuler et al (36) had similar findings.

Fetal thrombotic vasculopathy is defined as vascular obstruction of arteries and veins in fetal circulation of the placenta. This may lead to necrosis of surrounding vessels and eventual stillbirth. We found statistically significant findings between the FSB and controls. AOR-6.4(1.73-26.03)P=0.016.Similar findings in Kraus et al(37) Pinar(27)was present in 23% of

stillbirths and 7% of live birth Anantha et al (27)Foetal vascular thrombi in the chorionic plate (30.58 vs. 14.12%; $p = 0.02$).

5.3. Objective 3:Secondary objective:Sociodemographic medical and obstetric factors

We found older maternal age >35 was associated with stillbirth. Advance maternal age had been associated with adverse maternal and neonatal outcome. This age group is affected adversely with acquisition of comorbid conditions including hypertension and diabetes. This age groups are expected to have good fetal and maternal antenatal follow up to screen for any comorbid conditions and plan for uneventful delivery. We found that Fresh stillbirth was more in cases that were above 35 years of age OR 6.5(1.32,31.91) p=0.043 Similar findings in Gwako et al 2020(12) and Zhu et al in China (13).

Education is social determinant of health and has a direct influence on health seeking behaviour of an individual as described in Gwako et al(18).. As such, they allow early diagnosis of any anomalies and timely interventions. We found lower education was associated with stillbirth OR 6.74(1.49,30.48) p=0.013 similar findings in Gwako et al. and Zhu et al and Ongeso et al (12)(13)(11).

There was an association between low birth weight and fresh stillbirth which was statistically significant. OR .5-(1.56,6.87) p=0.046.36.4% of the cases compared to 18.2% of the controls had low birth weight. Similar studies including Gardosi et al found that low birth weight prematurity and IUGR were greatly correlated to stillbirth(38). Similar study in Tanzania by Chuwa et al found that fetus with low birth weight have increased risk of intrapartum stillbirth, acclaimed that is associated with under developed respiratory systems (16).

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1. CONCLUSION

From our findings FSB had lower placental weights, had significant green coloured membranes and retro placental hematoma. The FSB placenta had significant villitis, villous vascularity and fetal thrombotic vasculopathy. In our secondary objective older maternal age of > 35, lower maternal education and lower birth weight were associated with fresh stillbirth.

6.2. RECOMMENDATIONS

Improved fetal surveillance at Pumwani maternity hospital with use of NST and CTG during labour avert adverse maternal and neonatal outcome (meconium-stained liquor and in cases of abruption placenta).

Introduce Placental examination in a case of stillbirth can detect/diagnose many maternal/fetal conditions and thereby can help in preventing future stillbirths.

Improve antenatal care for mothers with advanced maternal age >35 where important screening for comorbidities, education on danger signs and planning for delivery should be emphasized.

Area for further research

Use of aspirin in cases of fetal thrombotic vasculopathy to avert stillbirth

Biomarkers of in cases of stillbirth

REFERENCES

1. STILL BIRTH -WHO.

2. Anzagra L. Stillbirth Rates in the Tamale Metropolis of Ghana. Public Heal Res [Internet]. 2014;4(5):160–5. Available from: The study estimated the stillbirth rates in the Tamale metropolis of Ghana over a five year period (from January, 2009 to June, 2013). It then investigated as to whether or not these rates significantly varied according to types and hospitals respectively

3. Blaikie K, Danna VA. Understanding the complexities of unexplained stillbirth in sub-Saharan Africa : a mixed-methods study. 2021;1206–14.

4. Wako BA, Epiu I, Otor S. Maternal factors associated with stillbirth among women in Marsabit County, Kenya. Afr J Midwifery Womens Health. 2021;15(1):1–11.

5. Causes of death among stillbirths. JAMA. 2011 Dec;306(22):2459–68.

6. Akombi BJ, Ghimire PR, Agho KE, Renzaho AM. Stillbirth in the African Great Lakes region: A pooled analysis of Demographic and Health Surveys. PLoS One. 2018;13(8):1–15.

7. De Bernis L, Kinney M V., Stones W, Ten Hoope-Bender P, Vivio D, Leisher SH, et al. Stillbirths: Ending preventable deaths by 2030. Lancet. 2016;387(10019):703–16.

8. Bjerregaard-andersen M, Lund N, Sofie A, Joergensen P, Jepsen FS, Unger HW, et al. Stillbirths in urban Guinea-Bissau : A hospital- and community-based study. 2018;866:1– 18.

9. Madhi SA, Briner C, Maswime S, Mose S, Mlandu P, Chawana R, et al. Articles Causes of stillbirths among women from South Africa : a prospective , observational study. Lancet Glob Heal. 7(4):e503–12.

10. Aminu M, Bar-Zeev S, White S, Mathai M, Van Den Broek N. Understanding cause of stillbirth: A prospective observational multi-country study from sub-Saharan Africa. BMC Pregnancy Childbirth. 2019;19(1).

11. Ongeso A, Lukorito M, Kabo J. Factors Influencing High Prevalence of Fresh Still Births in Mbagathi County Hospital, Nairobi - Kenya. Int J Adv Res. 2018;6(4):36–48.

12. Gwako GN, Obimbo MM, Gichangi PB, Kinuthia J, Gachuno OW, Were F. Association between obstetric and medical risk factors and stillbirths in a low-income urban setting. Int J Gynecol Obstet. 2020;(May):1–6.

13. Zhu J, Liang J, Mu Y, Li X, Guo S, Scherpbier R, et al. Sociodemographic and obstetric characteristics of stillbirths in China: A census of nearly 4 million health facility births

between 2012 and 2014. Lancet Glob Heal [Internet]. 2016;4(2):e109–18. Available from: http://dx.doi.org/10.1016/S2214-109X(15)00271-5

14. Idowu AA, Death AF. Socio-Demographic Determinants of. 2017;3:15–8.

15. Ashish KC, Wrammert J, Ewald U, Clark RB, Gautam J, Baral G, et al. Incidence of intrapartum stillbirth and associated risk factors in tertiary care setting of Nepal: A case-control study. Reprod Health [Internet]. 2016;13(1):1–11. Available from: http://dx.doi.org/10.1186/s12978-016-0226-9

16. Chuwa FS, Mwanamsangu AH, Brown BG, Msuya SE, Senkoro EE, Mnali OP, et al. Maternal and fetal risk factors for stillbirth in Northern Tanzania: A registry-based retrospective cohort study. PLoS One. 2017;12(8):e0182250.

17. Saidi F, Chiudzu G, Milala B, Jennifer H. Factors associated with stillbirths among women delivering at a resource limited tertiary hospital in. 2021;

18. Gwako GN, Were F, Obimbo MM, Kinuthia J, Gachuno OW, Gichangi PB. Association between utilization and quality of antenatal care with stillbirths in four tertiary hospitals in a low-income urban setting. Acta Obstet Gynecol Scand. 2020;(May):1–8.

19. Afulani PA. Determinants of stillbirths in Ghana: Does quality of antenatal care matter? BMC Pregnancy Childbirth [Internet]. 2016;16(1):1–17. Available from: http://dx.doi.org/10.1186/s12884-016-0925-9

20. Kulkarni AD, Palaniappan N, Evans MJ. Placental Pathology and Stillbirth: A Review of the Literature and Guidelines for the Less Experienced. J Fetal Med. 2017;4(4):177–85.

21. ACOG Practice Bulletin No. 102: management of stillbirth. Obstet Gynecol. 2009 Mar;113(3):748–61.

22. Owino A, Gachuno O, Tamooh H, Rogena EA. GROSS PRESENTATION AND HISTOMORPHOLOGICAL CHANGES OF PLACENTAE IN PATIENTS PRESENTING WITH INTRAUTERINE FOETAL DEATH AT KENYATTA NATIONAL HOSPITAL. 2014;91(7).

23. Machin G, Ackerman J, Gilbert-Barness E. Abnormal Umbilical Cord Coiling Is Associated with Adverse Perinatal Outcomes. Pediatr Dev Pathol. 2000 Sep 1;3:462–71.

24. Ananthan A, Nanavati R, Sathe P, Balasubramanian H. Placental Findings in Singleton Stillbirths: A Case-control Study. J Trop Pediatr. 2019;65(1):21–8.

25. Mecacci F, Serena C, Avagliano L, Cozzolino M, Baroni E, Rambaldi MP, et al. Stillbirths at term: Case control study of risk factors, growth status and placental histology. PLoS One. 2016;11(12):1–11.

26. Tiwari P, Gupta MM, Jain SL. Placental findings in singleton stillbirths: a case-control study from a tertiary-care center in India. J Perinat Med. 2021;

27. Pinar H, Goldenberg RL, Koch MA, Heim-Hall J, Hawkins HK, Shehata B, et al. Placental findings in singleton stillbirths. Obstet Gynecol. 2014 Feb;123(2 Pt 1):325–36.

28. Hug L, You D, Blencowe H, Mishra A, Wang Z, Fix MJ, et al. Global , regional , and national estimates and trends in stillbirths from 2000 to 2019 : a systematic assessment. Lancet [Internet]. 2021;398(10302):772–85. Available from: http://dx.doi.org/10.1016/S0140-6736(21)01112-0

29. Maiti K, Sultana Z, Aitken RJ, Morris J, Park F, Andrew B, et al. Evidence that fetal death is associated with placental aging. Am J Obstet Gynecol. 2017;217(4):441.e1-441.e14.

30. Minimally Invasive Tissue Sampling (MITS) Standard Operating Procedure (SOP) Incentive Grant Awardees. 2019;(October):1–44.

31. Leftwich H, Nicasio E, Masiero J, Novak B, Leung K, Vanguri V. Signs of Poor Placental Perfusion In Placental Pathology in Stillbirth Fetuses [19B]. Obstet Gynecol [Internet]. 2018;131. Available from: https://journals.lww.com/greenjournal/Fulltext/2018/05001/Signs_of_Poor_Placental_Perfusion_In_Placental.81.aspx

32. Tasew H, Zemicheal M, Teklay G, Mariye T. Risk factors of stillbirth among mothers delivered in public hospitals of Central Corresponding author : 2020;(January).

33. Lee J, Romero R, Lee KA, Kim EN, Korzeniewski SJ, Chaemsaithong P, et al. Meconium aspiration syndrome: a role for fetal systemic inflammation. Am J Obstet Gynecol. 2016 Mar;214(3):366.e1-9.

34. Jaiman S, Romero R, Pacora P, Jung E, Bhatti G, Yeo L, et al. Disorders of placental villous maturation in fetal death. 2020;48(4):345–68.

35. Sung DK, Baergen RN. Focal Chorangiosis: Does It Have Clinical and Pathologic Significance? Pediatr Dev Pathol [Internet]. 2019 Feb 13;22(5):406–9. Available from: https://doi.org/10.1177/1093526619830866

36. Altshuler G. Chorangiosis. An important placental sign of neonatal morbidity and mortality. Arch Pathol Lab Med. 1984;108(1):71–4.

37. Kraus FT. Fetal Thrombotic Vasculopathy: Perinatal Stroke, Growth Restriction, and Other Sequelae. Surg Pathol Clin [Internet]. 2013 Mar;6(1):87–100. Available from: https://pubmed.ncbi.nlm.nih.gov/26838704

38. Gardosi J, Madurasinghe V, Williams M, Malik A, Francis A. Maternal and fetal risk factors for stillbirth: Population based study. BMJ. 2013;346(7893):1–14.

39. Mondal D, Galloway TS, Bailey TC, Mathews F. Elevated risk of stillbirth in males: Systematic review and meta-analysis of more than 30 million births. BMC Med. 2014;12(1).

40. Muglu J, Rather H, Arroyo-manzano D, Id SB, Id JZ, Id ST. Risks of stillbirth and neonatal death with advancing gestation at term : A systematic review and meta-analysis of cohort studies of 15 million pregnancies. 2019;1–16.

29. Rogers MS, J.M.Mongelli, K.H.Tsang. Lipid peroxidation in cord blood at birth : the effect of labour. 1998;105(July):739–44.

30. S. Arikan,D Konokoglu,C Arikan,T Akcay,I Davas. Lipid Peroxidation and Antioxidant Status in Maternal and Cord Blood. Gynecol Obstet Invest 2001;51:145–149

APPENDICES

Appendix 1: Data Collection Form

Case Group *Series No. ……Or,* **Control Group** *Series No. ……..*

Before proceeding with data collection, the research assistant will identify form for either case group or control group.

Complete the data collection with relevant data abstracted from the patient files, gathered from the patient, or as observed from the placenta assessment.

Part A: Maternal Demographic Data

1. Maternal age in years ……..
2. Marital status
    i) Single
    ii) Married
    iii) Widow
    iv) Separated
3. Level of education
    i. No formal education
    ii. Primary
    iii. Secondary
    iv. University/College
    v. Postgraduate
4. Occupation
    i. Student
    ii. Formal employment
    iii. Self-employed
    iv. Casual laborer
    v. Unemployed
5. Religion

i. Christian

ii. Muslim

iii. Other

iv. None

6. County of residence ----------

Part B: Maternal Characteristics

7. Current parity …… + ……

8. Gravidity ……

9. LMP ……EDD……..

10. Gestation in weeks and days

a. By dates …… weeks …… days *Or*

b. By the earliest possible Ultrasound …… weeks …… days

11. Presence of any of these maternal conditions

	Maternal Conditions /obstetric condition	Present	Absent
a.	Pre-eclampsia		
b.	Chronic Hypertension		
c.	Thrombocytopenia		
d.	Thyroid Disease		
e.	Gestational Diabetes		
f.	Asthma		

12.NO OF ANC VISIT

a)none

b)1

c)2

d)3

e-4 and above-_____

Part C: Delivery Outcomes.

12. Mode of delivery
    a. Spontaneous vertex delivery …….
    b. Caesarean section ……..
13. Birth weight in kgs ……
14. Sex of the new-born
    i. Male ……..
    ii. Female …….
15. Viability of the fetus
    i. Alive …….
    ii. Fresh stillbirth ……
16. Did the new-born has intrauterine growth restriction
    i. Yes
    ii. No

Part D: Placental Morphology Assessment

17. Cord length in centimetres……
18. NO of coils per 5cm…
19. Placenta weight in grams ……
20. Cord Insertion type
    a. Central
    b. Eccentric
    c. Marginal
    d. Velamentous
21. Number of blood vessels
    a. Normal count (two arteries and one vein)
    b. Abnormal count
22. Placental completeness
    a. Complete/intact
    b. Incomplete
23. Abnormalities of the shape
    a. No abnormality (single lobe)
    b. Bilobate
    c. Multi-lobed
    d. Succenturiate
24. Abnormalities of maternal placental surface
    a. Presence of placenta infarcts Yes or No
    b. Adherent blood clots Yes or No
    c. Chorioangioma Yes or No
25. Others notable characteristics …….

Part E: Histopathology Assessment Report

26.histopathology

parameter	Case	control
Delayed villous maturity		
Accelerated villous maturity		
Avascular villi		
Villous edema		
Syncytial knots		
vilitis		
Villous vascularity		
Fetal thrombotic vasculopathy		
Fetal inflammatory		

a.

Appendix 2: Dummy Tables

Table I: Maternal Characteristics

Factor	Categories	Case Group N (%)	Control Group N (%)	P-value
Maternal Age (Years)	≤ 20			
	21–25			
	26–30			
	31–35			
	≥ 36			
Gestational Age (weeks)	≥28 -<37			
	≥37- <40			
	≥40- ≤42			
Parity				

Gravidity				
Mode of Delivery	SVD			
	CS			
Smoking	Yes			
	N0			
No of ANC visit				
Occupation	Student			
	Self-employment			
	Formal employment			
	Unemployed			

Table II: Association between obstetric/ medical condition and fsb

Factor	Categories	FSB N (%)	Live birth N (%)	Odds Ratio (95% CI)	P-Value
Pre-eclampsia	Mild				
	Severe				
Chronic Hypertension	Yes				
	No				
IUGR	Yes				
	No				
Thyroid Disease	Yes				
	No				

Gestational Diabetes	Yes				
	No				
Asthma in pregnancy	Yes				
	No				

Table III: Placental Morphology Assessment Findings

Factor		**FSB Mean**	***Live birth* Mean**	**Odds Ratio**	**P-value**
Cord length in centimeters					
Placental weight in grams					
Factor	**Subcategories**	**Case GroupN%**	**Control Group N%**	**Odds Ratio**	**P-value**
Cord insertion type	Central				
	Eccentric				
	Marginal				

	Velamentous					
Coiling of cord	hypercoiled					
	undercoiled					
	normal					
Number of cord blood Vessels	Normal count					
	Abnormal count					
Placental completeness	Complete/intact					
	Incomplete					
Abnormalities of placenta Shape	Normal shape					
	Bilobate					
	Multilobed					
	Succenturriate					
Abnormalities of maternal placenta surface	Placenta infarcts	Yes				
		No				
	Adherent blood clots	Yes				
		No				

Appendix 3: Budget

Item	**Description**	**Quantity**	**Amount (Ksh)**	**Total (Kshs.)**
Personnel	Research assistants	5	12000	60,000
	Statistician	1	35000	35,000
Supplies/ Materials	Draft proposals printing	70 pages x 3 copies	10 per page	2100
	Final proposal printing	70 pages x 3 copies	10 per page	2100
	Questionnaires printing	4 pages x 50 copies	10 per	2000
	Lab form	50 copies	10 per	500
	Lab cost			150,000
	Specimen containers	92	100	9200
	Airtime and Bundles	3gb per month for 4months	5000	15,000
	Training of research team	2	5000	10,000
	Laptop	1		70,000
Transport and Lunch	Within Nairobi			5000
KNH/UON ERC	Submission to ERC (twice)			4,000
Miscellaneous costs				50,000
Total				414,900

Appendix 4: Study timeframe

	December 2020	January 2021	February to May 2021	June - december2021-April 2022	January to May-2022	June 2022
PROPOSAL DEVELOPMENT						
PROPOSAL PRESENTATION						
ETHICS						
DATA COLLECTION						
ANALYSIS						
RESEARCH PRESENTATION						
MANUSCRIPT WRITING						

Appendix 5: Consent Form

PARTICIPANT INFORMATION AND CONSENT FORM SAMPLE ADULT CONSENT FOR ENROLLMENT IN THE STUDY

(To be administered in English or any other appropriate language e.g Kiswahili translation) **Title of Study: DETERMINING MARKERS OF OXIDATIVE STRESS IN PLACENTAE OF PATIENT WITH FRESH STILLBIRTH AT PUMWANI MATERNITY HOSPITAL**

Principal Investigator\and institutional affiliation: DR PAUL OMAGWA / UNIVERSITY OF NAIROBI

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in medical research: i) Your decision to participate is entirely voluntary ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal
iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol No._____

WHAT IS THIS STUDY ABOUT.

The researchers listed above are interviewing individuals who have a live birth or fresh still birth. The purpose of the interview is to find out if there are markers of oxidative stress in placenta of patients with fresh stillbirth as opposed to live birth. Participants in this research study will be asked questions bio data and health related history.

There will be approximate 96 participants in this study randomly chosen. We are asking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen:

You will be interviewed by a trained interviewer in a private area where you feel comfortable answering the questions. The interview will last a p p r o x i m a t e l y 20 minutes on questions such as your age, marital status, level of education, occupation, and county or residence.

We will ask for a telephone number where we can contact you in the process of the data seeking clarification when necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others. Also, instead of your placenta being disposed after delivery as this is the standard practice, we will obtain it and store it for investigations since this is the main source of the study samples.

ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer

database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

You may benefit by receiving free counselling at Pumwani maternity hospital. Psychological support to mothers who would have had FSB will receive grief counselling. We will work in tandem with grief counsellor to assist as in this scenario Also, the information you provide will help us better understand risk factors and causation of fresh stillbirth This information is a contribution to science and will greatly improve screening and future management of patients

WILL BEING IN THIS STUDY COST YOU ANYTHING?

The study will involve recruiting patients for information on socio -demographic and obstetric risk factors

No financial contribution is required for study participant.

WILL YOU GET REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?

No financial appreciation will happen in this study

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email

uonknh_erc@uonbi.ac.ke. Or you can call the principal investigator for this study,

Dr. Paul Omagwa +254 715664783

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study:	**Yes**	**No**
I agree to have (define specimen) preserved for later study:	Yes	No
I agree to provide contact information for follow-up:	Yes	No

Participant printed name: _

Participant signature / Thumb stamp_____ **Date** _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher 's Name:_____ **Date**: _____

Signature_____

Role in the study: _____*[i.e. study staff who explained informed consent form.]*

For more information contact_____at_____from

_____to _____

Witness Printed Name (*If witness is necessary, A witness is a person mutually acceptable to both the researcher and participant*)

Name_____ **Signature /Thumb stamp:** _____

Contact information…….. _ Date; _____

Kiambatisho 5: Fomu ya Idhini

TAARIFA YA MSHIRIKI NA FOMU YA KIRATIBISHO KIBALI CHA MTU MZIMA WA WAKUU WA KUJIANDIKISHA KATIKA MAFUNZO

(Itasimamiwa kwa Kiingereza au lugha nyingine yoyote inayofaa mfano tafsiri ya Kiswahili) Kichwa cha Somo: KUJITAMBUA ALAMA ZA MSONGO WA KUPATIKANA KATIKA KUWEKA KWA MGONJWA NA UTHIBITISHO WA KIASI KWENYE HOSPITALI YA TAIFA YA KENYATTA NA HOSPITALI YA WAZAZI

Mchunguzi Mkuu \ na ushirika wa kitaasisi: DK PAUL OMAGWA / CHUO KIKUU CHA NAIROBI

Utangulizi:

Ningependa kukuambia juu ya utafiti unaofanywa na watafiti walioorodheshwa hapo juu. Madhumuni ya fomu hii ya idhini ni kukupa habari utakayohitaji kukusaidia kuamua ikiwa ni mshiriki wa utafiti huo au la. Jisikie huru kuuliza maswali yoyote juu ya madhumuni ya utafiti, nini kinatokea ikiwa unashiriki katika utafiti, hatari na faida zinazowezekana, haki zako kama kujitolea, na chochote kingine kuhusu utafiti au fomu hii ambayo haijulikani Wakati tumejibu maswali yako yote kukuridhisha, unaweza kuamua kuwa kwenye somo au la. Utaratibu huu unaitwa 'idhini ya habari' Mara tu utakapoelewa na kukubali kuwa kwenye utafiti, nitakuomba utie sahihi jina lako kwenye fomu hii. Unapaswa kuelewa kanuni za jumla ambazo zinatumika kwa washiriki wote katika utafiti wa matibabu:

i) Uamuzi wako wa kushiriki ni wa hiari kabisa ii) Unaweza kujiondoa kwenye utafiti wakati wowote bila kutoa sababu ya kujiondoa kwako

iii) Kukataa kushiriki katika utafiti hakutaathiri huduma unazostahiki katika kituo hiki cha afya au vituo vingine. Tutakupa nakala ya fomu hii kwa kumbukumbu zako.

Naweza kuendelea? NDIO LA

Utafiti huu umeidhinishwa na Itifaki Na.

HAYA NI MAFUNZO GANI KUHUSU

Watafiti walioorodheshwa hapo juu wanawahoji watu ambao wamezaliwa moja kwa moja au kuzaliwa upya. Kusudi la mahojiano ni kujua ikiwa kuna alama za mafadhaiko ya kioksidishaji kwenye kondo la wagonjwa walio na kuzaliwa upya bila kufa kwa kuzaliwa. Washiriki katika utafiti huu wataulizwa maswali biodata na historia inayohusiana na afya.

Kutakuwa na washiriki wa takriban katika utafiti huu waliochaguliwa kwa nasibu. Tunaomba idhini yako kuzingatia kushiriki katika utafiti huu.

NINI KITATOKEA UKIAMUA KUWA KWENYE UTAFITI HUU WA UTAFITI?

Ikiwa unakubali kushiriki katika utafiti huu, mambo yafuatayo yatatokea:

Utahojiwa na mhojiwa aliyefunzwa katika eneo la kibinafsi ambapo unahisi raha kujibu maswali. Mahojiano hayo yatachukua takriban dakika 20 kwa maswali kama umri wako, hali yako ya ndoa, kiwango cha elimu, kazi, na kaunti au makazi.

Tutauliza nambari ya simu ambapo tunaweza kuwasiliana na wewe katika mchakato wa data kutafuta ufafanuzi inapobidi. Ikiwa unakubali kutoa anwani yako ya mawasiliano, itatumika tu na watu wanaofanya kazi kwa utafiti huu na hawatashirikiwa na wengine kamwe. Pia, badala ya kondo lako kutupwa baada ya kujifungua kwani hii ndio kawaida, tutapata na kuihifadhi kwa uchunguzi kwani hii ndio chanzo kikuu cha sampuli za utafiti.

KUNA ATHARI ZOZOTE, ZINAZIDHARAU HASARA ZINAZOHUSIANA NA UTAFITI HUU?

Utafiti wa kimatibabu una uwezo wa kuanzisha hatari za kisaikolojia, kijamii, kihemko na kiafya. Jitihada inapaswa kuwekwa kila wakati ili kupunguza hatari. Hatari moja ya kuwa katika utafiti ni kupoteza faragha. Tutaweka kila kitu unatuambia kama siri iwezekanavyo. Tutatumia nambari ya nambari kukutambulisha kwenye hifadhidata ya kompyuta inayolindwa na nywila na tutaweka rekodi zetu zote za karatasi kwenye kabati la faili lililofungwa. Walakini, hakuna mfumo wowote wa kulinda usiri wako ambao unaweza kuwa salama kabisa, kwa hivyo bado

inawezekana kwamba mtu anaweza kugundua kuwa ulikuwa kwenye utafiti huu na angeweza kupata habari kukuhusu.

Pia, kujibu maswali kwenye mahojiano inaweza kuwa mbaya kwako. Ikiwa kuna maswali ambayo hautaki kujibu, unaweza kuyaruka. Una haki ya kukataa mahojiano au maswali yoyote yanayoulizwa wakati wa mahojiano.

KUNA FAIDA ZOZOTE ZINAKUWA KATIKA UTAFITI HUU?

Unaweza kufaidika kwa kupata ushauri wa bure. Pia, habari unayotoa itatusaidia kuelewa vyema sababu za hatari na sababu ya kuzaliwa upya kwa mtoto mchanga Habari hii ni msaada kwa sayansi na itaboresha sana uchunguzi na usimamizi wa baadaye wa wagonjwa

JE, KUWA KWENYE UTAFITI HUU KGHARIMIA CHOCHOTE?

Utafiti huo utahusisha kuajiri wagonjwa kwa habari juu ya hatari za kijamii na idadi ya watu na hatari za uzazi

Hakuna mchango wa kifedha unaohitajika kwa mshiriki wa utafiti.

JE, UTARUDISHA KWA PESA YOYOTE ILIYOTUMIWA KWA SEHEMU YA UTAFITI HUU?

Hakuna shukrani ya kifedha itakayotokea katika utafiti huu

NINI KAMA UNA MASWALI BAADAYE?

Ikiwa una maswali zaidi au wasiwasi juu ya kushiriki katika utafiti huu, tafadhali piga simu au tuma ujumbe mfupi kwa wafanyikazi wa utafiti kwa nambari iliyotolewa chini ya ukurasa huu.

Kwa habari zaidi juu ya haki zako kama mshiriki wa utafiti unaweza kuwasiliana na Katibu / Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-Chuo Kikuu cha Nairobi Maadili na Kamati ya Utafiti Nambari ya simu 2726300 Ext. Barua pepe 44102 uonknh_erc@uonbi.ac.ke. Au unaweza kumpigia simu mchunguzi wa kanuni hii, Dk Paul Omagwa +254 715664783

Wafanyakazi wa utafiti watakulipa malipo yako kwa nambari hizi ikiwa simu ni ya mawasiliano yanayohusiana na utafiti.

CHAGUO ZAKO ZINGINE NI NINI?

Uamuzi wako wa kushiriki katika utafiti ni wa hiari. Uko huru kukataa kushiriki katika utafiti na unaweza kujiondoa kutoka kwa utafiti wakati wowote bila udhalimu au kupoteza faida yoyote.

FOMU YA MAJALIZO (TAARIFA YA MAJIBU)

Taarifa ya mshiriki

Nimesoma fomu hii ya idhini au habari hiyo imesomwa kwangu. Nimekuwa na nafasi ya kujadili utafiti huu wa utafiti na mshauri wa utafiti. Nimejibiwa maswali yangu kwa lugha ambayo ninaelewa. Hatari na faida zimeelezewa kwangu. Ninaelewa kuwa ushiriki wangu katika utafiti huu ni wa hiari na kwamba ninaweza kuchagua kujiondoa wakati wowote. Ninakubali kwa hiari kushiriki katika utafiti huu wa utafiti.

Ninaelewa kuwa juhudi zote zitafanywa kutunza habari kuhusu kitambulisho changu binafsi kuwa siri.

Kwa kusaini fomu hii ya idhini, sijatoa haki yoyote ya kisheria ambayo ninayo kama mshiriki katika utafiti wa utafiti.

Ninakubali kushiriki katika utafiti huu: Ndio Hapana

Ninakubali kuwa (fafanua kielelezo) kilichohifadhiwa kwa masomo ya baadaye: Ndio Hapana

Ninakubali kutoa habari ya mawasiliano kwa ufuatiliaji: Ndio Hapana

Jina la mshiriki aliyechapishwa:

Saini ya mshiriki / Stempu ya Thumb

Kauli ya mtafiti

Mimi, aliyesainiwa chini, nimeelezea kabisa maelezo yanayofaa ya utafiti huu kwa mshiriki aliyetajwa hapo juu na ninaamini kwamba mshiriki ameelewa na kwa hiari na kwa hiari ametoa idhini yake.

Jina la Mtafiti: ……..Tarehe:……..

Sahihi _____

Jukumu katika utafiti:……[i.e. wafanyikazi wa utafiti ambao walielezea fomu ya idhini ya habari.]

Kwa habari zaidi wasiliana na ……..kutoka…….

Kwa ……..

Jina Lililochapishwa la Shahidi (Ikiwa shahidi ni lazima, Shahidi ni mtu anayekubalika kwa mtafiti na mshiriki wote)

Name …….. saini/stempu ya kidole gumba: ……

Maelezo ya mawasiliano ……...… .. Tarehe;……

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/126

12th April 2021

Dr.Paul Oganda Omagwa
Re. No.H58/11135/2018
Dept. of Obstetrics and Gynaecology
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Omagwa

RESEARCH PROPOSAL - DIFFERENCES IN PLACENTAE STRUCTURE OF PATIENT WITH FRESH STILLBIRTH VERSUS LIVE BIRTH AT PUMWANI MATERNITY HOSPITAL (P711/12/2020)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 12th April 2021 – 11th April 2022.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website**http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information Dept, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Obstetrics and Gynaecology, UoN
Supervisors: Prof. Eunice Cheserem, Deptof Obstetrics and Gynaecology, UoN
Prof. Omondi Ogutu,Dept.of Obstetrics and Gynaecology, UoN
Dr. Obimbo Moses,Dept.os of Human Anatomy, Obstetrics and Gynaecology, UoN