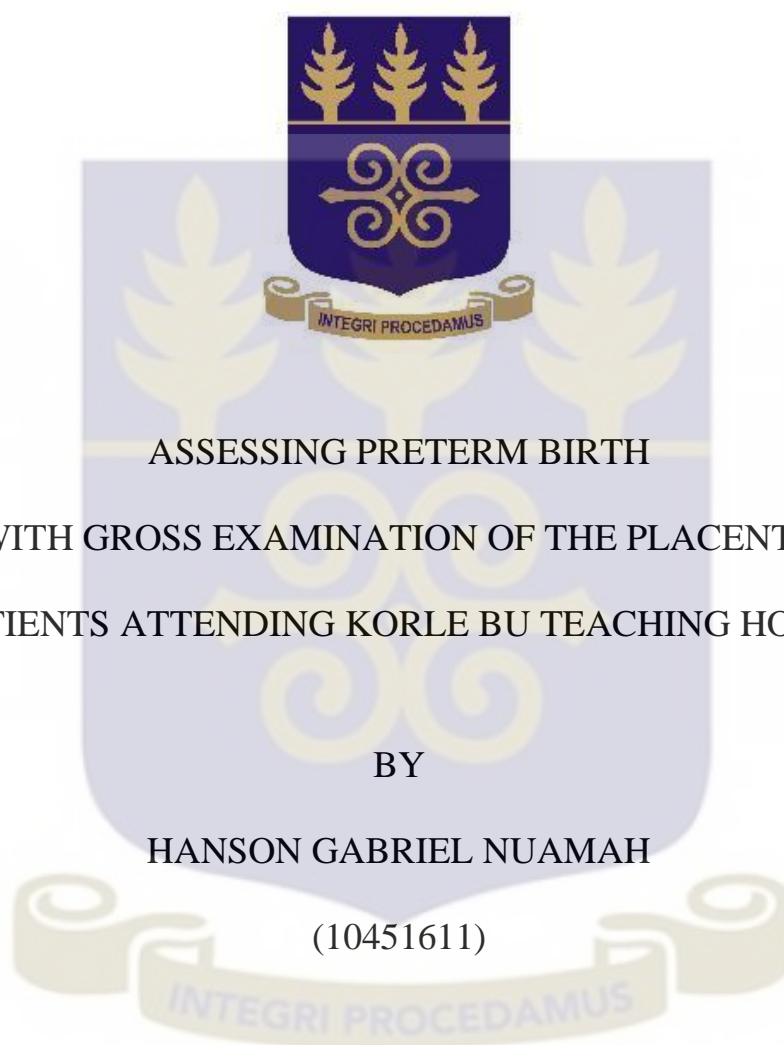


SCHOOL OF PUBLIC HEALTH
COLLEGE OF HEALTH SCIENCES
UNIVERSITY OF GHANA



ASSESSING PRETERM BIRTH
WITH GROSS EXAMINATION OF THE PLACENTA
OF PATIENTS ATTENDING KORLE BU TEACHING HOSPITAL
BY
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THIS DISSERTATION IS SUBMITTED TO THE UNIVERSITY OF GHANA,
LEGON IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE
AWARD OF MASTER OF PUBLIC HEALTH DEGREE

JULY, 2019

DECLARATION

I, HANSON GABRIEL NUAMAH, hereby declare that with the exception of the references made to other peoples' work which I have duly acknowledged, this dissertation which is my original work has neither in whole nor in part been presented to the University or elsewhere for another degree.

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DEDICATION

I dedicate this dissertation to God Almighty, my parents, Mr. and Mrs. Nuamah; my siblings, Ruth, Joseph, David, and Jonathan. They have all been a source of constant inspiration.

ACKNOWLEDGEMENT

I wish to express my sincere gratitude to my academic supervisors Dr. Bismark Sarfo and Dr. Mercy Anna Nuamah, for the immense academic guidance and support you gave me during my time in the school and my research work.

My sincere thanks to Magdalene Torto, Clara Dsane, Theophilus Brocke, Emmanuel Korankye, Deborah Doe, and Cynthia Oyekule for assisting with the data collection.

I am grateful to Dr. John Ahenkorah and Dr. Patience B. Tetteh-Quarcoo. You have been great inspiration and mentors to me.

A special thanks to my diverse and vibrant study group “MPH GENGING.” You made learning interesting and enjoyable.

God richly bless you all.

ABSTRACT

Background: Preterm births are the single greatest direct cause of neonatal deaths, responsible for 35% of the world's 3.1 million deaths a year. Preterm deliveries in Ghana is unacceptably higher than that of global estimates. An understanding of the placental morphological characteristics is essential for advancing our knowledge of the cause and mechanisms through which placental characteristics influence preterm births as well as identifying pregnancies at risk of these adverse perinatal outcomes.

General Objective: The objective of this study was to assess preterm births with gross examination of the postpartum placenta of pregnant women who deliver preterm at Korle Bu Teaching Hospital.

Methods: This was a cross sectional study which involved the consecutive sampling of pregnant women with preterm labor attending Korle Bu Teaching Hospital. After obtaining the patient's consent, demographic characteristics were collected from the patient's folder. Once the baby was delivered and the placenta was removed from the womb, various morphological characteristics of the placenta and its associated structure were recorded. Information on the pregnancy (preterm or term deliveries) was also recorded. The associations between dependent variable and each selected independent variable were analyzed using a multiple logistic regression.

Results: The prevalence of preterm deliveries among the study population during June 2019 was 12.6% (99 of the 785 singleton deliveries). The results revealed that umbilical cord pseudoknots are strong predictors of preterm delivery. The odds of preterm birth are 2.17 times greater when a pseudoknot is present on the umbilical cord as compared to when it is absent [Adjusted Odds Ratio (AOR) = 3.17 (95% CI = 1.19 – 8.48), p=0.02].

Conclusion: Proportion of preterm deliveries in the study population is high. Umbilical cord pseudoknots are strong predictors of preterm deliveries. Early detection of umbilical cord pseudoknots through ultrasonography and close monitoring may assist in management.

Keywords: Preterm, Placenta morphology, Pseudoknots, Determinants, Gross Examination

LIST OF ABBREVIATIONS

CI	Confidence Interval
IUGR	Intrauterine Growth Restriction
NICU	Neonatal Intensive Care Unite
COR	Crude Odds Ratio
AOR	Adjusted Odds Ratio
KBTH	Korle Bu Teaching Hospital

TABLE OF CONTENTS

<u>Contents</u>	<u>Pages</u>
DECLARATION	ii
DEDICATION	iii
ACKNOWLEDGEMENT	iv
ABSTRACT.....	v
TABLE OF CONTENTS.....	viii
LIST OF FIGURES	x
LIST OF TABLES	xi
CHAPTER ONE.....	1
1.0 INTRODUCTION	1
1.1 Background	1
1.2 Problem statement.....	4
1.3 Justification	4
1.4 Conceptual Framework.....	5
1.5 Study Objectives	8
1.5.1 General Objective	8
1.5.2 Specific Objectives	8
CHAPTER TWO	9
2.0 LITERATURE REVIEW	9
2.1 Preterm Delivery	9
2.2 Maternal Factors and Preterm Births	9
2.3 Obstetric Factors and Preterm Births	10
2.4 Lifestyle factors and Preterm Births	10
2.5 Placental/Umbilical Cord Abnormalities and Preterm Births.....	10
2.6 Placental Morphology	11
2.7 Maternal Factors Affecting Placenta Morphology	12
2.8 Obstetric Factors Affecting Placenta Morphology	12
2.9 Lifestyle Factors Affecting Placenta Morphology.....	13
2.10 Benefits of a Histological Examination	13
2.11 Setbacks of a Histological Examination	14
2.12 Gross Examination.....	14

3.0 METHODS	15
3.1 Study Design.....	15
3.2 Study Site	15
3.3 Study Population.....	15
3.4 Sample Size Calculation	16
3.5 Data Collection Method.....	17
3.5.1 Participant Recruitment	17
3.5.2 Placenta Examination.....	17
3.5.3 Fetal Parameters.....	17
3.6 Variables	18
3.6.1 Dependent Variable	18
3.6.2 Independent Variable	18
3.7 Data Processing and Analysis.....	19
3.8 Ethical Approval and Participant’s Consent.....	19
CHAPTER FOUR.....	20
4.0 RESULTS	20
4.1 Preterm Delivery.....	20
4.2 Descriptive Analysis of the Study Participants.....	20
4.3 Morphological Features Associated with Preterm Deliveries	22
CHAPTER FIVE	24
5.0 DISCUSSION	24
5.1 Preterm Deliveries	24
5.2 Morphological Features Associated with Preterm Deliveries	24
5.3 Strength.....	26
5.4 Limitations	26
CHAPTER SIX.....	27
6.0 CONCLUSION & RECOMMENDATIONS	27
6.1 CONCLUSION.....	27
6.2 RECOMMENDATIONS.....	27
REFERENCES	28
APPENDIX A: CONSENT FORM	35
APPENDIX B: QUESTIONNAIRE.....	37

LIST OF FIGURES

Figure 1: Conceptual Framework of Determinants of Preterm Delivery

Figure 2: Present and Absent Umbilical Cord Pseudoknot

LIST OF TABLES

Table 1: Operational Definition of the Independent Variables

Table 2: General Characteristics of Women with Preterm and Term Births at KBTH

Table 3: Morphological Features Associated with Preterm Deliveries

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

The magnitude and burden of perinatal complications, notably preterm births (<37 completed weeks of gestation), can be observed on different scales. A study on the global rates of preterm deliveries reveal 14.9 million babies (11.1%) that of the 135 million live births worldwide in 2010 were born prematurely (Blencowe *et al.*, 2012). Preterm deliveries are the greatest direct cause of neonatal mortality, accounting for 35% of the world's 3.1 million deaths annually (Liu *et al.*, 2012). Majority (60%) of preterm babies were born in sub-Saharan Africa and south Asia (Blencowe *et al.*, 2012). In 2019, a study conducted in Ghana reported 18.9% prevalence of preterm deliveries among pregnant women visiting Korle Bu Teaching Hospital, Accra (Adu-Bonsaffoh, Gyamfi-Bannerman, Opong, & Seffah, 2019).

Several factors are known to directly influence the occurrence of preterm deliveries: Maternal factors such as the age (Lisonkova, Janseen, Sheps, Lee, & Dahlgren, 2010). sickle cell anemia (Kuo & Caughey, 2016), diabetes (Johnson, Rottier, Luellwitz, & Kirby, 2009; Crump, Winkleby, Sundquist, & Sundquist, 2011) and hypertension (Premkumar, Baer, Jelliffe-Pawlowski, & Norton, 2017). have been linked to preterm birth. Associations between preterm deliveries and obstetric factors such as multiple gestation (Xiong, Dickey, Pridjian, & Buekens, 2015; Wagura, Wasunna, Laving, Wamalwa, & Ng'ang'a, 2018), parity (Nabavizadeh *et al.*, 2012), pre-eclampsia (Aseidu *et al.*, 2019) and premature rupture of membrane (PROM) (Mekonen, Yismaw, Nigussie, & Ambaw, 2019) have been reported. Behavioral factors associated with preterm birth include smoking, (Miyake, Tanaka, & Arakawa, 2013), and

excessive alcohol intake during pregnancy (Aliyu, Lynch, Belogolovkin, Zoorob, & Salihu, 2010; Patra *et al.*, 2011). Studies done on the placenta have also reported association between preterm deliveries and several placenta abnormalities (Vahanian, Lavery, Ananth, & Vintzileous, 2015) and umbilical cord abnormalities (Räisänen, Georgiadis, Harju, Keski-Nisual, & Heinonen, 2013). Based on the above literature, it is apparent that causes of premature delivery are multifactorial.

The placenta provides several functions during the different stages of pregnancy and has a sensitive morphology which slightly varies among pregnant women. Using data from healthy infants with a mean birth weight of 3.02kg, a study reported the following morphological characteristics: mean placenta weight of 0.535kg (ranged between 0.35 to 0.77 kg), and mean placental diameter of 18.64cm (ranged between 15 to 23 cm) (Abdelrahman, 2013). The findings of a study reported that the umbilical cord does not often insert in the center of the disc nor is the placenta discoid in shape (Pathak *et al.*, 2010). In some cases, knots can form in the umbilical cord. True knots that became vascular obstruction have been associated with premature birth, neonatal intensive care, and fetal death (Räisänen *et al.*, 2013). Pseudoknots are redundancies of vessels that irregularly form on the cord's surface. Studies report of pseudoknots having no clinical significance (Moshiri *et al.*, 2014; Chang & Aw, 2019).

Maternal demographic, obstetric factors, and lifestyle factors are known to affect the morphology of the placenta. The maternal age has been reported to affect the placenta weight (Haavaldsen, Samuelsen, & Skild, 2011). Another study reports sickle cell anemia disease adversely affecting the placenta (Baptista *et al.*, 2016). Hypertension (Salmani *et al.*, 2014) and gestational diabetes mellitus (GDM) (El Sawy, Iqbal, & Alkushi, 2018) are reported to cause alterations to the placenta morphology. Different works on obstetric factors and the placenta morphology observed

multiple gestation (Freedman *et al.*, 2019), parity (Wallace, Bhattacharya, & Horgan, 2013) and pre-eclampsia/eclampsia (Akhlaq, Nagi, & Yousaf, 2012) cause morphological and pathological changes to the placenta. Smoking and excessive alcohol consumption have been reported to alter the function of the placenta (Ortigosa *et al.*, 2012; van Oppenraaij, 2012; Wang *et al.*, 2014). Other possible factors which may alter the placenta morphology and its functions are widely unknown.

Histological examination of the placenta may be used to assist pathological studies of perinatal complications. On a study of still birth, researchers concluded that examining the placenta may assist in the classification of stillbirth and recommended that histological analysis of placental tissue be offered in all cases of stillbirth (Heazell & Martindale, 2009; Kidron, Bernheim, & Aviram, 2009). A different study on fetal mortality concluded that a placenta examination, among the other diagnostic tests, contributed the largest role in determining the causes of death (Korteweg *et al.*, 2012). Despite the benefits of performing a histological examination, researchers report poor utilization of this practice in health institutions (Al Harazi & Frass, 2011). The high cost and involving procedures are reported as contributing factors to the poor utilization of histological examination (Roberts, 2013; Struck, Baumgarten, & Wittmann, 2014).

Gross examinations of the placenta can also assist pathological studies of perinatal complications. Jaiman (2015) demonstrated the usefulness of placental examination for investigating perinatal death. Abnormal placenta shapes have been linked to reduced placental efficiency (Salafia *et al.*, 2010). A different study reported associations between gross patterns of umbilical cord coiling, placental histology and perinatal outcomes (Ernst, Minturn, Huang, Curry, & Su, 2013). Umbilical cord abnormalities have been correlated with significant perinatal morbidity and mortality (Kaplan, 2013).

1.2 Problem statement

Preterm birth in Ghana remains unacceptably high (Adu-Bonsaffoh *et al.*, 2019). Perinatal complications not only affect the pregnant woman emotionally but also financially affect the health care institutions (Hodek, von der Schulenburg, & Mittendorf, 2011; Baía *et al.*, 2016). Despite the valuable information from gross placental examination which could be used for investigating adverse perinatal outcomes, many health institutions do not mandate the practice of examining the placenta (Sills *et al.*, 2013). Therefore, there is paucity of information on the clinical significance of the placenta morphology.

1.3 Justification

Preterm birth in Ghana (18.9%) is higher than the global report (11.1%) (Blencowe *et al.*, 2012; Adu-Bonsaffoh *et al.*, 2019). A thorough understanding of the placental morphological characteristics is essential for advancing our knowledge of the cause and mechanisms through which placental characteristics influence preterm births and other perinatal outcomes. This knowledge can aid in identifying pregnancies at risk of adverse perinatal outcomes through intrauterine ultrasonography (if discovered before birth) and could also provide guidance in management of preterm babies if morphologies are discovered at delivery. Although several studies have examined the relationship between placental morphology and perinatal outcome, none have comprehensively assessed possible relationships between preterm births and morphological characteristics that can be studied with a gross examination.

1.4 Conceptual Framework

Preterm delivery is influenced by several factors. The factors of interest have been presented in the conceptual framework (Figure 1). This framework takes into account maternal demographic factors, obstetric factors, maternal life style factors, and factors related to placental/umbilical cord abnormalities.

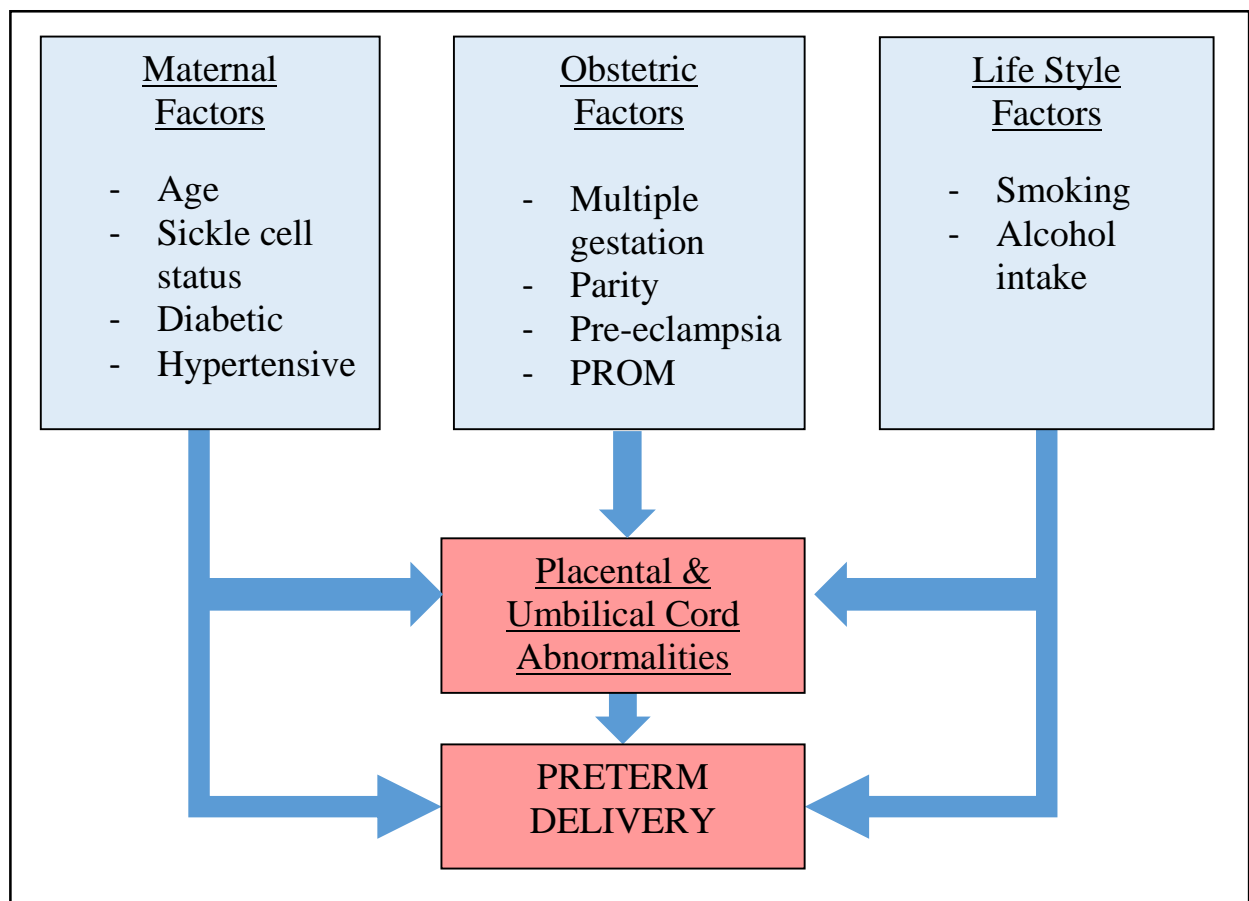


Figure 1: Conceptual Framework of Determinants of Preterm Delivery

This framework illustrates how maternal factors, obstetric factors, lifestyle factors, and placenta/umbilical cord abnormalities can independently or collectively influence the outcome of preterm deliveries. Old aged (Lisonkova *et al.*, 2010), sickle cell anemic (Kuo & Caughey, 2016), diabetic (Johnson *et al.*, 2009; Crump *et al.*, 2011), and hypertensive (Premkumar *et al.*, 2017) women have higher risk of preterm deliveries. Obstetric factors such as multiple gestation (Xiong *et al.*, 2015; Wagura *et al.*, 2018), parity (Nabavizadeh *et al.*, 2012), pre-eclampsia (Aseidu *et al.*, 2019), and premature rupture of membrane (PROM) (Mekonen *et al.*, 2019) have commonly been linked with preterm deliveries. Behavioral factors associated with preterm birth include smoking, (Miyake *et al.*, 2013) and excessive alcohol intake during pregnancy (Aliyu *et al.*, 2010; Patra *et al.*, 2011). Study conducted on the placenta have observed a correlation between preterm deliveries, several placenta abnormalities (Vahanian *et al.*, 2015), and umbilical cord abnormalities (Räisänen *et al.*, 2013). Based on the above literature, it is apparent that there is no single factor that causes premature delivery.

The framework also reveals how these factors can indirectly influence preterm deliveries by affecting the placenta morphology and its functions. Maternal age (Haavaldsen, Samuelsen, & Skild, 2011), sickle cell anemia disease (Baptista *et al.*, 2016), hypertension (Salmani *et al.*, 2014), and gestational diabetes mellitus (GDM) (El Sawy, Iqbal, & Alkushi, 2018) are reported to cause alterations to the placenta morphology. Morphological and pathological changes of the placenta are also observed with obstetric factors such as multiple pregnancies (Freedman *et al.*, 2019), parity (Wallace, Bhattacharya, & Horgan, 2013), and pre-eclampsia/eclampsia (Akhlq, Nagi, & Yousaf, 2012). Smoking and excessive alcohol intake are reported to alter the function of the placenta (Ortigosa *et al.*, 2012; van Oppenraaij, 2012; Wang *et al.*, 2014). Other possible factors which may alter the placenta morphology and its functions are widely unknown.

A thorough understanding of the placental characteristics is essential for advancing our knowledge of the cause and mechanisms through which placental characteristics influence preterm births and other perinatal outcomes.

1.5 Study Objectives

1.5.1 General Objective

Assess preterm births with gross examination of the postpartum placenta of pregnant women attending Korle Bu Teaching Hospital.

1.5.2 Specific Objectives

1. To determine the proportion of preterm births in pregnant women at Korle Bu Teaching Hospital during the study period.
2. To examine the association between preterm births and various morphological characteristics of the placenta.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Preterm Delivery

The magnitude and burden of perinatal complications, notably preterm births (<37 completed weeks of gestation), can be observed on different scales. A study on the global rates of preterm deliveries reveal 14.9 million babies (11.1%) of the 135 million live births worldwide in 2010, were born prematurely (Blencowe *et al.*, 2012). Preterm deliveries are the greatest direct cause of neonatal mortality, accounting for 35% of the world's 3.1 million deaths annually (Liu *et al.*, 2012). Majority (60%) of preterm babies were born in sub-Saharan Africa and South Asia (Blencowe *et al.*, 2012). A recent study conducted in Ghana reported 18.9% prevalence of preterm deliveries among pregnant women visiting Korle Bu Teaching Hospital, Accra (Adu-Bonsaffoh *et al.*, 2019). Other perinatal complications include still birth, low APGAR score and small/large birth weight for gestational age.

2.2 Maternal Factors and Preterm Births

Several maternal factors are known to directly influence the occurrence of preterm deliveries. A cohort study on singleton birth in British Columbia revealed that older women were at greater risk of several perinatal complications including preterm birth (Lisonkova *et al.*, 2010). Infants born to women with sickle cell anemia are at greater risk of preterm deliveries (Kuo & Caughey, 2016). Among African-American women from 2007-2011 in the birth cohort file maintained by the California Office of Statewide Health Planning and Development, chronic hypertension advancing to pre-eclampsia was observed to increase the risk for preterm birth (Premkumar *et*

al., 2017). Different studies recorded an increased risk of preterm birth among diabetic women (Johnson *et al.*, 2009; Crump *et al.*, 2011).

2.3 Obstetric Factors and Preterm Births

Obstetric factors have long been associated with preterm births. Different studies have established a link between multiple gestations and preterm deliveries (Xiong *et al.*, 2015; Wagura *et al.*, 2018). Parity and pre-eclampsia have also been reported as having an association with preterm deliveries (Nabavizadeh *et al.*, 2012, Aseidu *et al.*, 2019). It was observed that those having premature rupture of membrane (PROM) were 3 times more likely to have a preterm birth (Mekonen *et al.*, 2019).

2.4 Lifestyle factors and Preterm Births

Many studies support a relationship between behavioral factors and the outcome of preterm deliveries. A study to assess the effect of maternal smoking throughout pregnancy in Japan demonstrated a positive linear trend between active maternal smoking and the risk of preterm birth (Miyake *et al.*, 2013). A systematic review and meta-analyses on the effects of maternal alcohol exposure on adverse perinatal outcome established a relationship between heavy alcohol consumption during pregnancy and the outcome of preterm deliveries (Patra *et al.*, 2011). A different study on alcohol intake during pregnancy observed spontaneous preterm birth increase with incremental rise in number of drinks consumed per week (Aliyu *et al.*, 2010).

2.5 Placental/Umbilical Cord Abnormalities and Preterm Births

Few studies have reported a relationship between preterm deliveries and different abnormalities of the placenta/umbilical cord structures. Strong associations between placenta implantation

abnormalities and preterm deliveries were reported in a systematic review (Vahanian *et al.*, 2015). A study on women delivering singleton pregnancy at Kuopio University Hospital revealed an association between the presence of true umbilical cord knots and perinatal complications including premature birth (Räsänen *et al.*, 2013). Hyper coiled umbilical cords have been associated with perinatal complication. (Patil, Kulkarni, & Lohitashwa, 2013). Research on the umbilical cord revealed a significant association between umbilical coiling index and perinatal complications including preterm deliveries (Chitra, Sushanth, & Raghavan, 2012). Based on the above literature, it is apparent that there is no single factor that influences the occurrence of premature delivery. Research on the umbilical cord of one thousand antenatal women revealed a significant association between umbilical coiling index and perinatal complications including preterm deliveries (Chitra *et al.*, 2012).

2.6 Placental Morphology

The placenta provides several functions during the different stages of pregnancy and has a sensitive morphology which slightly varies among pregnant women. From healthy infants with a mean birth weight of 3.02kg, a study reported the following morphological characteristics: mean placenta weight of 0.535kg (ranged between 0.35 to 0.77 kg), mean placental diameter of 18.64cm (ranged between 15 to 23 cm) (Abdelrahman, 2013). It has been suggested that the difference in the placenta shape may be influenced by maternal factors or the uterine environment (Haeussner, Schmitz, Koch, & Frank, 2013). A study on the umbilical cord reported that the umbilical cord does not normally insert centrally nor is the placenta normally round in shape (Pathak *et al.*, 2010). Placentas with a displaced cord possess a less efficient transport of blood and nutrients (Yampolsky *et al.*, 2009). In some cases, knots can form in the umbilical cord. True knots which become vascular obstruction have been associated with premature birth,

neonatal intensive care, and fetal death (Räisänen *et al.*, 2013). Pseudo-knots are redundancies of vessels that irregularly form on the cord's surface. Some report that pseudo-knots have no clinical significance (Moshiri *et al.*, 2014; Chang & Aw, 2019).

2.7 Maternal Factors Affecting Placenta Morphology

Different studies have investigated associations between maternal demographic factors and the placenta's morphology. A study conducted on all singleton birth in Norway reported maternal age having an effect on the placenta weight (Haavaldsen, Samuelsen, & Skild, 2011). Maternal age may also influence the development of succenturiate lobes along the main placenta disc (Suzuki & Igarashi, 2008). Research on gene expression profile illustrated how sickle cell anemia disease among pregnant women may lead to improper placental development (Baptista *et al.*, 2016). Pregnancy complicated by hypertension adversely affects the placenta by reducing the weight and dimensions which may cause placental insufficiency (Salmani *et al.*, 2014). The mean weight of gestational diabetes mellitus (GDM) placentae were greater than the normal placentae (El Sawy, Iqbal, & Alkushi, 2018).

2.8 Obstetric Factors Affecting Placenta Morphology

Several works have been published on obstetrics factors that affect placenta morphology. A study evaluating associations between features of placental morphology and birth weight within twin pairs, reported significant associations between surface area and birthweight (Freedman *et al.*, 2019). Another study identified an association between parity and the placenta weight (Wallace, Bhattacharya, & Horgan, 2013). Morphological and pathological differences were observed in patients with pre-eclampsia/eclampsia and normotensive controls. (Akhlq, Nagi, & Yousaf, 2012).

2.9 Lifestyle Factors Affecting Placenta Morphology

Lifestyle factors are known to affect the morphology and proper function of the placenta. A histomorphometric study on 225 placentas observed a non-significant reduction of placental vascularization in cocaine and opiates using mothers (Ortigosa *et al.*, 2012). Examination of the placenta of smoking and non-smoking women revealed that chorionic villous vascularization is already compromised during the early stage of pregnancy in women who smoke both before and during pregnancy (van Oppenraaij *et al.*, 2012). Research conducted on singleton deliveries from the Tasmanian Infant Health Survey observed an association between smoking and lower placental weight. The same study also observed an association between alcohol intake and lower placenta-to-birth weight ratio (Wang *et al.*, 2014). Other possible factors which may alter the placenta morphology and its functions are widely unknown.

2.10 Benefits of a Histological Examination

Histological examination of the placenta has been used to assist pathological studies of perinatal complications. From assessing 71 consecutive cases of stillbirth, researchers concluded that post-mortem examination of the placenta can aid in classification of stillbirth (Heazell & Martindale, 2009). A retrospective review of singleton still birth supported the report that a pathological analysis of the placenta is essential in investigating causes of stillbirth (Kidron *et al.*, 2009). A different study on fetal mortality concluded that a placenta examination, among the other diagnostic tests, contributed the largest role in determining the causes of death (Korteweg *et al.*, 2012).

2.11 Setbacks of a Histological Examination

Despite the benefits of performing a histological examination, researchers report poor utilization of this practice in health institutions. A review of the 2007 delivery records at tertiary care hospital in San'a, Yemen revealed placental pathological examination was under-utilized with only 73 (4.9%) of the 1501 placentas expected to be pathologically examined were ultimately assessed (Al Harazi & Frass, 2011). A research to demonstrate the value of perinatal pathology identified limited financial and manpower resource as contributing factor to the poor utilization of a histological examination. The same study then suggested assessments which could be implemented in areas with limited resources (Roberts, 2013). It has been suggested that implementation pathological services have cost implications and are not available to all obstetric units in the United Kingdom (Struck *et al.*, 2014). These studies suggest the high cost and involving procedures as contributing factors to the poor utilization of histological examination.

2.12 Gross Examination

A Gross examination of the placenta can also assist pathological studies of perinatal complications. A study by Jaiman (2015) demonstrated the usefulness of placental examination for investigating perinatal death. Abnormal placenta shapes have been linked to reduced placental efficiency (Salafia *et al.*, 2010). A different study reported associations between gross patterns of umbilical cord coiling, placental histology and perinatal outcomes (Ernst *et al.*, 2013). Umbilical cord abnormalities were correlated with significant perinatal morbidity and mortality (Kaplan, 2013).

CHAPTER THREE

3.0 METHODS

3.1 Study Design

This study was a cross sectional study which involved a consecutive sampling and examination of the postpartum placenta of women delivering preterm to identifying associations between various morphological characteristics of the placenta and outcomes of preterm deliveries.

3.2 Study Site

Subjects for this study were recruited at the labor ward of the Department of Obstetrics and Gynecology of Korle Bu Teaching Hospital (KBTH). KBTH is the largest tertiary referral hospital in Ghana and the department serves mainly as a referral center for the southern half of the country.

3.3 Study Population

All pregnant women who delivered at the KBTH labor wards. The inclusion criteria consisted of all pregnant women expecting to be deliver live singleton birth. However, those who were not willing to give their consent to participate in the study, those with incomplete postpartum placenta (having one or more missing cotyledons), those with incomplete maternal data essential for the study were excluded.

3.4 Sample Size Calculation

The Korle-Bu Teaching Hospital Annual Statistical Report of 2017 recorded a 11.2% prevalence of singleton preterm birth out of the 5,235 deliveries. The sample size was calculated using the Cochran formula by

$$n = \frac{Z^2(p)(1-p)}{E^2}$$

where

n = estimated sample size

E = desire margin of error (0.05)

Z = critical z score based on the desired level of confidence (95%)

P = prevalence of preterm deliveries (11.2%)

$$n = \frac{(1.96)^2(0.112)(1 - 0.112)}{(0.05)^2}$$

$$n = 152.83$$

153 Patients was the minimum number of subjects considered representative of the population for this study.

3.5 Data Collection Method

3.5.1 Participant Recruitment

Recruitment of the patients was done by the data collector as they waited to deliver at the labor ward of the Department of Obstetrics and Gynecology of KBTH. A summary of this research project was explained to the patients. Once the patient agreed to participate in the study, a structured questionnaire was given or read to collect essential data such as their socio-demographic characteristics and medical information. The information given by the patient were verified from the maternal health record book. Pregnant women who met the inclusion criteria were recruited into the study.

3.5.2 Placenta Examination

Examination of placenta was conducted by the data collector at the labor ward within an hour after the placenta was removed from the womb. With water, the blood stains and any blood clots on the surface of the placenta was washed off with water. After trimming the membrane, morphological parameters such as the placenta shape, the mode of cord insertion, the presence of succenturiate lobes, umbilical cord pseudoknots, and umbilical coils were recorded.

3.5.3 Fetal Parameters

After examining the placenta and its associated structures, information such as the birth weight, APGAR score, and gestational age documented by the doctors and midwives were obtained by the data collector from the neonatal card (pink card) and the in-patient folder.

3.6 Variables

3.6.1 Dependent Variable

Characteristics of births were the dependent variable of this study.

3.6.2 Independent Variable

Various morphological characteristics of the placenta and its associated structures were the independent variables.

Table 1: Operational Definition of the Independent Variables

VARIABLE	OPERATIONAL DEFINITION	SCALE OF MEASURE	DATA SOURCE
Placenta Shape	The dimension of the placenta disc	Categorical: Central, Oval, Bilobed, Other	Examination
Succenturiate Lobe	A smaller accessory lobes attached to the main disc of the placenta	Binary: Present or Absent	Examination
Umbilical Cord Insertion	The cord insertion site into the fetal surface of the placenta	Categorical: Centric, Eccentric, Marginal, Velamentous	Examination
Umbilical Pseudoknots	Focal redundancies in the umbilical cord	Binary: Present or Absent	Examination
Umbilical Coiling	Coiling of the umbilical cord	Binary: Present or Absent	Examination

3.7 Data Processing and Analysis

The data from the patient questionnaire, the placenta examination, and the perinatal outcome were transferred and stored digitally in Microsoft Excel 2016 (Microsoft company, USA). The stored data were then exported into a Stata (version 15) statistical software for analysis. Descriptive analyses were expressed in the form of frequencies and percentages. A Chi-square test was used to assess for associations between general characteristics of women and the birth outcome (preterm or term birth). Associations between preterm birth and each selected independent variables were analyzed using a multiple logistic regression analysis with 95% confidence intervals (CI) and p-values <0.05.

3.8 Ethical Approval and Participant's Consent

Approval to conduct this study was obtained from the Ethical and Protocol Review Committee of the College of Health Sciences, University of Ghana under protocol identification number CHS-Et/M.6 C/2018-2019. All participants signed a written informed consent or gave verbal consent (Appendix A). Participants were adequately informed of the objective and procedures of the study. Non-participation did not affect clinical management of the patients.

CHAPTER FOUR

4.0 RESULTS

4.1 Preterm Delivery

During June 2019, there were 785 live birth deliveries in the hospital. Ninety-nine (12.6%) of these birth were preterm deliveries. Out of the preterm deliveries, 17.2% (17/99) were classified as very preterm (28 weeks - 31 weeks 6 days gestation) and 82.8% (82/99) were moderate to late preterm (32 weeks - 36 weeks 6 days gestation) base on the WHO classification. Of the 154 pregnant women recruited into this study, 36 women were preterm deliveries.

4.2 Descriptive Analysis of the Study Participants

The general characteristics of women who delivered preterm were not significantly different ($p>0.05$) from those who delivered term (Table 2). A large portion of the study population between the ages of 25-29 years had preterm deliveries (9/28) as compare with other age groups. Fifteen of the 47 patients who delivered preterm were giving birth for the first time whilst the remaining 32 patients gave birth during term. Most of the study participants (121/154) were sickle cell negative whilst those who had a positive status or were not aware of their status were (24/154) and (9/154) respectively. The life style factors of women in the sampled population were similar between the two delivery groups.

Table 2: General Characteristics of Women with Preterm and Term Births at KBTH.

Characteristics	Preterm n (%)	Term n (%)	Total n=154	P-value
Age Group				0.53
≤24	6 (18.5)	16 (72.7)	22	
25-29	9 (32.1)	19 (67.8)	28	
30-34	10 (18.5)	44 (81.5)	54	
≥35	11 (22.0)	39 (78.0)	50	
Parity				0.14
0	15 (31.9)	32 (68.1)	47	
1	5 (13.2)	33 (86.8)	38	
2	10 (29.4)	24 (70.6)	34	
≥3	6 (17.1)	29 (82.9)	35	
Sickle Cell Status				0.94
Negative	28 (23.1)	93 (76.8)	121	
Positive	6 (25.0)	18 (75.0)	24	
Unknown	2 (22.2)	7 (77.8)	9	
Smoke During Pregnancy				1.00
Yes	0	1	1	
No	36 (23.4)	117 (76.6)	153	
Alcohol Intake During Pregnancy				1.00
Yes	1 (16.7)	5 (83.3)	6	
No	35 (23.6)	113 (76.4)	148	

4.3 Morphological Features Associated with Preterm Deliveries

Pseudoknots were present on 25 of the 154 (16.2%) umbilical cords. Eleven (44.0%) pseudoknots were present on the umbilical cords of preterm deliveries (Table 3). After adjusting for placenta shape, succenturiate lobes, umbilical cord coils, and umbilical cord insertion, the results revealed umbilical cord pseudoknot (Figure 2) to be a strong predictor of the outcome of preterm delivery because the odds of preterm birth is 2.17 times greater when a pseudoknot is present on the patient's umbilical cord as compared to when it is absent [AOR = 3.17 (95% CI = 1.19 – 8.48), $p=0.02$].

Other measured morphological features were not significantly associated with the outcome of preterm deliveries.

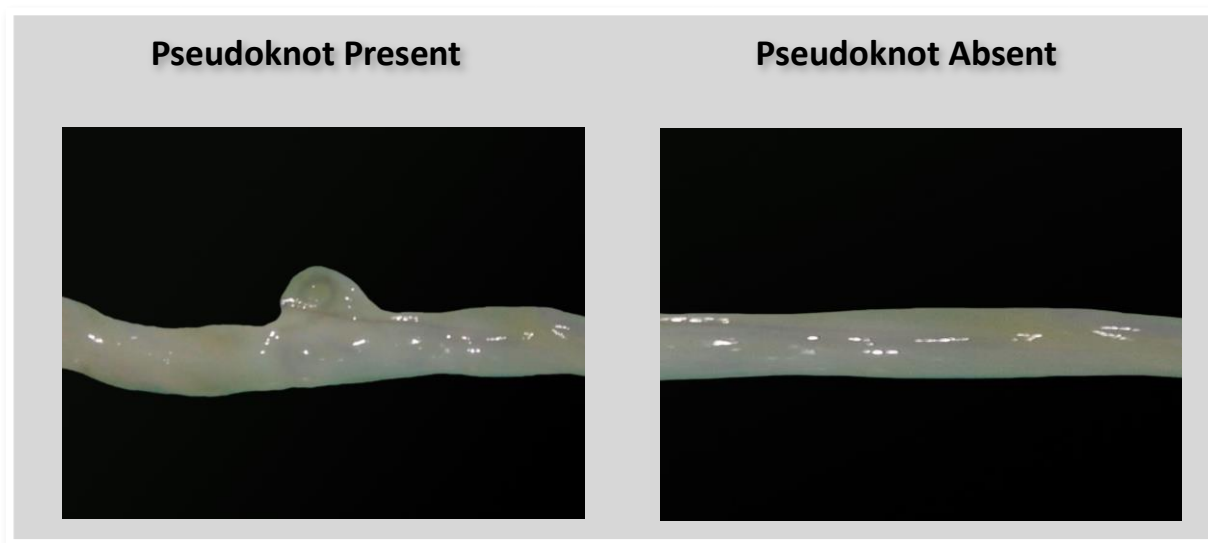


Figure 2: Present and Absent Umbilical Cord Pseudoknot

Table 3: Morphological Features Associated with Preterm Deliveries

MORPHOLOGICAL FEATURES	Total No.	Preterm No.	%	COR (95% CI)	P-Value	AOR (95% CI)	P-Value
Placenta Shape					0.38		0.83
Discoid	87	21	24.1	1		1	
Oval	41	11	26.8	1.15 (0.49-2.69)		1.02 (0.41-2.53)	
Bilobed	5	1	20.0	0.79 (0.08-7.42)		0.89 (0.08-9.70)	
Other	21	2	14.3	0.52 (0.14-1.96)		0.53 (0.14-2.07)	
Succenturiate Lobe					0.55		0.88
Absent	129	29	22.5	1		1	
Present	25	7	28.0	1.34 (0.51-3.52)		1.09 (0.35-3.37)	
Umbilical Pseudoknots					0.01		0.02
Absent	129	25	19.4	1		1	
Present	25	11	44.0	3.27 (1.33-8.06)		3.17 (1.19-8.48)	
Umbilical Cord Coils					0.11		0.06
Absent	112	30	26.8	1		1	
Present	42	6	14.3	0.46 (0.17-1.19)		0.38 (0.14-1.04)	
Umbilical Cord Insertion					0.39		0.57
Eccentric	101	26	25.7	1		1	
Central	26	4	15.4	0.52 (0.17-1.66)		0.53 (0.16-1.75)	
Marginal	17	5	29.4	1.20 (0.39-3.74)		1.25 (0.36-4.31)	
Velamentous	10	1	10.0	0.32 (0.04-2.64)		0.39 (0.04-3.38)	

*CI = Confidence Interval

*COR = Crude Odds Ratio

*AOR = Adjusted Odds Ratio

CHAPTER FIVE

5.0 DISCUSSION

5.1 Preterm Deliveries

The prevalence of preterm birth in this study is smaller than the 18.9% established by a recent study (Adu-Bonsaffoh *et al.*, 2019). However, this prevalence is higher than the 9.3% rate reported over a decade ago (Nkyekyer, Enweronu-Laryear, & Boafor, 2006). A systematic review reported 10.6% as the global preterm rate for 2014 (Chawanpaiboon *et al.*, 2019). The global estimates reveal wide variations in preterm birth with the majority being reported from sub-Saharan Africa and South Asia (Blencowe *et al.*, 2012). The wide variations may also be as a result of the different definitions and clinical guidelines employed in the various regions (Lawn *et al.*, 2010; Kramer *et al.*, 2012). These variations, however, may hinder efforts to acquire an accurate estimate of the true burden of preterm births.

5.2 Morphological Features Associated with Preterm Deliveries

To the best of our search, this is the first study investigating associations between characteristics of the placenta morphology and the outcome of preterm deliveries. Several studies on umbilical cord abnormalities have established an association between true knots and adverse fetal outcome (Baergen, 2013; Räisänen *et al.*, 2013; Chan & Baergen, 2014). The findings of the current study differ from other studies which report pseudoknots as not being of any clinical significance (Moshiri *et al.*, 2014; Chang & Aw, 2019). The mechanism behind the high number of pseudoknots among the preterm deliveries in this study is unknown. Therefore, more research is needed to elucidate the mechanism.

Certain morphological features of the placenta form during the early stages of pregnancy (Salafia, Yampolsky, Shlakter, Mandel, & Schwartz, 2012). Although several studies have been published on the morphological features and perinatal outcomes, most have not directly investigated these placenta features with the outcome of preterm births.

Studies have associated umbilical coiling with adverse perinatal outcome. One prospective study recorded a significant correlation between the hyper coiled cords and perinatal complication such as IUGR, low Apgar score and NICU admission (Patil, Kulkarni, & Lohitashwa, 2013). Research on the umbilical cord revealed a significant association between umbilical coiling index and perinatal complications including preterm deliveries (Chitra, Sushanth, & Raghavan, 2012). Umbilical coils in the present study was not significantly associated with the occurrence of preterm deliveries which may be attributed to the difference in the assessment. This study assessed the presence or absence of umbilical coiling as opposed to umbilical coiling index.

The findings of this study was in agreement with previous studies, which also observed most umbilical cords not being inserted in the center of the placenta disc (Yampolsky *et al.*, 2009, Pathak *et al.*, 2010). These displacements of the cord are known to reduce transport efficiency (Yampolsky *et al.*, 2009). According to Fick's law of diffusion, exchange efficacy, depends on the concentration difference of the substance across the membrane, as well as on the area and thickness of the membrane. Thus, for passive diffusion of oxygen, carbon dioxide, and water, reduction of the distance between maternal and fetal blood is of crucial importance for the maternofetal diffusional exchange which may influence perinatal outcome.

This current study recorded majority of the study population as having discoid shaped placentas. This was in agreement with a previous study which also reported discoid placentas (round in shape) (Pathak *et al.*, 2010).

Placenta lobes are not common and are influenced by the maternal age and the women's history of using *in vitro* fertilization (Suzuki & Igarashi, 2008). The reason behind the higher occurrence of placenta lobes in the current study population is unknown but may have been influenced by the high proportion (50/154) of women over 35 years.

5.3 Strength

The comprehensive assessment of placenta morphological characteristics is the major strength of this study. This permitted for the assessments of several variables which are lacking in literature.

5.4 Limitations

The limitation of this study is that it employed a consecutive sampling method, and the study findings cannot be generalized. In addition, the availability of data was dependent on what was recorded in the patient's maternal folder. This resulted in the need to exclude several participants from the study. Another challenge of the study was the self-reporting nature of life style factors. This could be influence by social desirability bias for smoking and alcohol intake during pregnancy.

CHAPTER SIX

6.0 CONCLUSION & RECOMMENDATIONS

6.1 CONCLUSION

The study reported preterm deliveries during June 2019 as 12.6% of the study population. Furthermore, after adjusting for confounders, umbilical cord pseudoknot remains a strong predictor of preterm delivery.

6.2 RECOMMENDATIONS

To build on this study, intrauterine examination with ultrasonography to detect umbilical cord abnormalities before birth can be employed to better prepare clinicians in the management of pregnancy at risk of preterm. Secondly, pathologists could conduct selective histological examinations to study more characteristics such as syncytial knot, villi syncytial necrosis, fetal capillaries, and inter-villous space on suspected cord.

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APPENDIX A: CONSENT FORM

Title: “Assessing Preterm Births with Gross Examination of the Placenta of Patients Attending Korle Bu Teaching Hospital.”

Investigator: Hanson Gabriel Nuamah. BSc, MPH

Principal investigator: Dr. Mercy Nuamah. MD, PhD

Address: Department of Obstetrics and Gynaecology, School of Medicine and Dentistry, College of Health Science, University of Ghana.

Dear volunteer,

We wish to ask you to take part in this study to investigate associations between preterm births and various morphological characteristics of the placenta. We are interested in your opinion because you are receiving care at the Korle-Bu Teaching Hospital and we wish to find ways to help improve the health of pregnant women and their babies.

Possible benefits

You will not be paid for participation in this study and you are also not expected to pay anything. However, if during the study we detect a condition that needs prompt attention, you will be referred for investigation and management.

Possible Risks

This research presents minimal risk to you or your baby. The main risks include, psychological distress from discussing potentially upsetting issues and loss of confidentiality, though none of the data to be collected are of a highly sensitive nature. Confidentiality will be protected as described in the following section.

Confidentiality

All information gathered would be treated in strict confidentiality. We will protect information about you taking part in this research to the best of our ability. You will not be named in any reports. If you have any questions, please feel free to ask.

Withdrawal from study

We would like to stress that this study is strictly voluntary. Should you decide not to participate in the study it will have no consequences for you.

Contacts

If you have any questions about the research study or study-related problems, you may contact Dr. Mercy Nuamah (Research Coordinator), at the Department of Obstetrics and Gynaecology, School of Medicine and Dentistry, College of Health Science, University of Ghana.

Telephone number: 0249298354/ 0502568057

E-mail: mercymgrinc7@gmail.com.

PARTICIPANT AGREEMENT

The above document describing the benefits, risks and procedures for the research, title: “Assessing Perinatal Complications with Gross Examination of the Placenta of Patients Attending Korle-Bu Teaching Hospital” has been read and explained to me. I have been given an opportunity to have any questions about the research answered to my satisfaction. I agree to participate as a volunteer.

Date
Signature or Thumbprint
(of the volunteer)

If a volunteer cannot read the form themselves, a witness must sign here:
I was present while the benefits, risks and procedures were read to the volunteer.
All questions were answered and the volunteer has agreed to take part in the research.

Date
Signature or Thumbprint
(of the witness)

I certify that the nature and purpose, the potential benefits, and possible risks associated with participating in this research have been explained to the above individual.

Date
Signature
(of the person who obtained the Consent)

APPENDIX B: QUESTIONNAIRE

1. Patient's Code:
2. Folder Number:
3. Contact Number:.....

SOCIO-DEMOGRAPHIC CHARACTERISTICS

4. Residence:
5. Age:
6. Highest education: None [] – Primary [] – JHS [] – SHS [] – Tertiary []
7. Occupation:
8. Blood group:
9. Gravidity:
10. Parity:
11. Maternal weight..... Kgdate weighed (dd/mm/yy)
12. Date of delivery..... (dd/mm/yy)
13. Mode of delivery: SVD [] – CS []

MATERNAL FACTORS

14. Smoked during pregnancy: Yes [] - No []
15. Alcohol consumed during pregnancy: Yes [] - No []
16. Diabetic: Yes [] - No []
17. Sickle cell status:
18. Other factors:

Patient's Code.....

Folder Number.....

PLACENTA MORPHOLOGY

19. Shape: Discoid [] - Oval [] - Bilobed [] - Other []

20. Succenturiate lobe present: Yes [] - No []

21. Number of cotyledons:

22. Weight: g

23. Placenta stretch (longest diameter)..... cm

24. Thickness..... cm

25. Volume: ml

26. Circumference.....cm

27. Other observations:

.....

UMBILICAL CORD

28. Insertion: Central [] – Eccentric [] – Marginal [] – Velamentous []

29. Coils: Present [] – Absent []

30. Other observations:

NEONATAL ACCESSMENT

31. Gestational age:..... weeks.....days

32. Birth weight Kg

33. APGAR score: 1min [] - 5min []

34. Genetic abnormalities: Present [] – Absent []

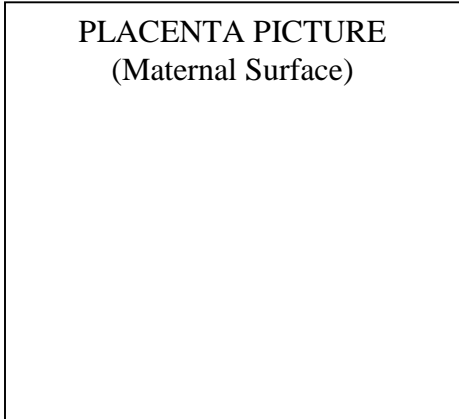
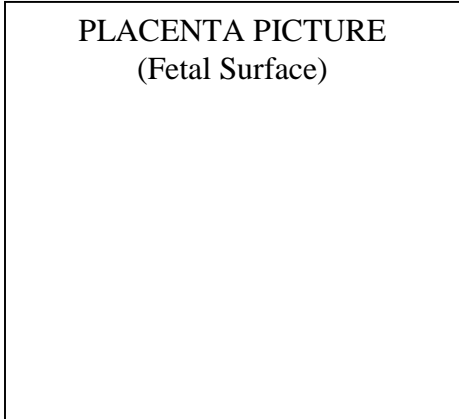
35. NICU admission. No [] - Yes []

36. Days of stay at hospital after delivery

37. Neonatal death: No [] - Yes []

38. If yes: Cause of Death.....

39. Other Observations:.....



Thank you for your participation.