KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE AND DENTISTRY
DEPARTMENT OF ANATOMY

PREDICTIVE MODELS FOR PLACENTAL, UMBILICAL CORD AND NEONATAL INDICES USING MATERNAL BOOKING VISIT BIOMETRIC INDICES

BY

SAMUEL BIMPONG

MARCH, 2020

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A THESIS SUBMITTED IN FULFILLMENT OF THE

REQUIREMENTS FOR THE DEGREE OF

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DECLARATION

The experimental work described in this thesis was carried out at the Department of Anatomy, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology. This work has not been submitted for any other degree.

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ACKNOWLEDGEMENTS

My profound gratitude goes to the Almighty God for His mercies, guidance and protection throughout the course of my study in this university.

I also wish to acknowledge the huge contributions, directions and mentorship offered me by my supervisor Professor Chrissie Stansie Abaidoo, for taking time off her busy schedule to read through the work and making the necessary corrections and suggestions to the realization of a successful work.

A special mention is made of Dr. Nana Kena Frimpong of the Mathematics Department, KNUST, for his support. Also, many thanks to Mr. Christopher Nkrumah, the Head of Laboratory Department, Wenchi Methodist Hospital, the Head and staff members of Victory Maternity Home and Clinic, I say God bless you for your patience and support.

I am indebted to all the staff members of Department of Anatomy, KNUST, for their immense support and encouragement.

I cannot forget my sweetheart Victoria Bimpong (Mama Vic), my daughters Sylvia Addo and Akosua Aniwaa Gyinadu and my sons Johnson Gyinadu Bimpong and Baffour Akoto Gyinadu for the special role they play in my life.

Finally, I am very grateful to my wonderful siblings and friends for their prayers and the peace of mind that enabled me to undertake this research work to a successful end.

DEDICATION

This thesis is dedicated first to the Almighty GOD, secondly to my late Father, Thomas Okyeame Bimpong and finally to my Wife, Victoria Quainoo and my Children.

ABSTRACT

The birth of a normal healthy baby is a reflection of healthy intrauterine environment that depends on the qualitative and quantitative characteristics of maternal, placental and umbilical cord that ensure survival, healthy growth and development of the foetus. This study sought to establish mathematical models to predict outcomes of placental, umbilical cord and neonatal indices using maternal booking biometric parameters. A total of 240 pregnant women attending antenatal care for the first time at Victory Maternity Home and Clinic at Tech-Junction – Kumasi were enrolled into the study. Significant difference was observed between the mean values of booking total cholesterol at various maternal educational levels while differences in mean booking low density lipoprotein among various ethnic groups was statistically significant. Significant differences in placental weight, diameter, area and number of cotyledons were observed between neonates with normal and short umbilical cord lengths. It was found that booking systolic blood pressure could influence neonatal body length. Also total cholesterol, triglyceride, high and low density lipoproteins could predict placental volume. Maternal booking diastolic blood pressure was found to influence umbilical cord length, while triglyceride, high density and low density lipoproteins could predict outcome of umbilical cord diameter. Triglyceride and high density lipoprotein were observed to predict cord area outcome. It was realized that, a unit increase in maternal booking systolic blood pressure could lead to 0.03 unit increase in neonatal body length while a unit increase in total cholesterol could increase umbilical cord length by 2.32 units. However, a unit increase in low density lipoprotein could decrease cord length by 3.31 units.

Conclusively, these models of maternal booking biometric indices could be used to screen and monitor pregnancies at risk and also predict possible outcomes of placenta, umbilical cord and neonatal indices.

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LIST OF ABBREVIATIONS

ABCA1	ATP-Binding Cassette Transporter A1
AC	Abdominal Circumference
ADP	Adenosine – 5 - Diphosphate
ANC	Antenatal Care
ApoB-100	Apo-protein B-100
ATP	Adenosine – 5 - Triphosphate
BL	Body Length
BP	Blood Pressure
BV	Booking Visit
BW	Birth Weight
DDA	Descriptive Discriminant Analysis
DHAP	Dihydroxyacetone Phosphate
DSP	Diastolic Blood Pressure
FANC	Focused Antenatal Care
FGF	Fibroblast Growth Factor
GSS	Ghana Statistical Service
GUSTO	Growing Up in Singapore Toward a Healthy Outcome
HB-EGF	Heparin Binding Epidermal Growth Factor
HC	Head Circumference
HDL-C	High Density Lipoprotein Cholesterol
HDP	Hypertensive Disorders of Pregnancy

HLA-G	Human Leucocyte Antigen – G
INTERGROWTH – 21ST	International Foetal and Newborn Growth Consortium for the 21st Century
IUGR	Intra Uterine Growth Restriction
JHS	Junior High School
LBW	Low Birth Weight
LDL-C	Low Density Lipoprotein Cholesterol
LDLR	Low Density Lipoprotein Receptors,
LDLR	Low-Density Lipoprotein Receptor
LGA	Large-for-gestational Age
LXR	Liver X Receptor
MANOVA	Multiple Analysis of Variance
MHC	Maternal Booking Hip Circumference
MHC-I	Major Histocompatility Complex Class – I
MHt	Maternal Booking Height
MWC	Maternal Booking Waist Circumference
MWt	Maternal Booking Weight
NCD-RisC	Non – Communicable Disease Risk Factor Collaboration
No. of COTYL	Number of Cotyledons
PA	Placental Area
PD	Placental Diameter
PEM	Protein – Energy Malnutrition
PI	Ponderal Index

PT	Placental Thickness
PV	Placental Volume
PW	Placental Weight
SBP	Systolic Blood Pressure
SGA	Small-for-gestational Age
SHS	Senior High School
SOS	Speed of Sound
SR BI	Scavenger Receptor Class B type I
SSCE	Senior Secondary School Certficate
TANC	Traditional Antenatal Care
TC	Total Cholesterol
TG	Triglycerides
UCA	Umbilical Cord Area
UCD	Umbilical Cord Diameter
UCI	Umbilical Cord Index
UCL	Umbilical Cord Length
UCV	Umbilical Cord Volume
UCW	Umbilical Cord Weight
VEGF	Vascular Endothelial Growth Factor
VEGFR	Vascular Endothelial Growth Factor Receptor
VLDLR	Very Low Density Lipoprotein Receptor
WHO	World Health Organization

CHAPTER ONE

GENERAL INTRODUCTION

1.1 Pregnancy Characteristics

Pregnancy is characterized by transitional stages of anatomical and physiological changes in the body of the pregnant woman for the purposes of meeting the high metabolic demands of the foetus, allowing for the full development of the foetus and to prepare the woman's body for childbirth (Bhatia and Chhabra, 2018). It is also affected by a number of problems originating from a variety of sources such as chromosomal and genetic disorders of the developing foetus, maternal health status and behaviour, environmental factors, placental and umbilical cord morphologic and functional characteristics (Rupa *et al.*, 2013; Paiker *et al.*, 2016). The success of perinatal outcome, survival status, growth and development of the foetus is characteristically expressed by different growth indices including body length, head, chest and abdominal circumferences which cumulatively contribute to birth weight (Haq *et al.*, 2017).

Pregnancy is also a period during which there is an intense maternal nutritional and hormonal change. For instance, maternal lipid profile experiences significant increase in levels with advancing gestational age (Sales *et al.*, 2015). The changes in lipid levels – total cholesterol (TC), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C) and triglycerides (TG) permit the mother to accumulate huge source of energy to provide for herself, the foetus and maintain a steady metabolic rate for healthy growth and development of the foetus (Herrera *et al.*, 2006).

1.2 Antenatal Care (ANC) and Booking Visit

Although pregnancy is deemed a positive and cherished experience for majority of women and families, it is not without associated problems including nausea and vomiting, ill health, malnutrition and even death. The antenatal period offers the best of times for the pregnant woman to access both preventive and curative health care (Gudayu *et al.,* 2014).

Antenatal care is an important part of the Safe Motherhood Programme that involves provision of systematic medical attention to the pregnant woman during pregnancy till child birth (Asah-Opoku *et al.,* 2019). One key factor proven to increase quality of pregnancy outcome has been antenatal care service (Asamoah and Agardh, 2017). This is due to the fact that, most interventions implemented at ANC are based on empirical evidence produced scientifically (Yeboah *et al.,* 2018).

Through education at ANC service, pregnant women deliver with skilled birth attendant and also become familiar with healthcare personnel, all of which promote improvement in pregnancy outcome (Asamoah and Agardh, 2017). Also, the ANC service targets safe delivery and parenthood as well as preventing, detecting, alleviating or managing three major health issues during pregnancy – pregnancy complication, chronic conditions that worsen in the course of pregnancy and effects of unhealthy lifestyles (Asah-Opoku *et al.,* 2019).

According to Yeboah *et al.* (2018), the first visit of a pregnant woman to the maternity unit of a hospital, clinic or health centre is described as booking visit (BV). It happens to be the first encounter with healthcare providers as well as being introduced to the maternity services. It is also the time when both obstetric and family histories are recorded for the purposes of determining any potential health risk during pregnancy.

Early booking visit intervenes in saving the lives of both the mother and foetus/newborn through promotion of good health seeking behaviours among pregnant women.

Two major forms of antenatal practices are the traditional antenatal care (TANC) and focused antenatal care (FANC). Whereas the traditional type involves a monthly visit for the first six months, followed by a fortnight visit for the following two months and a weekly visit until delivery, the FANC initiated in 2002 by WHO requires a maximum of four visits scheduled as follows: the first visit is before week 16, the second visit comes between weeks 20 and 24 while the third visit is between week 28 and 32 and finally fourth visit comes off between 36 and 40 weeks of gestation. This was implemented in Ghana in 2002. However, WHO in 2016 developed another ANC model following evidence emanated from the 2002 model;

1. the recommended four ANC visits in the 2002 model was associated with an increased perinatal death.

2. high level of maternal satisfaction was derived from increasing the number of ANC visits irrespective of the country.

Based on these observations, the current WHO recommended minimum ANC visits is eight contacts, scheduled as one visit in the first trimester before week 12 described as Contact 1, two visits in second trimester – week 20, Contact 2; in week 26, Contact 3 and five visits in the third trimester with Contact 4 in week 30, contact 5 in week 34, Contact 6 in week 36, Contact 7 in week 38 and Contact 8 in week 40 (WHO, 2018). Ghana, on the other hand implemented an inverse version of this recommendation with more visits in early parts of the pregnancy which requires of the pregnant woman visiting every month till week 28, fortnight

visits from weeks 28 to 36, then weekly visits until delivery (Ansah-Opoku *et al.,* 2018) which totals 13 visits.

1.3 Placental Characteristics

Placental morphometric index, which is defined as a measure of diameter, thickness, area, volume, weight and number of cotyledons, is gaining keen interest among obstetricians and anatomists on the basis of understanding the biological complexity and uniqueness of these organs (Sabita and Gugapriya, 2014). Studies over the years have paid attention to the increasing importance of normality or pathology associated with the placenta. This is because, the placenta is an extra organ that develops in the female due to pregnancy and permits efficient transfer and exchange of materials between the mother and foetus (Abramowicz and Sheiner, 2008; Bhatia and Chhabra, 2018). The placenta is an organ that connects the growing foetus to the uterine wall at the maternal side (Agarwal *et al.,* 2015).

The birth of a healthy child and successful pregnancy outcome are dependent on the qualitative and quantitative properties of the placenta and umbilical cord which ensure the survival, healthy growth and development of the foetus (Kowsalya *et al.,* 2013). The functional and morphologic capacities of the placenta are known to determine the path of prenatal development which in turn influences birth weight. Placental and umbilical cord parameters have traditionally been described in qualitative terms which are also known to have clinical association with pregnancy outcome. Essentially, having these parameters described in quantitative terms is likely to enhance the accuracy of diagnosis among surgical pathologists (Salafia *et al.,* 2005).

Hypertensive disorders such as hypertension, gestational diabetes, preeclampsia and eclampsia which affect the health of the mother also in a similar fashion influence the vascular

development and functional capacity of the placenta. Thus, valuable information about perinatal health of both the neonate and mother could be obtained by critically examining the placenta (Agarwal *et al.,* 2015). It has been reported that, developmental and functional abnormalities associated with the placenta during various stages of pregnancy are accountable for adverse pregnancy outcomes including stillbirth, early miscarriage, midtrimester foetal death, preterm birth, intrauterine growth restriction, placental abruption and *placenta praevia* (Moran and McAuliffe, 2011).

Gross placental measures entail more than just its weight but also the diameter, thickness, shape, volume and other structural growth of different placental parts which in theory influence birth weight by different mechanisms (Salafia *et al.,* 2008; Kulandaivelu *et al.,* 2014). For example, placental lateral growth, defined to include the largest diameter, smallest diameter and chorionic-plate area, is known to be involved in bulk transport of foetal blood exchanged within the villi capillary bed. Placental area is a reflection of the size of the uterine lining in contact within the placenta and which also depicts the quantity of maternal spiral arteries supplying the placenta (Baptiste-Roberts1 *et al.,* 2009). Placenta could be referred to as the "black box recorder" organ that maintains exact and efficient recordings of intrauterine life experiences of the neonate from pregnancy to birth. It has been hypothesized that, in mothers who fail to attend antenatal care, a careful examination of the placenta could assist in prompt diagnosis of intrauterine growth restriction risk of foetuses (Kulandaivelu *et al.,* 2014).

1.4 Umbilical Cord Characteristics

The umbilical cord is an intra – amniotic structure developed from the allantois and stalk of yolk sac which connects at one end of the placenta and inserts into the foetal abdomen at the umbilicus (Sabnis *et al.,* 2012). Characteristically, a fully developed term umbilical cord ranges from 1 to 2 cm in diameter, 50 – 60 cm in length with two arteries that carry deoxygenated blood and metabolic by-products towards the placenta and one vein which transports oxygenated blood containing essential nutrients from the placenta to the foetus embedded within large quantity of Wharton's jelly (Kumar *et al.,* 2017; Tsegah and Asante, 2018). The umbilical cord is described as the foetal lifeline and an important component of the foetoplacental unit which is flexible, mobile and strong to withstand compression and to permit foetal movement during intrauterine life (Sabnis *et al.,* 2012; Nandini *et al.,* 2015; Masarat, 2017).

The influence exerted by the umbilical cord on the development and well-being of the foetus has been extensively studied. Significantly positive relationship between umbilical cord length with neonatal birth weight, body length and head circumference has been reported (Petekkaya1 *et al.,* 2011). Several umbilical cord morphometric indices and that of its vessels have shown statistically significant correlation with neonatal birth weight, body length and abdominal circumference among normotensive and hypertensive mothers while significant differences in body length between short and normal umbilical cord lengths of neonates have been observed (Bimpong *et al.,* 2019). Evidence exists that, perinatal mortality is significantly high among short and long umbilical cord neonates than their normal counterparts (Kumar *et al.,* 2017). Umbilical cord diameter is known to positively correlate with placental and neonatal birth weights. This implies that, thin umbilical cords could result in low placental and neonatal birth

weights (Proctor *et al.,* 2013). Also, foetuses at risk of adverse pregnancy outcomes can be identified using umbilical cord thickness and area. This is because, they have been found to show significant relationship with intrauterine growth restriction, low birth weight and meconium staining (Tahmasebi and Alighanbari, 2011).

1.5 Maternal Anthropometric Indices

The pregnant woman is the sole provider of all the requirements for a successful pregnancy outcome. Therefore, maternal anthropometric indices are valuable determinants in pregnancy evaluation. For example, expectant mother's anthropometric parameters such as booking weight and height are known to influence birth weight. A poor socioeconomic characteristic affects maternal nutritional status, extremes of maternal age adversely influence foetal development and birth weight outcome while low educational level leads to poor knowledge on nutrition and morbidities such as severe anaemia. Parity is also known to relate positively with birth weight outcome (Haq *et al.,* 2017; Shariff and Prakash, 2019). Low booking BMI has been reported to strongly predict unfavourable pregnancy outcomes (Hassan *et al.,* 2011).

1.6 Maternal Booking Biometric Indices

Progression of pregnancy is associated with remarkable increase in maternal circulating lipids. It has been reported that, plasma cholesterol concentrations rise from 25 to 50% while triglyceride level increases from 200 to 400% from first to third trimesters, HDL-C level also increases up to 40% from the 14 to 28 weeks while LDL-C shoots to 70% in level (Huda *et al.*, 2009). The variations in maternal plasma lipid profile lead to changes in foetal growth and developmental processes. This is evident in the biochemical and physiological influence exerted

by cholesterols on foetal membranes and neurodevelopment (Aghaie *et al.,* 2018). Also, the increased concentrations of plasma lipids return to their booking levels after delivery, suggesting that, the rise in concentrations might play important physiological or biochemical role in the development of the foetus (Geraghty *et al.,* 2016).

The functional role played by cholesterol during foetal development is crucial since it is a major constituent of cell membranes, regulates metabolism (oxysterols), important in hedgehog signaling modulation and a precursor of steroid hormones. Though there is endogenous synthesis of cholesterol by the foetus, maternal cholesterol is vigorously transported across the placenta in the early stage of pregnancy to serve as the main source of energy (Zhang *et al*., 2017). At the embryonic stage, cholesterol contributes significantly to cellular proliferation, differentiation and cellular communication. It has therefore been proposed that, a unit kilogramme increase in body tissue of the developing foetus must correspondingly be accompanied by 1.5 to 2.0 g net deposition of cholesterol (Zeng *et al*., 2017).

However, the increase in levels of total cholesterol, LDL-C and HDL-C is not so significant during the first trimester, probably due to decreased food intake following frequent vomiting and nausea which characterize the early stages of pregnancy (Mankuta *et al.,* 2010). It has been reported that, early pregnancy lipid levels lower or higher than the ranges considered to be normal is associated with poor health consequences for the mother and her developing foetus. For this reason, early rise in cholesterol and triglyceride levels are known to predict development of hypertensive disorders of pregnancy (HDP) (Geraghty *et al.,* 2016).

A similar study to this current one, which correlated first prenatal visit lipids with foetal growth outcome found TG level correlating positively with neonatal birth weight, body length and

shoulder circumferences (Liu *et al.,* 2016). It has also been reported that, while low maternal booking cholesterol levels associate with preterm delivery and low birth weight, elevated LDL-C predicts development of atherosclerosis in later adult life (Mendelson *et al.*, 2016). On the contrary, HDL-C level has been found to negatively correlate with birth weight, body length and chest circumference while TG and LDL-C only showed positive relationship with body length and chest circumferences (Mitra *et al.*, 2012).

1.7 Neonatal Anthropometry

Neonatal anthropometric indices consisting of birth weight, body length, head and abdominal circumferences are key quality control parameters in evaluating foetal growth, intrauterine life and maternal nutritional status during pregnancy. These indices are routinely measured at the obstetric and neonatal units for the purposes of assessing peri- and postnatal physical development in clinical practice and probable prediction of development of chronic disease later in adult life (Hajianfar *et al.,* 2018).

Impaired development of these neonatal anthropometric indices at birth are known to associate with high risk of developing chronic diseases in adult life such as obesity, diabetes, cardiovascular disease (Kuhle *et al.,* 2017), endothelial dysfunction (Visentin *et al.,* 2014), non-alcoholic fatty liver and kidney diseases (Hirano *et al.,* 2016). The outcome of specific neonatal anthropometric index impairment has been observed. For example, low birth weight could be as a result of iron deficiency anaemia which in turn leads to impaired neurodevelopment at term (Long *et al.,* 2012). Also, poor growth of head circumference is associated with the neonate not achieving optimal neurodevelopmental potential (Sicard *et al.,* 2017).

Morphometric evaluation of these neonatal anthropometric indices at birth is important to properly differentiate between normal and IUGR neonates. In the case of ―false positives‖, an otherwise healthy neonate is misclassified as unhealthy, resulting in special monitoring which in reality is needless while parental anxiety and misuse of limited clinical resources are the end results. Also, in the "false negatives", small neonates needing special care are wrongly classified as growing normally. As such, health risks facing these neonates are clearly ignored (Janssen *et al.*, 2007).

1.7.1 Birth Weight

Birth weight is considered the most appropriate, easy to apply, and low cost tool to diagnose foetuses at risk of intrauterine growth restriction and compromised intrauterine environment (Salavati *et al.,* 2019). However, birth weight can be modulated by both maternal and foetal characteristics with maternal factors being blood pressure, BMI, gestational diabetes, chronic hypertension and dysmetabolic conditions. The foetal factors include utero–placental activities, impaired intrauterine growth, premature birth and infections (Lim *et al.*, 2014). Admittedly, maternal conditions during pregnancy such as anaemia, hypoxia, malnutrition; utero-placental dysfunctions like poor implantation, insufficient placental transfer, preeclampsia; and adverse foetal states as seen in infections and poor growth and development significantly associate with poor birth weight outcomes (Salavati *et al.,* 2019). High concentration of insulin-like growth factor-1 (IGF-1) has been found to positively correlate with birth weight following its ability to alter the composition and concentration level of lipoproteins at birth (Aletayeb *et al.,* 2013). Birth weight has been found to cause changes in blood pressure of the neonate within 72 hours after delivery. In the said study, it

was reported that, birth weight predicted mean blood pressure of 1.0 mmHg for every 100 g increase in birth weight between 25 and 72 hours after delivery. This anatomical association between birth weight and neonatal blood pressure could be explained in terms of the transition from foetus to neonate that involves reduced activity and increased production of vasodilation factors. This is important in both foetal survival and intrinsic alteration in the functional role played by the vascular smooth muscles (LeFlore and Engle, 2002). There is also another study which recorded rise in blood pressure for neonates with birth weights ranging from 2.5 to 3.5 kg at 25 – 48 hours after birth, but remained constant beyond 3.5 kg. The deduction from these studies is that, birth weight is a key determinant of blood pressure and could influence its levels in early life of the neonate (Nwokoye *et al.*, 2015).

Geraghty *et al.* (2016) reported a thrilling finding, where it was found that, birth weight was positively associated with triglyceride levels in late pregnancy. Significant positive association of birth weight with total cholesterol and triglyceride levels has also been reported (Kulkarni *et al.*, 2013). This presupposes that, the developing foetus uses lipids in addition to glucose as sources of energy for growth. Evidence of inverse risk for the relation between birth weight and maternal lipids has been observed in a prospective study and was more pronounced in the White population. Particularly, triglyceride levels were associated with high risk of low birth weight in the Whites (Harville *et al.*, 2018).

1.7.2 Body Length

Body length at birth is fundamental in determining nutritional status of the neonate. Characteristically, it is sensitive, easy to obtain and interpret and could be used in identifying neonates who are malnourished and or have other health related problems (Wood *et al.*,

2013). It has been observed that, poor growth and undernutrition are linked to an adverse outcome in adult life including short adult stature, dysfunctional cognitive ability, morbidity and mortality (Victora *et al.,* 2008). Both body length and birth weight therefore become the foundation upon which future growth measures are compared and critical decisions on interventions are formulated when these are used to plot standard growth curves. It is often treated secondarily to birth weight due to low level or lack of understanding of its significance. Consequently, it is either measured incorrectly or completely ignored in clinical practice following perceived difficulty in taking length measurements (Wood *et al.,* 2013). Body length is useful in assessing the timing and severity of "*in utero*" growth restriction, since comparing length and head circumference permits differentiation of symmetric and asymmetric growth patterns (Janssen *et al.,* 2007). It has been reported that, maternal high – quality diet during the first trimester positively associates with both birth weight and body length while carbohydrate intake relates inversely with body length and head circumference (Hajianfar *et al.,* 2018).

Maternal serum lipid concentration probably exerts appreciable influence on neonatal anthropometric indices. Whereas cholesterol is known to regulate cell membrane, tissue and organ development, maternal TG have shown significant positive relationship with neonatal body length and birth weight. On the contrary, HDL – C negatively related with birth weight (Ghiasi *et al.,* 2014). Another study also observed that, 0.0037 mmol/L rise in HDL – C in pregnancy was associated with a decrease of 0.22 g in birth weight, 0.24 cm in body length and 0.24 cm in head circumference while 0.028 mmol/L rise in TG was associated with an increase of 0.13 g in birth weight and 0.19 cm in head circumference. However, TC and LDL-C never associated with the neonatal anthropometric indices (Boghossian *et al*., 2017).

1.7.3 Head and Abdominal Circumferences (HC and AC)

The size of brain both *in utero* and after delivery could be determined indirectly by measuring head circumference (Singh *et al.,* 2018). Relationship between head circumference at birth and intellectual capacity of the child during early school-going age has been reported (Obel *et al.,* 2003). Head circumference rapidly increases in the first year of life and in conjunction with other neonatal indices, could be used in identification of macrocephalic or microcephalic conditions. For instance, head circumference-for-age is a marker for identifying severe chronic protein-energy malnutrition (PEM) or severe chronic malnutrition in children during early few months. PEM leads to decreased brain growth which also could result in abnormally small head circumference (Cape Town Metropole Paediatric Interest Group, 2009).

Abdominal circumference (AC) is the only neonatal anthropometric parameter not routinely measured at obstetric and neonatal units. Standard reference values for abdominal circumference are difficult to determine because AC measurement is affected by the resistance of the abdominal wall, time of feeding or defaecation, amount of fat deposit and different phases of breathing (Meldere *et al.,* 2017). However, measurement of abdominal circumference is clinically relevant in determining the size of abdominal viscera in a healthy neonate, pathological organs and other disease conditions of the abdominal cavity. For example, greater abdominal circumference is associated with each clinical stage of necrotizing enterocolitis (NEC). Therefore, AC could play a significant role in clinical diagnosis (Guner *et al.,* 2008).

1.8 Statement of the Problem

Major observations key to hindrances in the practice of modern obstetrics have been early detection of pregnancy at risk of early onset of hypertensive disorders of pregnancy and taking the needed measures applicable to minimizing morbidity and mortality relating to pregnancies (Poon and Nicolaides, 2014). HDP is ranked second as the direct cause of maternal deaths around the globe, but places first in certain tertiary referral hospitals and contributes 19% and 40% to maternal morbidity and mortality respectively in Ghana (Amoakoh-Coleman *et al.*, 2017). Also in Columbia, 7,482 cases of severe maternal morbidity was reported in 2016 for first trimester pregnancies which represented 27.9 mothers for every 1000 live births and 182 cases of maternal mortality also corresponding to 49.2 mothers for every 100, 000 live births. These morbidity and mortality cases were attributed to hypertensive disorders in pregnancy (62.4% and 15.5%) and haemorrhagic complications (15.5% and 18.0%) respectively (Cortés-Vásquez *et al.*, 2018).

Evidentially, relationships exist between maternal TC, HDL-C, LDL-C and TG and HDP as well as risks of changes in the processes leading to the perinatal outcomes (Aghaie *et al.*, 2018). Increased total cholesterol and triglyceride concentration levels are reported to serve as markers for identification of poor maternal and foetal health outcomes. For example, elevated level of triglyceride in early pregnancy associates with pregnancy induced hypertension, preeclampsia, preterm birth, foetal body length, birth weight and fat mass (Geraghty *et al.*, 2016).

Blood pressure is known to decrease in the early part of pregnancy and rises approximately after 18 to 20 weeks of gestation. As such, pregnant women who experience HDP have high booking blood pressure. Also, elevated systolic and diastolic blood pressures from 18 to 30 weeks of

gestation associate with low birth weight and small-for-gestational age (Macdonald-Wallis *et al.,* 2014). Similarly, elevated BP is found to associate with small neonatal head circumference, femoral length and birth weight.

Although, a number of risk factors relating to adverse maternal and perinatal outcomes have been identified, two things still remain; assessing the risks and predicting outcomes have not been quantified and also, poor understanding of the mutual relationships among risk factors makes it difficult in predicting pregnancy outcome. An approach that will identify patients at risk of HDP early enough would assist in intervening appropriately and cut down cost on unnecessary and potentially distressful interventions which the patients do not even need (Poon and Nicolaides, 2014).

The lipid biomarkers when elucidated and proven could easily be implemented in most clinical establishments because majority of clinical laboratories are already equipped with facilities to conduct lipid profile tests in order to identify pregnancies at risk of HDP (Boghossian *et al.*, 2017). In fact, the biochemical basis for the relationships among placental, umbilical cord and neonatal indices using maternal booking visit biometric parameters is yet to be explored.

This study uses simple mathematical models to hypothesize on how maternal booking biometric indices could exert influences experienced by foetal, placental and umbilical cord tissues which induce adaptive remodeling on the tissues and the ultimate changes in functional efficiency. This approach of studying the perinatal triad (that is maternal-placental-foetal) allows for building a simple picture in the functioning of materno-placental and foeto-placental circulations that permit the sinologist, paediatrician and anatomist to effectively predict the outcome of foetal, placental and umbilical cord

morphology and morphometry. For this reason, there is the need to develop accurate, easy to use and cost effective pregnancy screening methods to identify pregnancies at risk of complications in early parts of the first trimester, especially in low income countries like Ghana (Ferreira *et al.,* 2011). This current study aims at establishing predictive models using maternal booking visit biometric parameters to predict the outcomes of placental, umbilical cord and the neonatal indices.

1.9 AIM AND SPECIFIC OBJECTIVES

1.9.1 Aim

To establish predictive models using maternal booking visit biometric indices to predict the outcome of placental, umbilical cord and the neonatal indices.

1.9.2 Specific Objectives

- To determine relationship between maternal sociodemographic and booking visit biometric indices.
- To establish Pearson correlations between placental and umbilical cord indices and also compare placental characteristics among neonates with short and normal umbilical cord lengths.
- To develop predictive models for the outcome of neonatal indices using maternal booking visit biometric indices.
- To develop predictive models for placental and umbilical cord indices using maternal booking visit biometric indices.

1.10. Ethical Consideration

Ethical approval was sought from the Committee on Human Research Publications and Ethics, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana. Also, permission was obtained from the authorities of Victory Maternity Home and Clinic as well as informed consent from prospective participants before sample collection.

CHAPTER TWO

RELATIONSHIP BETWEEN MATERNAL SOCIODEMOGRAPHIC AND BOOKING VISITS BIOMETRIC INDICES

2.1 LITERATURE REVIEW

2.1.1 Maternal Sociodemographic Characteristics

A limited number of studies have been conducted on the impact of maternal sociodemographic parameters on pregnancy outcomes. These studies have shown that, maternal sociodemographic characteristics are associated with increased risk of adverse pregnancy outcomes including preterm birth, low birth weight and foetal growth restriction (López and Bréart, 2013). Maternal sociodemographic characteristics is defined to include the age of the mother, parity, education, occupation, religion, marital status, ethnicity, family size and income levels (Mosha and Napendaeli, 2010). It has been observed that, among the high risk factors for adverse pregnancy outcomes are the maternal sociodemographic characteristics (Baskaradoss *et al.*, 2012; Ganchimeg *et al*., 2014).

Identification of these predisposing factors of adverse pregnancy outcomes is justified by the reasons that; it permits the identification of pregnant women at risk who need particular attention and treatment. Secondly, it contributes to the study of specific population and the exact interventions to be applied. Lastly, it contributes to the in-depth understanding of the mechanisms which result in low birth weight and preterm delivery (Ganchimeg *et al.,* 2014).

The age range which is perceived to be appropriate to conceive with no or little obstetric complications is 20 – 35 years. Therefore, ages below or above this range could endanger the life of the mother and her foetus (Mosha and Napendaeli, 2010). Adverse pregnancy outcome is

commonly associated with age below or above this bracket. High postnatal mortality has been found to be highest among the youngest and oldest group of mothers with mothers less than 20 years recording the maximum limit followed by mothers above 35 years (Bratati and Hazra, 2004). The incidence of low birth weight neonates has been observed to be strongly associated with adolescent mothers than older women. It was reported that, neonates born to mothers less than 19 years were at 60% risk of dying in the first year of life than neonates born to mothers older than 19 years (Ayuba and Ibukun, 2012),. In another study, it was observed that, low birth weight neonates' mothers were less than 20 years and formed 33.8% of the study population, whereas the age range of 21 – 30 years was found to be ideal for giving birth to normal birth weight neonates. Maternal age greater than 31 years constituted 38.6% of the population and they also gave birth to low birth weight neonates (Sabir *et al.*, 2013).

Childbearing age is regarded as a global social issue and developed countries have been experiencing an increased trend of childbearing at an advanced maternal age of 35 years or more. Several studies have associated advanced maternal age with a number of high risk pregnancy complications such as miscarriage, stillbirth, preterm births, delivery of small-for-age or large-for-age neonates and emergency or elective caesarian deliveries. These studies reported that, advanced age mothers forgo the normal childbearing age to undertake higher education, improved career opportunities and reliance on assisted reproductive technologies (Odibo *et al.,* 2006; Huang *et al.,* 2008; Wang *et al.,* 2011; Khalil *et al.,* 2013). Significant association of age with ineffective contractility of the uterus and malfunctioning of endothelia has been observed in advanced age mothers. The biological basis of this observation is the dysfunctioning uterine tissues due to various physiological aging processes such as changes in hormonal level and secretions associated with the age of the mother (Blomberg *et al.*, 2014).

Developing countries experience highest incidence rate of teenage pregnancy globally. For example, a Tanzanian National survey found that, 25% of mothers gave birth at the age of 17 years which rose to about 40% among those who were 18 years. Growing evidence suggests that, young maternal age significantly correlates with increasing risk of pregnancy complications involving low birth weight, stillbirth, preterm birth, intrauterine growth restriction and neonatal mortality. In one study, it was found that, the rate of neonatal mortality was high among neonates born to teenage mothers, which could be attributed to financial and social difficulties. Little or no child medical care, immature anatomical and physiological development of uterus and narrow pelvic bones of teenage mothers could be contributing factors (Mousumi, 2014). Consequently, risky childbearing and inexperience in caring for neonates become the associated factors to the high neonatal mortality among these mothers. These findings are very similar to a studies conducted which used the Third round of National Family Health Survey (2005-06) data‖ of India (Mousumi, 2014; Selemani *et al.*, 2014).

Education level of mothers has been found to influence the feeding practices and choice of food of the household. Mothers with low level of education were found to show poor understanding of nutrition and feeding patterns (Mosha and Napendaeli, 2010). Maternal education is a known key factor in determining the survival of a child. A comparative demographic health survey study in three African countries namely Tanzania, Zimbabwe and Malawi observed that, the mechanisms through which mother's education influences a child's survival include: enlightened child health knowledge, compliance of prescribed principles of child's feeding practices and proper management and control of resources. In this study, one significant observation was the use of the "wasting model" to establish minimum threshold levels of maternal education below which mother's education does not contribute to reducing child's

malnutrition status. The required minimum threshold levels of a mother's education to significantly impact on the reduction of a child's malnutrition was junior secondary school which corresponded to a minimum of nine and eight years of schooling in Malawi and Zimbabwe respectively. However, in Tanzania, the level was upper primary school, corresponding to a minimum of five years in school. When the traditional stunting and underweight methods of measuring a child's nutritional status were used, the minimum threshold level was the same for Malawi (Junior Secondary School) but rose to senior secondary or higher for Tanzania and Zimbabwe (Makoka, 2013). Maternal malnutrition status during gestation shows a significant relationship with permanent damage of the central nervous system of the neonate resulting in mental retardation (Mosha and Napendaeli, 2010). Foetal growth and development completely depend on the supply of energy and nutrients from the mother in order to balance the varied demands of the foetus as well as reducing future development of poor health (Prentice, 2011). It has been reported that, mothers who spend less than six years in education are more susceptible to giving birth to low birth weight neonates with low placental weight, volume, surface area and thickness. This study observed that, undernourished mothers showed consistently significant lower placental weight, volume, surface area and thickness as against the normal group. Another study also found maternal malnutrition status before and during gestation to predict positive association between birth weight and placental weight and could contribute to variations in the metabolic activities of the foetus with subsequent development of hypertension during adult life. In all these findings, it has been shown that, education only plays an indirect role in determining the birth weight and perinatal outcome (Barker *et al.,* 2010a; Balihallimath *et al.,* 2015).

The finding of well educated pregnant woman not at high risk of giving birth to low birth weight neonates could result from the high levels of awareness and knowledge of available medical facilities and services which impact positively on her health seeking behaviour and maternal nutritional status (Amosu *et al.,* 2014).

The morphology of the spiral arteries of the uterus is known to undergo irreversible structural variations after gestation. This contributes significantly to the efficient vascular remodeling thereby facilitating migration of trophoblast in subsequent pregnancies. In this sense, maternal parity has direct influence in the development of placental morphology and morphometry. This is evident in a study which recorded significantly high values of placental weight, volume, surface area and thickness among multiparous mothers than observed in primiparous mothers (Balihallimath *et al.,* 2015). The huge maternal constraint that occurs in the uterus at every first pregnancy leads to uterine adaptation which permits the mothers to effectively support subsequent pregnancies. Though the mechanism supporting this observation is unclear, it is believed that, variations in the gene expression of the placenta among multiparous mothers could explain the changes in uterine environment. These changes have been observed to enhance efficiency in blood supply and hence, variation in placental gene expression may account for differences in nutrient availability. Primiparous mothers having high incidence rate of giving birth to low birth weight neonates and or lower placental weight has been reported (Day *et al.,* 2015). Another study observed that, although statistically not significant, the percentage distribution of low birth weight neonates was 26.8%, 28.6% and 18.3% among primiparous, biparous and multiparous mothers respectively (Sabir *et al.,* 2013).

Maternal parity is also found to relate with pregnancy wastages. In one such study, it was reported that, first time pregnancies stand at increased risk of experiencing pregnancy wastage

and the risk decreases after two to four pregnancies. However, the risk rises with the 5th birth order and above. The rise could be explained in terms of reproductive compensation where it was realized that, mothers who experienced frequent abortive pregnancies tend to have more pregnancies than mothers without abortions. Reproductive compensation instead of real birth order effect is found to contribute to the increased rate of abortion among advanced maternal age and high birth orders (Bratati and Hazra, 2004).

Maternal marital status is one demographic factor recognized to pose high risk to maternal and neonatal health outcomes. This employs social supports and stress mechanisms to exert its influence on small-for-gestational age deliveries. Neuroendocrine or immune response is found to be regulated by psychological stimuli and these biological operators are found to associate psychosocial stress with small-for-gestational age birth. It is speculated that, marital partner could probably play a significant role in the stress involved in childcare (Auger *et al.,* 2008). It has been observed that, neonates of single mothers have increased risk of experiencing low birth weight, preterm delivery, stillbirths, neonatal mortality and sudden infant death syndrome which are linked to poor and delayed prenatal care (Farbu *et al.,* 2014). Single pregnant women face a lot of socioeconomic challenges including poor mental health and psychosocial stress, stigmatization, discrimination, job loss and violence which contribute to the low patronage at free prenatal care service offered by government institutions. Reports of married pregnant women unlikely to be involved in smoking, drinking alcohol or the use of illicit drugs that adversely influence birth outcomes of the neonate are evident (Rondo *et al.,* 2003; Bilszta *et al.,* 2008; Zain *et al.,* 2015).

The findings of a study on the impact of unmarried pregnant women on obstetric outcomes were observed to include high risk of premature neonates, low birth weight, small-for-

gestational age and infant deaths. Among the theories associating marital status with perinatal outcomes are; the absence or low levels of psychosocial support, insecure relationship of unmarried women, high risk behaviour exposures including drinking of alcohol, substance abuse, illicit sexuality and stigmatization as a result of low social acceptance of the unmarried status. The risk posed by unmarried status on birth indices is considered as a surrogate marker for other potential risk factors. In fact, it has been observed that, pregnancies of unmarried women could encourage discontinued visits to a physician who could have given adequate information on prenatal care and other relevant pregnancy related issuses and safe motherhood (Kirchengast *et al.,* 2007; Balayla *et al.,* 2011).

Maternal occupation has been identified as one of the sociodemographic risk factors associated with low birth weight. The occupation of mothers at the time of becoming pregnant or in the first trimester affects neonatal birth weight. It has been reported that, mothers who work as labourers during gestation are at 7.14 times risk of delivering low birth weight babies relative to their counterparts in the service class (Shahnawaz *et al.,* 2014). Initiation of early prenatal care is critical for successful pregnancies and healthy perinatal outcomes such as delivering normal birth weight babies. However, various barriers need to be overcome by pregnant women working on the farm; these include poor transport systems, frequent movements due to work nature, low educational level, financial difficulties and pregnant women not having health insurance as well as proper documentations. Also, the musculoskeletal system of pregnant women experiences a lot of strain which changes their centre of gravity making them more susceptible to musculoskeletal injuries. Additional risks of injury are work related such as heavy workload, continuous bending and or squatting, frequent hand and body movements, long hours of standing, intensive physical work like lifting and psychological stress (Runkle *et al.,* 2014).

Nutritional and emotional status of the pregnant woman is believed to affect the development of the foetus. As a result, it becomes imperative in ensuring healthy physical and psychological environment before and during pregnancy. The influences exerted by maternal work strains on the foetal outcome have been found to include preterm delivery and low birth weight. A 2011 Korean study on impact of a mother's job strain observed significant association between adverse pregnancy outcomes and work stress as indicated by 39% of female doctors responding affirmatively to experiencing one adverse pregnancy outcome or the other, including pregnancy complications, abortion and infertility (Kim *et al.,* 2015). Naidoo *et al.* (2011) reported on association between occupational exposures and poor reproductive outcome among mothers in various categories of work. The findings specifically indicated high risk of spontaneous abortion among healthcare workers who came in contact with chemicals such as disinfectants, antineoplastic and anaesthetic drugs. Also, women working in industries who were exposed to heavy metals and solvents were at high risk of experiencing spontaneous abortion. Ergonomic exposures like standing three hours a day, lifting and heavy workload were found to associate with preterm delivery and low birth weight neonates.

Two theories have been identified as the possible explanations of the mechanisms underlying the association between prenatal maternal stress and neonatal outcome. In one theory, described as the hypothalamic-pituitary-axis (HPA) model, it was found that, cortisol levels alter maternal stress which in turn alters the control of 11-beta hydroxysteroid dehydrogenase type 2 (11β-HSD2) in the placenta. This biomarker regulates neonatal exposure to cortisol by the conversion of active cortisol into inactive form which otherwise could adversely influence foetal development. The other theory is the autonomic nervous system and uterine blood flow. Two observations made with this theory are first; stress was found to induce neonatal sympathetic

nervous functioning. As a result, it changes the autonomic nervous system balance. Secondly, the induction of high levels of adrenal hormones due to stress stimulates vasoconstrictions in the uterus and hypoxic foetal disorder (Kim *et al.*, 2015).

The health and life span of the individual is linked with active participation in religious services, but very few studies have explored this fact to determine if the health benefits derived from religious involvement could be passed on from the mother to her neonate. The result of a study that analyzed data from the US Fragile Families and Child Wellbeing observed lower odds of low birth weight among neonates of unmarried urban mothers who at least involved themselves in religious service once a week, but the same was not found in neonates of unmarried urban mothers not involved in religious attendance (Reichman *et al.*, 2008).

The connection between religion and health of the individual is more pronnounced in the African setting, where sicknesses and deaths have been attributed to spiritual powers for many years. In this context, the Christian, Islamic and traditional beliefs and practices play crucial roles in pregnancy and childbirth. During pregnancy, expectant mothers seek possible spiritual and traditional alternatives to be sure of their protection, safe delivery and good health of their neonates. Therefore, pregnant women make use of various religious artifacts to impact positively on their fate. Among these artifacts are holy water, anointing oils, handkerchiefs, religious leader's stickers, blessed sand, bibles and rosary. Some of the artifacts are used once and others are used even after delivery (Aziato *et al.*, 2016) .

The potential factors intervening between maternal religious involvement and low birth weight neonates are speculated to include the mental health and health behaviour of the mother. It is assumed that, poor mental health is a predisposing factor to a number of adverse birth outcomes. However, better mental status promotes social and psychological benefits including

optimism as well as a sense of meaning and purpose and also takes away a number of harmful moody conditions such as anger, depression, anxiety and nonspecific psychological distress. Religious involvement therefore probably protects against low birth weight by promoting a healthy mental status of the expectant mothers (Reichman *et al.,* 2008; Burdette *et al.,* 2012).

It has been speculated that, religious involvement could reduce the reccurence of low birth weight in neonates through promotion of healthier behavioural practices and avoidance of inappropriate lifestyles among expectant mothers. Reasons have been suggested that, expectant mother's religious attendance could influence birth outcome through promotion of enhanced healthy behaviour and the sanctioning of specific unsafe behaviour. Certain religious doctrines and sanctifications are very relevant to healthy behaviour among pregnant women as they religiously and spiritually stimulate proper caring for their bodies and adhere to pregnancy advices offered them by health professionals or medical experts and reduction of involvement in acts considered unhealthy and which may impact negatively on the health of both the mother and neonate (Burdette *et al.,* 2012). Religion is also known to create supportive environment and social communities which are essential to the health status of pregnant women. Indeed, a direct relationship between social support and birth consequences have been reported (Elsenbruch *et al.,* 2007).

Study of minority racial populations in advanced countries had found increased adverse pregnancy outcomes. These adverse conditions range from miscarriage, stillbirth, preeclampsia, gestational hypertension, gestational *diabetes mellitus*, preterm delivery, small-for-gestational age or large-for-gestational age neonates (Khalil *et al.,* 2013). Significant differences in maternal characteristics have been observed among ethnic groups. Differences in behaviour, medical, nutritional, cultural and social factors have been proposed to account for the nativity

variations. A comparative study among African, US born black women and US born white women in Illinois reported lower risk of African born black women delivering low birth weight neonates than US born white women. In the same study, the association between maternal and neonatal characteristics and low birth weight outcomes were found to vary with ethnicity (Fucntes-Afflicks *et al.*, 1998).

Ethnic variations in maternal cholesterol and triglyceride levels have been studied in six ethnic groups staying in Amsterdam including Dutch, Surinam-Hindustani, African- Caribbean, Turkish, Moroccan and Ghanaian pregnant women. It was observed that, the African-Caribbean, Moroccan and Ghanaian women showed statistically significant lower levels of total cholesterol relative to the Dutch women. Also, the Ghanaian women had lower levels of triglyceride as compared with the other ethnic groups (Schreuder *et al.*, 2011).

Evidence from cultural and traditional practices points to the fact that, maternal ethnicity offers possible explanations to variations in gestation and neonatal mortality among different ethnic populations. Black and Asian women were found in a study to have shorter gestational period than their white European counterparts. This observation is assumed to result from differences in socio-economic, behavioural and physiological characteristics. The association between gestational age and birth weight is seen in the rate of neonatal mortality resulting from low birth weight (Lorch and Enlow, 2016).

2.1.2 Maternal Anthropometry

Anthropometry is the only known most popular applicable approach which is less expensive and non-invasive in the determination of size, proportions and composition of the human body as well as predicting into future performance, growth and well-being and the survival of the individual (WHO Expert Committee, 1995). The maternal anthropometric parameters are

described to include the measurements of the mother's height, weight, body mass index, pre-pregnancy weight, weight-gain in pregnancy, skinfold thickness, waist and hip circumferences (Jananthan *et al.,* 2009). Anthropometric indices of the mother are essential determinants of birth outcome. They may predict both past and future events, reflect present nutritional status, indicate associated socioeconomic disparities, a risk or a reaction to an intervention. In other words, anthropometric indices draw clearly distinctive lines between the concepts of risk, benefits and response at various levels of development (WHO Expert Committee, 1995). Reports from studies conducted in developed and less developed worlds have proven that, maternal anthropometric characteristics positively correlate with neonatal birth weight. For instance, stature, pre-pregnancy weight, pre-pregnancy body mass index and weight gain in pregnancy show strong significant association with birth weight (Kotingo *et al.,* 2015).

Maternal anthropometric parameters serve as easier, cheaper and readily available alternative in identifying birth outcome with excellent reliability. For example, low pregnancy weight in the first trimester is an indication of poor maternal nutritional status which in turn correlates linearly with placental size and foetal abdominal circumference at term (Thame *et al.,* 2004). In developing countries, the impact of maternal anthropometry on birth outcome has been explained in terms of levels of poverty, chronic malnutrition and poor living standards which adversely affect maternal nutrition. Maternal nutritional status significantly determines the nutrient made available to the foetus. It is known that, nutrient supply to the foetus is a key influential factor for prenatal outcome (Mohsen and Wafey, 2007; Ugwa, 2014).

An Association between maternal height and birth weight has been reported, where mothers whose height measured above 155 cm (1.55 m) gave birth to normal weight babies (Mean birth weight of 3.6 kg) as compared to short-stature mothers (mean birth weight 2.6 kg). Indeed, poor

maternal anthropometry is considered as a potential predisposing risk factor for low birth weight (Tabrizi and Saraswathi, 2012). In medical terms, short stature is defined as the height of an adult more than 2 standard deviations below the mean for age and sex; whereas World Health Organization (WHO) recommendation indicates a height of 145 cm as the standard measure to differentiate between short and normal stature persons (Kotingo *et al.,* 2015).

The determination of foetal size is traditionally done with the use of four key foetal parameters, namely head circumference, abdominal circumference, femoral length and biparietal diameter. These foetal parameters have been reported to be positively associated with weight gain in early pregnancy. It has been observed that, mothers who showed lower rate of weight gain had smaller neonates and placental volumes as compared to mothers who had higher weight gain rate (Thame *et al.,* 2004).

Birth weight has been the most preferred parameter for determining foetal size globally due to the simplicity and availability of weight scale in all health facilities. However, body length, head circumference, abdominal circumference and mid – upper arm circumference which could substitute for weight determination in the absence of weighing scale are less applied in developing world than the developed countries (Vaano, 2014).

The identification of birth weight as an adverse birth outcome is manifested in one of the following; low birth weight (LBW), small-for-gestational age (SGW), large-for-gestational age (LGW), and macrosomia. The onset of abnormal birth weight could be visualized from the maternal anthropometry such as the booking BMI and pregnancy weight gain. Excessive increase in pre-pregnancy BMI and gestational weight gain are associated with high risk of macrosomic birth (Du *et al.,* 2016). Indeed, studies have reported that, in developing countries, the most frequently cited figure as a cut-off point for booking weight below which the

mother is three times likely to deliver a low birth weight neonate is 40 kg. In one study, it was observed that, mothers whose booking weight was < 40 kg gave birth to the lowest birth weight neonates than mothers whose booking weight was > 40 kg. It was also realized that, every 1 kg rise in pregnancy weight was associated with a corresponding 0.2 kg increase in birth weight (Tripath *et al.,* 1987; Kardjati *et al.,* 1988; Nahar *et al.,* 2005).

Waist circumference is an essential and accurate means of evaluating regional fat distribution in an adult and therefore a key indicator of identifying cardiovascular diseases and type 2 diabetes. It has been found that, waist circumference has high ability to predict beyond bodymass index, people at risk of health problems, as it strongly measures abdominal adiposity (Janssen *et al.*, 2002). Together with its importance as better measure of abdominal adiposity are other advantages such as simplicity in self-measuring of waist circumference and its reliability among middle –aged people (Visscher *et al.,* 2001), easy interpretation, only tape measure is needed which makes it cost effective, and only a single measurement is made as against averages or ratios associated with other measurements (Dobbelsteyn *et al.,* 2001). A study involving 225,000 participants reported a strong association of waist circumference with lung cancer and chronic respiratory disease-associated deaths and speculated that, physiologically, lung cancer and chronic respiratory disease mortalities involve biochemical pathways relating to insulin resistance and other metabolic disorders including excess production of proinflammatory and prothrombotic factors; all of which positively correlate strongly with abdominal adiposity (Leitzmann *et al.,* 2011).

A number of national and international studies including that of World Health Organization and other International Associations have reported a waist circumference less than 80 cm to be the normal cut off point for women with diverse ethnicity, above which it may become indicative of

weight management (Dobbelsteyn *et al.,* 2001; Lear *et al.,* 2010; Stevens *et al.,* 2010; Liu *et al.,* 2011).

Body mass index (BMI), defined as the ratio of weight in kilogrammes to the height square in metres (kg/m^2) has been the traditional method of determining weight status in public health and clinical operations (Liu *et al.,* 2011). Prospective Studies Collaboration of more than 66,000 deaths estimated an optimal survival BMI range of 22.5 – 25.0 kg/m^2, and reported that, individual's life expectancy is reduced by 3 and 10 years for moderate obesity BMI range of 30 – 35 kg/m^2 and morbid obesity BMI range of 40 – 50 kg/m^2 respectively (Huxley *et al.,* 2010). The World Health Organization (2000) in classifying body weight status categorized BMI into underweight with BMI < 18.5 kg/m^2, normal with 18.5 – 24.9 kg/m^2, overweight as 25.0 – 29.9 kg/m^2, obese class I (moderate) as 30.0 – 34.9 kg/m^2 and obese class II (extreme) to be ≥ 35.0 kg/m^2.

Indeed, overweight and obesity in Ghana is on ascendancy, especially among females and has become a great public health concern (Addo, 2010). On the basis of the WHO BMI categorization, a study conducted in the Accra Metropolitan Area on 2, 814 Ghanaian women aged 18 years and above observed that, 3.9% were underweight, 31.5% had normal weight, 27.8% were overweight and 37.1% were obese (Benkeser *et al.,* 2012). In a similar study involving 186 women in the Kumasi Metropolitan Area, it was found that, 8.0% were underweight, 62.8% normal weight, 18.1% overweight and 11.2% obese (Owiredu *et al.,* 2011). One other study which was carried out on nurses in Tamale Metropolis of Ghana, also reported that, 12.7% of the nurses were underweight, 44.0% were normal weight, 26.4% were overweight and 16.9% were obese (Aryee *et al.,* 2013).

Pre-pregnancy body mass index according to Institute of Medicine (IOM) recommendation could be used to ascertain weight gained in pregnancy. With this categorization, BMI less than 19.8 kg/m^2 corresponds to total weight gain range of 12.5 – 18.0 kg while BMI between 19.8 – 26.0 kg/m^2 is equivalent to total weight gain ranging from 11.5 kg to 16.0 kg. BMI range greater than 26.0 – 29.0 kg/m^2 correspond to total weight gain from 7.0 kg to 11.5 kg (Addo, 2010). Increased prepregnancy BMI and weight gain in pregnancy have been identified to be crucial as these predict high risk of postpartum morbidity and increased level of postpartum weight retention (Gupta *et al.*, 2015). It has also been reported that, BMI not only associates with high pregnancy complications, but also results in high numbers and long stay of maternal hospital admission and the cost of health services. The results here showed that underweight, overweight and obese women had higher mean maternal numbers of inpatient admissions and stayed longer on admission than women with normal BMI which automatically translated into high cost of health services (Denison *et al.,* 2014).

It has also been observed that, overweight and obese mothers stand increased chance of transferring their disorders to the neonates and this is clearly evident in the high BMI of children born to overweight and obese mothers. Therefore, normalization of childhood obesity is a principle in the management of maternal BMI (Gademan *et al.,* 2014).

2.1.3 Maternal Biometric Parameters

Following the intense hormonal changes associated with pregnancy, the lipid profile of the pregnant woman is adjusted to meet the rising levels of physiological changes throughout the pregnancy. Pregnant woman having normal increased physiological lipid levels obtains sufficient energy to provide for herself and the foetus and also maintain steady metabolic rate

which allows for the healthy growth and development of the foetus (Sales *et al.,* 2015). The circulating lipid concentrations of non-pregnant women is recommended to be lower than 5 mmol/L for total cholesterol, 3 mmol/L for low-density lipoprotein cholesterol (LDL-C), 2 mmol/L for triglycerides and above 1 mmol/L for high-density lipoprotein cholesterol (HDL- C). However, these blood lipid levels naturally rise during pregnancy (Geraghty *et al.,* 2016).

Maternal cholesterol and triglyceride levels in early pregnancy are crucial in determining the health status of both the foetus and the placenta. Both high and low levels of cholesterol and triglyceride are known to be associated with poor pregnancy consequences. It has been found that, reduced level of total cholesterol during pregnancy is linked to preterm delivery and intrauterine growth restriction. However, overly elevated levels of total cholesterol and triglycerides are also linked to the development of preeclampsia and other adverse pregnancy outcomes (Schreuder *et al.,* 2011).

In a third trimester lipid profile study, it was observed that, maternal cholesterol level approximately 200 mg/L corresponded to neonatal birth weight of 3.0 kg, while cholesterol levels up to 250 mg/L associated with birth weight measuring up to 3.5 kg and cholesterol levels of 300 mg/L corresponded with birth weights of 3.5 kg to 4.0 kg. Similarly, the triglyceride levels approximately 200 mg/L associated with birth weight of 3.0 kg and birth weight of 3.5 kg corresponded with the triglyceride levels of 250 mg/L. Also, triglyceride levels of 300 mg/L and above corresponded to birth weight of 3.5 to 4.0 kg. This supports the observation that, maternal circulating lipids (cholesterol and triglycerides) in the third trimester exhibits significantly positive associations with neonatal birth weight (Nisa *et al.,* 2011).

Geraghty *et al.* (2016) hypothesized that, in addition to glucose, triglycerides probably serve as source of fuel for the growth of the developing foetus. This study reported that, high level of maternal triglyceride during pregnancy possibly contributes to the development of larger placenta, which reflected in the observation of significant association of high triglyceride levels with birth weight.

High density lipoprotein – cholesterol (HDL-C) is known to significantly affect the total cholesterol balance necessary to ensure suitable steroid homeostasis to enable the extra-embryonic tissues to offer the much needed support for the developing foetus. Although, HDL-C is unable to cross the placenta, it is capable of altering foetal metabolism and growth through the influence it exerts on the foetal extra-embryonic tissue metabolic activities. It has been observed that, a decrease in maternal HDL-C concentration results in the extra-embryonic tissues undertaking compensatory mechanisms to ensure adequate circulating lipid uptake for foetal growth (Misra *et al.,* 2011).

Apart from its importance in the transport of cholesterol and maintaining circulating lipid balance, HDL-C exhibits antioxidant, anti-inflammatory and anti-thrombotic characteristics which could result in altered placental circulation and foetal growth. In this way, associations of low levels of maternal HDL-C with placental vasculopathy, possible development of preeclampsia and oxidative stress have been reported. These observations were believed to be as a result of vascular endothelial dysfunction leading to pathophysiological development of these perinatal outcomes (Bayhan *et al.,* 2005; Uzun *et al.,* 2005),

Findings of association between HDL-C and birth weight have been reported. One study observed inverse relationship of HDL-C with birth weight and indicated that, lower concentrations of HDL-C predicted for large-for-gestational age neonates (Krame *et al.,*

2013). Other studies made similar findings where it was observed that, high levels of HDL-C significantly associated with small-for-gestational age infants. These observations probably point to the fact that increased levels of HDL-C can lead to low birth weight neonates (Krame *et al.*, 2013; Ye *et al.*, 2015; Geraghty *et al.*,2016).

2.2 AIM AND SPECIFIC OBJECTIVES

2.2.1 Aim

To determine relationships between maternal sociodemographic and booking biometric indices.

2.2.2 Specific Objectives

- To determine relationship between maternal sociodemographic characteristics and anthropometric parameters.
- To determine the relationship between maternal biometric factors and sociodemographic characteristics.

2.3 MATERIALS AND METHODS

2.3.1 Study Design and Area

A descriptive cross-sectional study was conducted at the Victory Maternity Home and Clinic in the Kumasi Metropolis between March, 2014 and October, 2018. A total of 369 pregnant women in their first trimester who consented to participate in the study were enrolled. However,

240 who consented to the blood sample collection were eventually used in this study. Among the variables of the study population were maternal sociodemographic, anthropometric and biometric indices. Ethical approval was sought from the Committee on Human Research Publications and Ethics, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology and the Komfo Anokye Teaching Hospital, Kumasi, Ghana. Also, permission was obtained from the facility as well as Informed Consent from the study participants before sample collection.

2.3.2 Inclusion and Exclusion criteria

Included in the study were mothers with singleton live birth, without pregnancy or delivery complications, whose anthropometric and socio-demographic records as well as the anthropometric parameters of their neonates were complete. Excluded in the study were those pregnant women who had multiple births or lost their babies, had pregnancy or delivery complications; whose anthropometric as well as socio-demographic records and neonatal anthropometries were incomplete.

2.3.3 Maternal Sociodemographic Variables

Maternal sociodemographic information including age, parity, education, religion, ethnicity, occupation, booking weight and marital status were collected through standard medical record forms completed at the Victory Maternity Home and Clinic, Tech-Junction, Kumasi at first antenatal visit.

2.3.4 Maternal Anthropometric Parameters

Maternal anthropometric parameters studied consisted of booking weight, height and body mass index (BMI). All maternal anthropometric parameters were performed by following standardized anthropometric protocol described by Lohman *et al.* (1988). The measurements were carried out with the pregnant woman wearing minimal amount of clothing.

The weight was measured by the use of an OM – 200 digital bathroom weighing scale (American Weighing Scales Inc, USA).

Height measurement was performed using stadiometer. The pregnant woman was told to stand upright and erect with both feet together and the back of heel touching the pole of the stadiometer. The horizontal headpiece was then lowered onto the head and the measurement recorded (Nahar *et al.,* 2005).

Maternal BMI was computed from booking weight and height recorded using the formula:

$\text{BMI} = \frac{Weight(kg)}{\text{Height}^2(\text{m})}$.

2.3.5 Sampling and Biochemical Analysis

Two hundred and forty blood samples were collected after an overnight fast of at least 12 hours into a 3.5 ml vacutainer (BD Plymouth, SST II Advance Tubes, UK) stored and transported to the Wenchi Methodist Hospital Laboratory for the serum preparation and analysis. Serum was stored at -80 ^{o}C after centrifugation at 2000 g for 5 minutes before assayed. Total Cholesterol (TC), Triglyceride (TG) and High Density Lipoprotein (HDL-C) were measured using Automated Chemistry Analyzer (Flexor junior, Vital Scientific N.V., The Netherland) with reagents from ELITech Group company, (SEPPIM S.A.S, France). Low Density Lipoprotein Cholesterol was calculated using the Friedewald equation incorporated in the auto – analyzer.

2.3.5.1 Total Cholesterol

The method for this assay is based on that described by Trinder (1969). Cholesterol esterase catalyses thehydrolyses of esters to free cholesterol and fatty acids. The free cholesterol produced plus the preformed cholesterol are then oxidized in the presence of cholesterol oxidase to cholest-4-en-3-one and hydrogen peroxide. The quinoneimine chromogen, with absorption maximum at 500 nm, is produced when phenol is oxidatively coupled with 4-aminophenazone in the presence of peroxidase. The intensity of the final red colour is directly proportional to the total cholesterol concentration.

Cholesteryl ester + $H_2O \xrightarrow{\text{Cholesterol esterase}}$ Cholesterol + Free Fatty acids

Cholesterol + $O_2 \xrightarrow{\text{Cholesterol oxidase}}$ Cholest-4-en-3-one + H_2O_2

$2H_2O_2$ + Phenol + 4-Aminoantipyrine $\xrightarrow{\text{Peroxidase}}$ Quinoneimine + $4H_2O$

2.3.5.2 Triglyceride

The method for this assay is based on a modified Barham and Trinder (1972) colour reaction to produce a fast linear endpoint reaction. Triglyceride in the sample is hydrolyzed by lipase to glycerol and fatty acids. Glycerol is then phosphorylated by adenosine-5-triphosphate (ATP) to glycerol-3-phosphate and adenosine-5-diphosphate (ADP) in a reaction catalyzed by glycerol kinase. Glycerol-3-phosphate is then converted to dihydroxyacetone phosphate (DHAP) and hydrogen peroxide (H_2O_2) by glycerophosphate oxidase. The hydrogen peroxide then reacts with 4-aminoantipyrine and 3, 5 dichloro-2-hydroxybenzene (Chlorophenol) in a reaction catalyzed by peroxidase to yield a red coloured quinoneimine dye. The intensity of the colour produced is directly proportional to the concentration of triglycerides in the sample.

Triglycerides + $H_2O \xrightarrow{\text{lipoprotein lipase}}$ Glycerol + free fatty acid

Glycerol + ATP $\xrightarrow{\text{glycerol kinase}}$ Glycerol-3-Phosphate + ADP

Glycerol-3-Phosphate + O_2 $\xrightarrow{\text{Glycerol-3-phosphate oxidase}}$ Dihydroxyacetone-P + H_2O_2

H_2O_2 + 4-Aminoantipyrine $\xrightarrow{\text{Peroxidase}}$ Quinoneimine

2.3.5.3 HDL- Cholesterol

Anti-human ß-lipoprotein antibody in reagent R1 binds to lipoproteins (LDL-C, VLDL-C and chylomicrons) other than HDL-C. The antigen-antibody complexes formed block enzyme reactions when reagent R2 is added. Cholesterol esterase and cholesterol oxidase in reagent R2 react only with HDL-C. Hydrogen peroxide produced by the enzyme reactions with HDL-C yields a blue colour complex upon oxidative condensation of F-DAOS (N-ethyl-N-(2-hydroxy-3-sulfopropyl)-3,5–dimethoxy-4-fluoroaniline, sodium salt) and 4-aminoantipyrine in the presence of peroxidase. By measuring the absorbance of the blue colour complex produced at the average wavelength of 600 nm, the HDL-C concentration in the sample can be calculated when compared with the absorbance of the HDL-C calibrator.

2.3.5.4 LDL – Cholesterol

The LDL- Cholesterol concentration (LDL-C) is automatically calculated from the total cholesterol concentration (TC), HDL- Cholesterol concentration (HDL-C) and the triglyceride concentration (TG) according to Friedewald equation (Friedewald *et al.*, 1972) incorporated in the auto - analyzer. LDL- Cholesterol (mmol/l) = [TC(mmol/l) – (TG (mmol/l)/2.2 + HDL-C (mmol/l).

2.3.6 Statistical Analysis

All variables were screened for normal distribution by visual analysis of histograms. Data were presented in tables with mean ± SD and in graphs with n%. The differences in means between maternal sociodemographic, anthropometric and biometric characteristics were tested using One-Way Aanalysis of Variance (One-Way ANOVA).

2.4 RESULTS

Maternal demographic characteristics are shown in Table 1 below. The mean maternal age was 27.42 ± 6.10 years (range: 15 – 43 years) and that of parity was 2.57 ± 1.42 births (range: 1 – 8 births). Mean gestational age was 36.60 ± 2.46 weeks (range: 24 – 50 weeks).

Table 1: Descriptive Statistics of Maternal Demographic Characteristics

Variable	Mean ± SD	Range
Age (Years)	27.42 ± 6.10	15 – 43
Parity	2.57 ± 1.42	1 – 8
Gestational Age (Weeks)	36.60 ± 2.46	24 – 50

SD = standard deviation

Maternal sociodemographic characteristics such as education, religion, ethnicity, occupation and marital status are presented using frequency distribution bar charts and Figures 1(A – E). About 21.4% of the study participants did not obtain formal education, 13.0% completed Primary education and 43.0% Junior High School, while 17.3% attained Senior High School

education. The percentage of those who completed or were students of tertiary institutions was 4.3% (Fig. 1A). The religion of the participants fell within the two dominant religions in Ghana; 71.8% were Christians and 28.2% were Moslems as shown in Fig. 1B.

The ethnic backgrounds of the study participants were categorized into Ashantis, Bonos, Ewes, Fantes and Northerners as indicated in Fig. 1C. The frequency distribution chart shows that, 50.7% were Ashantis; 1.1% Bonos; 6.1% Ewes; 8.1% Fantes and 35.0% Northerners. The occupations of the pregnant women studied were grouped into seven categories. Farmers constituted 1.4% and 7.9% were Hairdressers. Housewives constituted 10.0% and the percentage of the Unemployed was 4.3%. Only one (2.2%) constituted the group tagged "Others'' which was meant to include radio presenters, nurses and fish mongers. Dress makers formed 7.0%, while Students and Teachers had the same percentage distribution (3.8%). In the light of the vibrant commercial activities in the Kumasi Metropolis, majority (59.6%) of the pregnant women in the study were Traders as presented in Fig. 1D. The frequency distribution of the study participants according to their marital status is shown in Fig. 1E where 86.2% were married as against 13.8% singles.

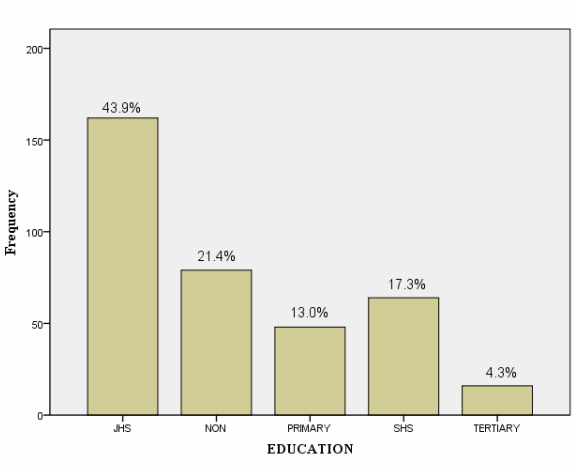


Figure A: Frequency Distribution of Participants by Education

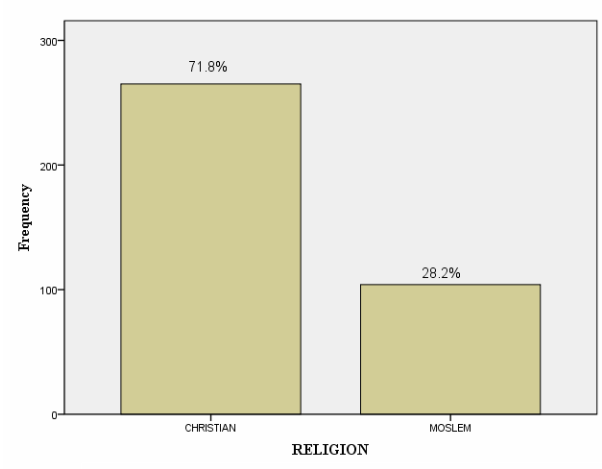


Figure B: Frequency Distribution of Participants by Religion

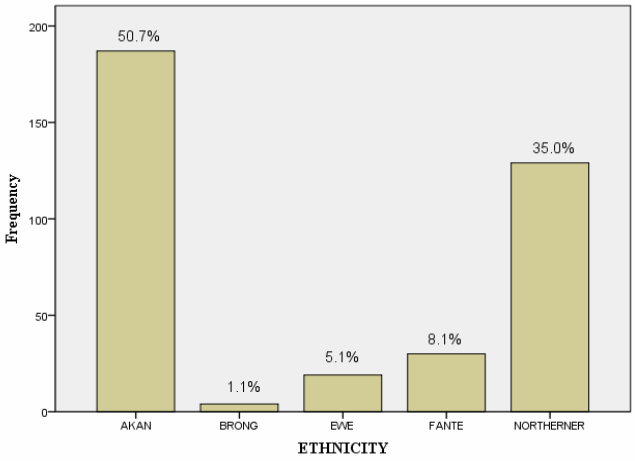


Figure C: Frequency Distribution of Participants by Ethnicity

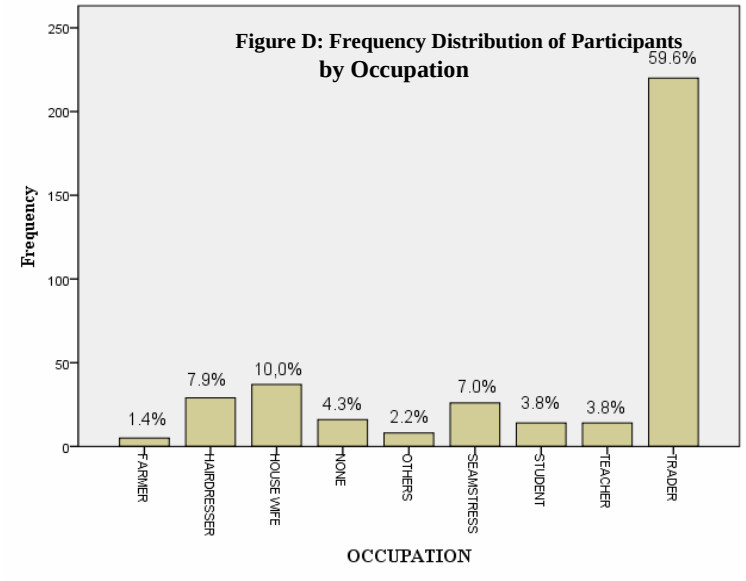
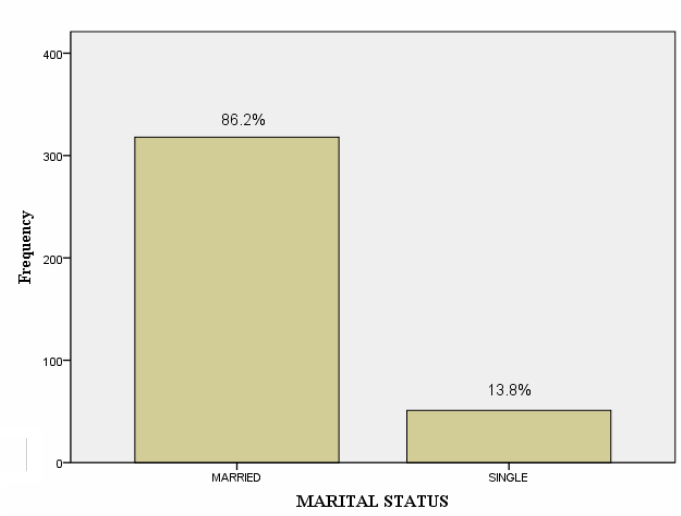


Figure D: Frequency Distribution of Participants by Occupation



E

Figure A: Frequency Distribution of Participants by Marital Status

Figure 1: Frequency Distribution of Maternal Sociodemographic Characteristics

Table 2 below shows maternal anthropometric parameters. The mean maternal booking weight was 66.26 ± 11.17 kg (37 – 95 kg). The mean maternal height was 1.60 ± 0.07 m (1.30 – 1.80 m). The mean waist circumference was 50.12 ± 12.08 cm (32 – 89 cm). Maternal booking BMI had mean of 25.80 ± 4.44 kg/m^2 (14.81 – 41.42 kg/m^2).

Table 2: Descriptive Statistics of Maternal Anthropometric Parameters

Variable	Mean ± SD	Range
MWt (kg)	66.26 ± 11.17	37 – 95
MHt (m)	1.60 ± 0.07	1.30 – 1.80
MWC (cm)	50.12 ± 12.08	32 – 89
BMI (kg/m^2)	25.80 ± 4.44	14.81 – 41.42

MWt = maternal booking weight, MHt = maternal Height, MWC = maternal booking waist circumference, MHC – maternal hip circumference, SD = standard deviation. cm = centimetre, m = metre

The maternal biometric parameters are presented in Table 3. The mean values of maternal prepregnancy systolic and diastolic blood pressures were 118.81 ± 25.15 mmHg (range: 90 – 250 mmHg) and 75.04 ± 14.02 mmHg (range: 50 – 120 mmHg) respectively. Total cholesterol and triglycerides had their respective mean and range to be 4.02 ± 0.09 mmol/L (range: 1.40 - 9.15 mmol/L) and 1.47 ± 0.05 mmol/L (range: 0.38 - 6.92 mmol/L). Similarly, the mean HDL-C was 1.11 ± 0.47 mmol/L (range: 0.50 - 2.98 mmol/L). The LDL-C mean was 2.24 ± 0.83 mmol/L (range: 0.36 - 5.68 mmol/L).

Table 3: Descriptive Statistics of Maternal Biometric Parameters

Variable	Mean ± SD	Range
SBP (mmHg)	118.81 ± 25.15	90 – 250
DBP (mmHg)	75.04 ± 14.02	50 – 120
TC (mmol/L)	4.02 ± 0.09	1.40 – 9.15
TG (mmol/L)	1.47 ± 0.05	0.38 – 6.92
HDL-C (mmol/L)	1.11 ± 0.47	0.05 – 2.98
LDL-C (mmol/L)	2.24 ± 0.83	0.36 – 5.68

SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = total cholesterol, TG = triglycerides, HDL-C = high density lipoprotein, LDL-C = low density lipoprotein, SD = standard deviation, mmHg = millimetre mecury, mmol/L = millimole per litre

In Table 4 below, the maternal sociodemographic characteristics were compared with their anthropometric parameters. When the anthropometric parameters and maternal education levels were compared using one-way analysis of variance (ANOVA), slight differences although statistically not significant, were observed in the means of maternal booking weight as follows; No formal education – 66.44 ± 11.29 kg; primary – 66.15 ± 9.89 kg; JHS – 66.03 ± 11.77 kg; SHS – 66.34 ± 11.34 kg and tertiary – 66.44 ± 6.72 kg ($p = 0.908$).

The differences in mean height values were: No formal education – 1.68 ± 0.58 m; primary – 1.61 ± 0.64 m; JHS – 1.63 ± 0.29 m; SHS – 1.70 ± 0.55 m and tertiary had 1.62 ± 0.67 m ($p = 0.587$). The means of waist circumference were; No formal education – 50.51 ± 12.25 cm; primary – 51.06 ± 10.81cm; JHS – 49.49 ± 12.30 cm; SHS – 50.23 ± 12.84 cm and tertiary – 51.31 ± 10.50 cm ($p = 0.915$). The maternal booking BMI mean values were: No formal education – 26.13 ± 4.30 kg/m^2; primary – 25.76± 4.26 kg/m^2; JHS – 25.64 ± 4.64 kg/m^2; SHS -

25.93 ± 4.64 kg/m^2 and tertiary – 25.29 ± 2.88 kg/m^2 (p = 0.922). Similarly, the anthropometric variables of the different maternal ethnic groups were compared. The observed mean values for the maternal booking weight were: Ashantis – 65.44 ± 10.53 kg; Fantes – 65.43 ± 13.00 kg; Northerners – 66.90 ± 11.59 kg; Ewes – 69.63 ± 10.52 kg and Bonos – 73.75 ± 13.07 kg (p = 0.196). The mean height differences were also: Ashantis – 1.68 ± 0.50 m; Fantes – 1.59 ± 0.06 m; Northerners – 1.61 ± 0.07 m; Ewes – 1.61 ± 0.05 m and Bonos with 1.57 ± 0.07 m (p = 0.484). The values of mean waist circumference were found to be: Ashantis – 49.97 ± 12.46 cm; Fantes – 45.97 ± 9.88 cm; Northerners – 51.01 ± 10.95 cm; Ewes – 52.53 ± 17.04 cm; with Bonos having 48.50 ± 14.82 cm (p = 0.286). Mean booking BMI values recorded among the various ethnicities were: Ashantis, 25.61 ± 4.34 kg/m^2; Fantes, 25.79 ± 5.17 kg/m^2; Northerners, 25.84 ± 4.35 kg/m^2; Ewes, 26.74 ± 3.90 kg/m^2 and the Bonos, 28.55 ± 8.61 kg/m^2 (p = 0.560), again the differences in mean values did not show any statistical significance.

The mean values of maternal anthropometric parameters with respect to their occupations showed that the booking weight of the unemployed was 67.41 ± 9.16 kg; Farmers had 58.25 ± 6.70 kg; Traders with 66.85 ± 10.83 kg; the Housewives 67.78 ± 13.16 kg; Hairdressers, Dress makers, Teachers and Students recorded 62.96 ± 10.63 kg, 64.32 ± 11.84 kg, 69.00 ± 10.53 and 62.00 ± 8.71 kg respectively. The professionals in the "Others" category (e.g. nurses, radio presenters, bankers etc) recorded booking weight of 74.50 ± 8.49 kg. These differences in mean booking weight values were not statistically significant (p = 0.267). Variations in the mean height values according to maternal occupation showed that, the unemployed mothers had 1.61 ± 0.05 m, the Farmers with 1.59 ± 0.08 m, Traders recorded 1.61 ± 0.07 m, Housewives, Hairdressers, Dress makers, Teachers and Students categories had 1.61 ± 0.08 m, 1.61 ± 0.09 m, 1.60 ± 0.08 m, 1.61

± 0.05 m and 1.58 ± 0.07 m respectively. The "Others" category had 1.59 ± 0.09 m; and again these differences in mean height values showed no statistical significance (p = 0.383). In terms of mean maternal waist circumference, the unemployed (None) category recorded 52.71 ± 16.17 cm, Farmers had 59.00 ± 20.17 cm, Traders with 50.13 ± 11.88 cm. Housewives recorded 51.16 ± 12.11 cm, the respective values for Hairdressers, Dress makers, Teachers, Students and "Others" were 48.56 ± 11.47 cm, 48.40 ± 13.36 cm, 49.36 ± 10.57 cm, 46.79 ± 5.45 cm and 49.00 ± 12.00 cm. The p – value of 0.717 indicates that, the difference in these mean values was not statistically significant. With regards to the maternal booking BMI, the mean value for Unemployed was 26.10 ± 4.40 kg/m^2, that of Farmers was 22.06 ± 0.79 kg/m^2, Traders with 25.93 ± 4.36 kg/m^2, and Housewives, 26.09 ± 4.16 kg/m^2. Hairdressers, Dress makers, Teachers, Students and "Others" accordingly had 24.54 ± 4.03 kg/m^2, 25.38 ± 5.50 kg/m^2, 26.63 ± 4.06 kg/m^2, 25.01 ± 3.48 kg/m^2 and 28.28 ± 6.18 kg/m^2. Statistically, the differences in mean values were not significant (p = 0.260).

Table 4: Comparison between Maternal Sociodemographic Characteristics and Anthropometric Parameters

Sociodemographic Characteristics	MWt (kg) Mean ± SD	p-Value	MHt (m) Mean ± SD	p-Value	MWc (cm) Mean ± SD	p-Value	BMI (kg/m^2) Mean ± SD	p-Value
Education								
No formal education	66.44 ± 11.29		1.68 ± 0.58		50.51 ± 12.25		26.13 ± 4.30	
Primary	66.15 ± 9.89		1.61 ± 0.64		51.06 ± 10.81		25.76 ± 4.26	
Junior High Sch.	66.03 ± 11.77	0.998	1.63 ± 0.29	0.587	49.49 ± 12.30	0.915	25.64 ± 4.64	0.922
Senior High Sch.	66.34 ± 11.34		1.70 ± 0.55		50.23 ± 12.84		25.93 ± 4.64	
Tertiary	66.44 ± 6.72		1.62 ± 0.67		51.31 ± 10.50		25.29 ± 2.88	
Ethnicity								
Ashantis	65.44 ± 10.53		1.68 ± 0.50		49.97 ± 12.46		25.61 ± 4.34	
Fantes	65.43 ± 13.00		1.59 ± 0.06		45.97 ± 9.88		25.79 ± 5.17	
Northerners	66.91 ± 11.59	0.196	1.61 ± 0.07	0.484	51.01 ± 10.95	0.286	25.84 ± 4.35	0.560
Ewes	69.63 ± 10.52		1.61 ± 0.05		52.53 ± 17.04		26.74 ± 3.90	
Bono	73.75 ± 13.07		1.57 ± 0.07		48.50 ± 14.82		28.55 ± 8.61	
Occupation								
Unemployed	67.41 ± 9.16		1.61 ± 0.05		52.71 ± 16.17		26.10 ± 4.40	
Farmers	58.25 ± 6.70		1.59 ± 0.08		59.00 ± 20.17		22.06 ± 0.79	
Traders	66.85 ± 10.83		1.61 ± 0.07		50.13 ± 11.88		25.93 ± 4.36	
Housewives	67.78 ± 13.16		1.61 ± 0.08		51.16 ± 12.11		26.09 ± 4.16	
Hairdressers	62.96 ± 10.63	0.267	1.61 ± 0.09	0.383	48.56 ± 11.47	0.717	24.54 ± 4.03	0.260
Dress makers	64.32 ± 11.84		1.60 ± 0.08		48.40 ± 13.36		25.38 ± 5.50	
Teachers	69.00 ± 10.53		1.61 ± 0.05		49.36 ± 10.57		26.63 ± 4.06	
Students	62.00 ± 8.71		1.58 ± 0.07		46.79 ± 5.45		25.01 ± 3.48	
Others	68.18 ± 13.37		1.59 ± 0.09		49.00 ± 12.00		28.28 ± 6.18	

MWt = maternal weight, MHt = maternal height, MWc = maternal waist circumference, BMI = body mass index, SD = standard deviation, kg =kilogramme, m =mwtre, cm = centimeter, kg/m^2=kilogramme per square metre

In Table 5 below, the means and standard deviations of maternal biometric indices using one-way ANOVA are compared. Within the sociodemographic characteristics, the differences in the mean systolic pressure (SP) observed at the educational levels were: No formal education, 116.9 ± 24.11 mmHg; primary, 124.70 ± 36.55 mmHg; JHS, 118.10 ± 20.39 mmHg; SHS, 120.10 ± 28.52 mmHg and tertiary with 112.30 ± 15.53 mmHg. The mean difference was not statistically significant ($p > 0.05$). The corresponding diastolic pressures (DP) showed that, No formal education had 74.18 ± 14.52 mmHg, primary with 78.33 ± 12.21 mmHg, JHS had 74.71 ± 14.36 mmHg, SHS recorded 75.44 ± 13.71 mmHg and tertiary had 71.19 ± 13.95 mmHg. The differences in these mean values were not statistically significant ($p = 0.368$).

The mean triglyceride (TG) values observed at different levels of maternal education levels were: "No formal education" – 3.95 ± 1.05 mmol/L; primary – 4.13 ± 1.37 mmol/L; JHS – 4.04 ± 1.03 mmol/L; SHS, 4.09 ± 1.07 mmol/L and tertiary, 3.41 ± 0.95 mmol/L. The differences in the mean values were found to be statistically significant ($p < 0.0001$). Triglyceride (TG) means recorded indicates that, "No formal education" group had 1.57 ± 0.83 mmol/L, primary with 1.29 ± 0.51 mmol/L, JHS had 1.46 ± 0.67 mmol/L with SHS recording 1.46 ± 0.77 mmol/L and the tertiary recording 1.84 ± 1.82 mmol/L. The p – value comparing the differences in mean values was 0.292 ($p > 0.05$). The mean value of low density lipoprotein (LDL-C) were found to be 1.20 ± 0.50 mmol/L for the "No formal education", 1.20 ± 0.49 mmol/L for primary, 1.12 ± 0.48 mmol/L for JHS, that of SHS was 1.10 ± 0.39 mmol/L and 0.83 ± 0.47 mmol/L for tertiary. These differences were not statistically significant ($p = 0.301$). The mean value of low density lipoprotein observed for the "No formal education", primary, JHS, SHS and tertiary were 2.14 ± 0.88 mmol/L, 2.35 ± 0.89 mmol/L, 2.27 ± 0.72 mmol/L, 2.32 ± 0.94 mmol/L and 1.74 ± 0.88 mmol/L respectively.

With respect to their ethnicity, the mean values obtained for systolic blood pressure showed that, the Ashantis recorded 117.40 ± 22.11mmHg, the Fantes with 114.90 ± 23.16 mmHg, Northerners had 122.00 ± 29.85 mmHg, Ewes with 117.00 ± 21.87 mmHg and the Bonos had 120.80 ± 21.65 mmHg. Although mean values observed were different, these were not statistically significant (p = 0.477). The mean diastolic blood pressure values observed among the ethnic groups were Ashantis – 74.46 ± 13.31 mmHg; Fantes – 72.07 ± 15.99; mmHg; Northerners – 76.58 ± 14.46 mmHg; Ewes – 75.05 ± 14.11 mmHg and Bonos – 74.75 ± 17.42 mmHg. The p – value obtained for the differences in means showed no statistical significance (p = 0.522). Mean total cholesterol values for the Ashantis was 4.07 ± 1.14 mmol/L, that of Fantes was 4.19 ± 0.70 mmol/L, Northerners had 3.98 ± 1.08 mmol/L, Ewes with 3.53 ± 1.30 mmol/L and Bonos had 3.16 ± 0.35 mmol/L (p = 0.348). Mean triglyceride of the Ashantis was 1.52 ± 0.85 mmol/L, the Fantes had 1.17 ± 0.48 mmol/L, Northern people had 1.44 ± 0.63 mmol/L, Ewes with 1.90 ± 0.94 mmol/L and the Bonos had 1.14 ± 0.28 mmol/L. The differences were not significant (p = 0.083). The high density lipoprotein mean values for the Ashantis was 1.09 ± 0.47 mmol/L, Fantes had 1.25 ± 0.38 mmol/L, Northerners obtained 1.09 ± 0.46 mmol/L, Ewes had 1.12 ± 0.66 mmol/L and the Bonos had 1.18 ± 0.34 mmol/L. The p – value observed for the differences in means was not statistically significant (p = 0.650). Mean low density lipoprotein for the various ethnicities were: Ashantis – 2.28 ± 0.89 mmol/L; Fantes – 2.46 ± 0.60 mmol/L; Northerners – 2.24 ± 0.77 mmol/L; Ewes – 1.54 ± 0.77 mmol/L and the Bonos with 1.46 ± 0.14 mmol/L. The p – value for the differences in mean observed among the ethnic groups was significant (p = 0.022).

The mean systolic and its corresponding diastolic blood pressure values observed for the different occupations of the mothers showed that, the unemployed obtained mean values of 133.40 ± 43.87 mmHg and 77.19 ± 15.29 mmHg while Farmers had 103.30 ± 15.28 mmHg and 66.67 ± 5.77

mmHg. The Traders had respective mean systolic and diastolic values of 117.00 ± 24.24 mmHg and 73.69 ± 12.96 mmHg and the Housewives had 129.50 ± 35.16 mmHg and 77.92 ± 15.77 mmHg respectively. The mean systolic and diastolic blood pressure values for Hairdressers, Dress makers, Teachers, Students and "Others" were 119.50 ± 30.57 mmHg and 72.86 ± 14.54 mmHg; 114.70 ± 24.12 mmHg and 68.42 ± 13.85 mmHg; 103.80 ± 9.16 mmHg and 65.00 ± 10.69 mmHg; 120.90 ± 31.45 mmHg and 76.36 ± 18.59 mmHg; and 116.30 ± 9.16 mmHg and 78.75 ± 6.41 mmHg respectively. These differences were not statistically significant ($p > 0.05$).

The values for mean total cholesterol among the mothers with different occupational backgrounds showed that, the unemployed had 3.84 ± 1.10 mmol/L, Farmers had 4.00 ± 0.96 mmol/L, Traders with 4.10 ± 1.15 mmol/L. The Housewives recorded 3.77 ± 1.10 mmol/L, Hairdressers with 3.81 ± 1.06 mmol/L and Dress makers scored 4.15 ± 1.06 mmol/L. The Teachers, Students and "Others' categories recorded 3.56 ± 0.83 mmol/L, 4.08 ± 0.67 mmol/L and 4.02 ± 1.08 mmol/L respectively. No statistical significance was observed in their mean differences ($p > 0.05$).

The mean triglyceride value for the unemployed was 1.47 ± 0.81 mmol/L, the Farmers had 1.43 ± 1.56 mmol/L, Traders with 1.44 ± 0.62 mmol/L, Housewives had 1.43 ± 0.77mmol/L. The value for Hairdressers was 1.62 ± 0.85 mmol/L, Dress makers had 1.48 ± 0.68 mmol/L. Teachers, Students and "Others" respectively obtained mean values of 1.22 ± 0.28 mmol/L, 1.89 ± 1.84 mmol/L and 1.48 ± 0.62 mmol/L. The mean difference was not significant ($p = 0.729$). Recordings of mean values of high density lipoprotein (HDL-C) in Table 5 below showed that, the unemployed had 0.99 ± 0.40 mmol/L while Farmers obtained 1.45 ± 0.24 mmol/L, Traders with 1.13 ± 0.50 mmol/L, Housewives had 0.99 ± 0.41 mmol/L, the Hairdressers had 1.02 ± 0.43 mmol/L. The value for Dress makers was 1.20 ± 0.32 mmol/L, that of Teachers was 0.95 ± 0.45

mmol/L, Students had 1.25 ± 0.53 mmol/L and "Others" category had 1.18 ± 0.42 mmol/L. Statistically, the differences in mean HDL-C values were not significant ($p = 0.340$).

Mean low density lipoprotein (LDL-C) values observed among the different occupations of the mothers indicated that, unemployed mothers had 2.15 ± 0.86 mmol/L, mothers who farm had 1.90 ± 0.53 mmol/L, trading mothers had 2.33 ± 0.86 mmol/L while Housewives had 2.10 ± 0.86 mmol/L. The Hairdressing mothers obtained 2.07 ± 0.89 mmol/L, Dress makers with 2.78 ± 0.75 mmol/L and Teachers had 1.96 ± 0.37 mmol/L. The values for Students and "Others" were 2.01 ± 0.62 mmol/L and 2.16 ± 1.01 mmol/L respectively. There was no statistically significant difference in their mean values ($p > 0.05$).

Table 5: Comparison of Maternal Sociodemographic Characteristics and Biometric Indices

Sociodemographic Characteristics	SP (mmHg) Mean ± SD	p-Value	DP (mmHg) Mean ± SD	p-Value	TC (mmol/l) Mean ± SD	p-Value	TG (mmol/l) Mean ± SD	p-Value	HDL-C (mmol/l) Mean ± SD	p-Value	LDL-C (mmol/l) Mean ± SD	p-Value
Education												
No formal education	116.90 ± 24.11		74.18 ± 14.52		3.95 ± 1.05		1.57 ± 0.83		1.20 ± 0.50		2.14 ± 0.88	
Primary	124.70 ± 36.55		78.33 ± 12.21		4.13 ± 1.37		1.29 ± 0.51		1.20 ± 0.49		2.35 ± 0.89	
JHS	118.10 ± 20.39	0.350	74.71 ± 14.36	0.368	4.04 ± 1.03	< 0.0001****	1.46 ± 0.67	0.292	1.12 ± 0.48	0.301	2.27 ± 0.72	0.243
SHS	120.10 ± 28.52		75.44 ± 13.71		4.09 ± 1.07		1.46 ± 0.67		1.10 ± 0.39		2.32 ± 0.94	
Tertiary	112.30 ± 15.53		71.19 ± 13.95		3.41 ± 0.95		1.84 ± 1.82		0.83 ± 0.47		1.74 ± 0.88	
Ethnicity												
Ashantis	117.40 ± 22.11		74.46 ± 13.31		4.07 ± 1.14		1.52 ± 0.85		1.09 ± 0.47		2.28 ± 0.89	
Fantes	114.90 ± 23.16		72.07 ± 15.99		4.19 ± 0.70		1.17 ± 0.48		1.25 ± 0.38		2.46 ± 0.60	
Northerners	122.00 ± 29.85	0.477	76.58 ± 14.46	0.522	3.98 ± 1.08	0.348	1.44 ± 0.63	0.083	1.09 ± 0.46	0.650	2.24 ± 0.77	0.0220*
Ewes	117.00 ± 21.87		75.05 ± 14.11		3.53 ± 1.30		1.90 ± 0.94		1.12 ± 0.66		1.54 ± 0.77	
Bono	120.80 ± 21.65		74.75 ± 17.42		3.16 ± 0.35		1.14 ± 0.28		1.18 ± 0.34		1.46 ± 0.14	
Occupation												
Unemployed	133.40 ± 43.87		77.19 ± 15.29		3.84 ± 1.10		1.47 ± 0.81		0.99 ± 0.40		2.15 ± 0.86	
Farmers	103.30 ± 15.28		66.67 ± 5.77		4.00 ± 0.96		1.43 ± 1.56		1.45 ± 0.24		1.90 ± 0.53	
Traders	117.00 ± 24.24		73.69 ± 12.96		4.10 ± 1.15		1.44 ± 0.62		1.13 ± 0.50		2.33 ± 0.86	
Housewives	129.50 ± 35.16		77.92 ± 15 77		3.77 ± 1.10		1.43 ± 0.77		0.99 ± 0.41		2.10 ± 0.86	
Hairdressers	119.50 ± 30.57	0.052	72.86 ± 14.54	0.132	3.81 ± 1.06	0.734	1.62 ± 0.85	0.729	1.02 ± 0.43	0.340	2.07 ± 0.89	0.694
Dress makers	114.70 ± 24.12		68.42 ± 13.85		4.15 ± 1.06		1.48 ± 0.68		1.20 ± 0.32		2.78 ± 0.75	
Teachers	103.80 ± 9.16		65.00 ± 10.69		3.56 ± 0.83		1.22 ± 0.28		0.95 ± 0.45		1.96 ± 0.37	
Students	120.90 ± 31.45		76.36 ± 18.59		4.08 ± 0.67		1.89 ± 1.84		1.25 ± 0.53		2.01 ± 0.62	
"Others"	116.30 ± 9.16		78.75 ± 6.41		4.02 ± 1.08		1.48 ± 0.62		1.18 ± 0.42		2.16 ± 1.01	

SP = systolic blood pressure, DP = diastolic blood pressure, TC = total cholesterol, TG = triglycerides, HDL-C = high density lipoproteins, LDL-C = low density lipoprotein, SD = standard deviation, p - value = significance level, mmHg = millimeter mercury, mmol/l = millimole per litre

2.5 DISCUSSION

2.5.1 Maternal Sociodemographic Characteristics

Maternal sociodemographic characteristics including age of the mother, parity, education, occupation, religion, marital status, ethnicity, family size and income levels are known to forecast valuable information to the pregnancy outcome. Therefore, early identification of anomalies of maternal sociodemographic factors could provide inexpensive amenable solutions to the prevention of adverse pregnancy outcomes (Mosha and Napendaeli, 2010; Ganchimeg *et al.*, 2014).

The present study recorded mean maternal age of 27.42 ± 6.10 years, while parity was 2.57 ± 1.42 (Table 1). The current findings are very similar to the mean values of 27.71 ± 5.95 years and 2.68 ± 1.71 observed for maternal age and parity respectively in the previous study at the same facility (Bimpong, 2012). Also, the present findings are similar to the maternal age (28.0 ± 5.2 years) and parity (2.0 ± 1.4) results observed by Ephraim *et al.* (2014) among the control population when studying the lipid profile and high maternal body mass index in the Cape Coast Metropolis. Another study conducted in North – West of Nigeria recorded a mean maternal age of 28.2 ± 5.7 years and parity of 3.0 ± 2.0 (Ugwa, 2014). A Sri Lanka based study also recorded mean maternal age of 28.2 ± 5.5 years and a mean parity of 2.0 ± 1.2 (Jananthan *et al.*, 2009). The relatedness in these results could be an indication of a common social factor that regulates child bearing age and parity such as not giving birth at teen age in order to gain the respect of society. The mean maternal age in this study could also place the participants within the range of ideal childbearing age of 21 – 30 years observed to be free of or less associated with adverse pregnancy outcomes (Mosha and Napendaeli, 2010). The age of study population could indicate that, majority of the

women were not so much concerned with or involved in higher education or top class careers that could have taken them into the advanced age as reported elsewhere (Odibo *et al.*, 2006; Huang *et al.*, 2008; Khalil *et al.*, 2013). A number of studies have identified adverse effects of maternal age below 20 years and also above 35 years. Such ages are adversely associated with birth outcomes including low birth weight, miscarriages, preterm and delivery of small for age neonates (Sabir *et al.*, 2013; Ayuba and Ibukun, 2012).

In the current study, mean parity was 2.57 ± 1.42 which showed that, majority of the mothers were expecting their third neonates. This might place the mothers in the state of low risk of adverse pregnancy outcomes such as low birth weight. Indeed, available evidence suggests that, primiparous mothers have high risk of delivering low birth weight neonates (Sabir *et al.*, 2013; Balihallimath *et al.*, 2015; Day *et al.*, 2015). The reason according to theory being that, the first pregnancy places huge constraint on the uterus resulting in uterine adaptation through expression of genes from the placenta to modify the uterus. The modification leads to efficient blood supply and hence adequate nutrient supply so that, the mother is now in a better position to provide effective and efficient support for her subsequent pregnancies (Day *et al.*, 2015). Notwithstanding, this theory being ideal for the second to fourth order pregnancies, the fifth order and above have been found to associate with adverse effects including abortion as observed by Bratati and Hazra (2004).

Maternal educational qualification is an important determinant of social class in Ghana because improved literacy is believed to lead to healthy lifestyle practices including proper health-seeking behaviour. The maternal education levels as observed by this study are presented in percentages in Figure 1A. The percentage distributions observed in the present study were different from the results of a similar study conducted among Ogu Speaking people of Badagry Area of Lagos State in Nigeria which found that, 35% of the respondents

had primary school education, 41.7% of the population had SSSCE qualification (Senior Secondary School Certificate), 16.7% had first degree qualification (tertiary education), while 6.7% had no formal education (Ajiboye and Adibayo, 2012). Another study in the Aminu Kano Teaching Hospital in the North – West Nigeria also found that, 49.5% had tertiary education, 42% had secondary education, 4.5% had primary education, 2% had Qua'ranic education and 1% had no form of formal education.

The differences observed in education levels of these studies could result from variations in their socio-political and educational systems. Whereas Badagry with its rich history in Trans-Atlantic slave trade serves as a major tourist destination in Nigeria, Kumasi is a major commercial city in Ghana where the inhabitants are often engaged in buying and selling. Also, the secondary education in Ghana is stratified into two; the Junior and Senior high levels but it is just one stream in Nigeria. Nevertheless, Nigeria with her huge population may have more women educated because of being well resourced economically than Ghana.

Maternal education could have huge influence on pregnancy outcomes as it might inform the behaviour in seeking healthcare and adequate nutrition among the pregnant women. In the Ghanaian context, where education levels define an individual's social status, it could play a role in influencing the pregnant woman's socialization which probably might have psychological effect on the pregnancy. One study has observed that, low level maternal education contributes to poor understanding of nutrition and feeding practices (Mosha and Napendaeli, 2010). This could be explained with the use of Demographic Health Survey findings from three African countries, namely Tanzania, Malawi and Zimbabwe. These findings suggested that, maternal education level impacts significantly on pregnancy outcome as education enlightens mothers on child health care, permits them to comply with

prescribed principles of feeding practices and judicious management and control of resources (Makoka, 2013). It has been reported that, high level of maternal education was not associated with delivering low birth weight neonate since well-educated mothers were aware and knowledgeable of available health facilities and services which positively influence their health seeking behaviour (Amosu *et al.*, 2014).

Religion is known to have protective effects on maternal health and survival as certain religious beliefs offer motivations to its members to desist from unhealthy practices including smoking, substance abuse and drinking. Evidence suggests that, health outcome derived from religious involvement could be transferred from mother to child such that, negative or positive religious practices could influence birth outcome in a like manner (Reichman *et al.,* 2008). In the present study, the religious affiliation of the participants was shown in Fig. 1B. The study participants were found to belong to two major religious institutions, namely Christianity and Moslems. The percentage distribution was 71.8% Christians and 28.2% Moslems. A study in Badagry Area of Lagos State in Nigeria also observed 63.2% Christians, 19.3% Islam and 17.5% belonged to other religions (Ajiboye and Adibayo, 2012). These observations presuppose that, Christians and Moslems dominated in both studies. Religious influence could contribute either positively or negatively to the outcome of pregnancy. Some of the religious believes could be beneficial to the pregnant women whereas others might endanger the lives of both the mother and her unborn foetus. Religious believes for centuries have been more observable in the African settings where diseases and deaths are attributed to supernatural powers, though Reichman *et al.* (2008), studying the US Fragile Family and Child Wellbeing data found that, low birth weight among neonates whose mothers involved themselves in religious service at least once a week had lower odds ratio than neonates with mothers who did not involve

themselves in religious service at all. Maternal religious involvement has been observed to impact positively on pregnancy outcomes through fate and healthy mental status and behaviour. Healthy mental state leads to good social and psychological practices that result in high optimism and sense of meaning and purpose to reduce depression, anxiety and fear which contribute to pregnancy outcomes. Religion is also known to play supportive and social roles to promote healthy pregnancy outcomes (Elsenbruch *et al.*, 2007; Burdette *et al.*, 2012).

Clearly, differences exist in maternal characteristics among ethnic groups. This could result from cultural and traditional practices observed among ethnic groups. Most ethnic studies on maternal characteristics are intercultural and cross border or are carried out in developed countries and appears to be little or none in Ghana.

The ethnic groupings according to this study were Ashantis, Bonos, Ewes, Fantes and Northerners whose percentage distributions were presented in Fig. 1C. The observation is not surprising as over half of the study population were Ashantis. Kumasi (Ashanti region capital) is the seat of all Twi speaking people in Ghana. The other observation where Northerners formed the second highest population confirmed the location of Kumasi as being situated between the perceived poorest regions up north and the rich south of Ghana and therefore attracts a lot of migrants from the northern parts of Ghana. Kumasi is also the major commercial capital of Ghana and attracts different tribes from various parts of the country (Baeyens, 2012), hence the various proportions contributed by the other tribes in this study. The few percentages of the Bonos, Ewes and Fantes found in the study could confirm the social dynamics existing between the traditional capital cities of these ethnic groups and Kumasi. Among the factors which could influence variations in study Participants' distribution are maternal age, marital status, both maternal and paternal social

statuses and access to health care delivery. It has been observed that, the Northerners migrate down south of Ghana at a much younger age than other tribes with majority of them being single in terms of marital status. Also, infrastructural development gap and provision of social amenities between the southern and northern Ghana probably explain the observed pattern (Ghana Statistical Service, 2008).

The type of occupation engaged in during pregnancy is critical in determining the outcome. The study population was found to belong to different occupational backgrounds as shown in Figure 1D. Other studies conducted elsewhere though did not specifically categorize the study population as done in this study, although the findings are closely related. One such study was conducted among 120 pregnant women in Badagry Area in Lagos State, 31.7% were Civil servants, 53.3% were into business and 15.0% were artisans (Ajiboye and Adibayo, 2012). Some studies also recorded 27.0% employed against 73.0% unemployed and 30.6% employed against 69.4% unemployed (Ugwa, 2014; Zain *et al.,* 2015). The current study findings would not be far different from these if it has been classified in the same way.

This finding of the present study showed that, the city of Kumasi is the business hub of Ghana and also the gateway because almost all key roads and railway networks from southern Ghana converge in Kumasi and diverge to the northern Ghana. The Kumasi Kejetia market is known to compete with the Onitsha open – air market in Nigeria as the largest of its kind in West Africa (Baeyens, 2012). Therefore, the 59.6% of the study population engaged in trading was an indication of economic viability of the Kumasi city with few people involved in farming. The nature of trading activities in Kumasi though seem economically good, it poses threat to the pregnant women in that, long hours of standing, lifting and carrying heavy loads and tight business schedules have been found to

associate with poor perinatal outcomes including preterm delivery and low birth weight (Naidoo *et al.*, 2011).

The social, traditional and psychological premium placed on marriage may have perinatal consequences both on the mother and the neonate. The percentage distribution of marital status among participants of this study was 86.2% married and 13.8% single (Fig 1E). The observation of current study was in line with studies in Montreal, Canada which recorded a higher percentage of married (61%) and a lower percentage of unmarried (39%) women, and a study in Brazil which also found 77.4% married and 22.6% unmarried among the study participants but contradicted with a study on Malaysian women which found 51.8% unmarried and 48.2% married (Auger *et al.*, 2008; De Carvalho *et al.*, 2009; Zain *et al.*, 2015). This could suggest cross cultural variations in attaching importance to marriage before birth. It has been reported that, unmarried status exerts psychosocial stress which influences the pregnancy through physiological alterations in neuroendocrine activities of the expectant mother (Auger *et al.*, 2008). Another theory also proposes that, unmarried status serves as a surrogate marker for other potential harmful practices such as discontinuous antenatal care services, smoking and drinking which endanger the lives of the foetus and the mother (Kirchengast *et al.*, 2007).

2.5.2 Maternal Anthropometric Characteristics

Maternal booking weight undoubtedly plays crucial role in the final outcome of pregnancy as it initiates the nutrient supply to foetus at the very critical stage of the foetal development before this is supported by additional weight gain or otherwise. The current study recorded mean maternal booking weight of 66.26 ± 11.17 kg and height of 1.60 ± 0.07 m which almost equals the 66.2 kg and 1.57 m result obtained among 1138 pregnant women studied

in Ibadan, Nigeria (Isiugo-Abanihe and Oke, 2011). The finding of this study is higher than findings from other similar studies in which mean maternal booking weight and height of 50.30 ± 6.80 kg, 1.53 ± 0.08 m; 58.71 ± 10.73 kg, 1.59 ± 0.01 m and 62.10 ± 10.00 kg, 1.62 ± 0.06 m were recorded for 160 Indian, 413 Brazilian and 155 Iranian pregnant women respectively (De Carvalho *et al.,* 2009; Juneja *et al.,* 2016; Nourbakhsh *et al.,* 2016). A study on 374 Jamaican women also found a mean booking weight and height of 65.50 ± 13.10 kg and 1.63 ± 0.13 m respectively, which is lower than the current finding in terms of booking weight (Thame *et al.,* 2004). However, the result of the present study is lower than that of a study conducted among 225 Nigerian pregnant women who recorded mean booking weight and height of 72.03 ± 11.00 kg and 1.64 ± 0.55 m respectively**.** Mohsen and Wafay (2007) also recorded respectively mean booking weight and height of 67.25 ± 14.25 kg and 1.63 ± 0.09 m among 30 control participants studied in Egypt. It could be assumed that, the finding of the current study adds up to the observation that, African women go into pregnancy with higher booking weight.

Waist circumference has been shown to be a superior sole predictor of abdominal fat redistribution (central adiposity) than the traditional body mass index or waist to hip ratio (Dobbelsteyn *et al.,* 2001). The mean value of waist circumference in the present study was 50.12 ± 12.08 cm. This observed mean value is lower than all the recommended waist circumference cutoff values. The finding could be attributed to cultural diversity, ethnic variations, socioeconomic and political disparities as well as diversity of mankind in general as also observed by Bolanle (2017). The International Diabetes Federation (IDF) places a waist circumference cut off point of 80 cm for women irrespective of ethnicity while the Adult Treatment Panel III (ATP III) places a limit of 88 cm for women, waist circumference above any of these values may necessitate weight management practices

(Stevens *et al.*, 2010). Similarly, the Canadian Clinical Practice guidelines place a cutoff point of 80.00 cm for Sub-Saharan African women (Lear *et al.*, 2010). A study involving Chinese population observed a mean waist circumference of 88.02 ± 12.23 cm which is almost equal to the recommended cutoff by the ATP III (Liu *et al.*, 2011). Another study conducted on 500 Colombian women had a mean waist circumference of 88.2 ± 13.0 cm and a cutoff point of 85.00 cm. This observed cutoff point according to the study was different from a cutoff point of 80 cm for Brazilian women (Mora-García *et al.*, 2014). A study that reported a waist circumference cutoff point for African women had 71.5 cm and 81.5 cm for Nigerian and Cameroonian women respectively (Lear *et al.*, 2010). In fact, Africa as a whole does not have an indigenous population-based waist circumference cutoff value as can be said of America, Europe and Asia. Therefore, for the purposes of scientific references, waist circumference studies in Africa adopt normal acceptable cutoff values of other continents to substitute for the people of African origin (Bolanle, 2017).

In epidemiological studies, the body mass index (BMI) has been the traditional method of choice in determining body size which has received World Health Organization (WHO) approval as the international standard of determining overweight and obesity in adult population (Dobbelsteyn *et al.*, 2001; Huxley *et al.*, 2010). The mean BMI recorded by the current study was 25.80 ± 4.44 kg/m^2. This result seems not too far away from other results obtained in studies carried out in Ghana. Owiredu *et al.* (2011) in studying the prevalence of metabolic syndrome among sport men and women and sedentary workers recorded a mean BMI of 24.82 ± 0.72 kg/m^2 for the total population. Similarly, Aryee *et al.* (2013) reported a mean BMI value of 26.0 ± 1.0 kg/m^2 for women when studying the prevalence and risk factors for overweight and obesity among nurses in the Tamale Metropolis. Arthur *et al.* (2012), studying the prediction of metabolic syndrome among postmenopausal

Ghanaian women using obesity and atherogenic markers recorded a mean BMI of 26.64 ± 0.32 kg/m^2. However, in studying the prevalence of overweight and obesity and perception of healthy and desirable body size in urban Ghanaian women, Benkeser *et al.* (2012) reported a mean BMI of 28.3 ± 6.7 kg/m^2. All these studies on Ghanaian women with different approaches at different places presuppose that, many of the women are overweight.

2.5.3 Maternal Biometric Parameters

The intense hormonal changes which occur during pregnancy mean that, biometric parameters of the pregnant woman are adjusted to correspond with the increasing physiological changes throughout the pregnancy. Pregnant woman having circulating lipids with normal rising physiological levels obtains sufficient energy to provide for herself and the foetus and also maintains steady metabolic rate which allows for the healthy growth and development of the foetus (Sales *et al.,* 2015). In the current study, the mean systolic blood pressure (SP) was 118.81 ± 25.15 mmHg and that of diastolic blood pressure (DP) was 75.04 ± 14.02 mmHg. Also, the mean values for the total cholesterol (TC), triglycerides (TG), high density lipoproteins (HDL-C) and low density lipoproteins (LDL-C) observed were 4.02 ± 0.09 mmol/L, 1.47 ± 0.05 mmol/L, 1.11 ± 0.47 mmol/L and 2.24 ± 0.83 mmol/L respectively. The systolic and diastolic blood pressures and triglyceride of the present study were a little above the 114.8 ± 17.2 mmHg systolic blood pressure and 70.0 ± 10.3 mmHg diastolic blood pressure and the 1.41 ± 1.08 mmol/l triglyceride result recorded among control group in studying body mass index, waist circumference and health risks. However, the total cholesterol (5.30 ± 1.16 mmol/L), high density lipoprotein (1.45 ± 0.39

mmol/L) and low density lipoprotein (3.21 ± 0.98 mmol/L) were higher than that observed in the present study (Janssen *et al.,* 2004). A study involving Singapore adult population also recorded 114.0 ± 13.7 mmHg and 74.0 ± 9.1 mmHg and 0.79 ± 0.00 mmol/L for systolic and diastolic blood pressures and triglyceride respectively which were lower, but had relatively higher mean values for total cholesterol (5.19 ± 0.91 mmol/l), high density lipoprotein (1.75 ± 0.41 mmol/l) and low density lipoprotein (3.02 ± 0.82 mmol/l) (Lam *et al.,* 2015).

In addition, the mean values of all the biometric parameters with the exception of triglyceride observed in the present study were lower than others that have been reported in Ghanaian population studies. For example, Arthur *et al.* (2012) reported mean systolic and diastolic blood pressures of 132.50 ± 1.19 mmHg and 86.30 ± 0.73 mmHg, total cholesterol of 4.40 ± 0.05 mmol/L, triglyceride of 1.20 ± 0.03 mmol/L, high density lipoprotein of 1.34 ± 0.02 mmol/L and low density lipoprotein of 2.51 ± 0.05 mmol/L when studying metabolic syndrome on premenopausal and postmenopausal women in Ghana. Also, studying the metabolic syndrome among sportsmen and women in the Kumasi Metropolis, Owiredu *et al.* (2011) recorded mean systolic blood pressure of 132.20 ± 1.71 mmHg and diastolic blood pressure of 79.18 ± 1.10 mmHg, the mean total cholesterol was 4.77 ± 0.09 mmol/l, triglyceride of 0.98 ± 0.04 mmol/l, the mean high density lipoprotein was 1.79 ± 0.07 mmol/L and that of low density lipoprotein was 2.62 ± 0.10 mmol/L. The differences in mean values of the biometric parameters of the current study and the other studies especially the Ghanaian studies could result from the age differences and the associated clinical conditions of the study populations. For instance, while the mean age of the present study was 27.42 ± 6.10 years, that reported by Owiredu *et al*. (2011) was 43.56 ± 1.06

years and that reported by Arthur *et al.*(2012), was 44.23 ± 0.90 years whose metabolic syndromes were studied.

2.5.4 Comparison between Maternal Sociodemographic and Anthropometric Indices

Information about the association between maternal anthropometric and sociodemographic indices is very scanty in Africa, more particularly in Ghana. This observation presents a huge deficit, given the significant role played by maternal anthropometric and sociodemographic parameters as key indicators of pregnancy outcome. Large volumes of literature on maternal anthropometric and sociodemographic parameters only establish relationships or associations between these indices and neonatal parameters (De Carvalho *et al.*, 2009; Mosha and Napendaeli, 2010; Juneja *et al.*, 2016; Nourbakhsh *et al.*, 2016).

The present study analyzed the results of different categories of maternal sociodemographic characteristics such as education, ethnicity and occupations with reference to their anthropometric parameters in order to establish associations between these parameters. The results indicated that, none of the maternal categories of education showed statistically significant association with weight, height, waist circumference or body mass index ($p > 0.05$). This finding was contrary to that of Hermann *et al.* (2011) which found a strong inverse association between maternal education levels and waist circumference where an average waist circumference was lowered by 5.20 cm among women with lowest educational level. That study also reported significant inverse association between BMI and education categories of women. 74% of the women who fell under lowest education category were either overweight or obese. This observation was explained in psychosocial terms than physiological, because there was underreporting among lowest education

category and also individuals with high BMI wanted to reduce weight. Therefore, it could be speculated by the present study that, where these psychosocial variables do not occur, maternal education level will not show association with maternal anthropometric indices. Molarius *et al.* (2000) in using the (WHO) MONICA Project data set observed an inverse relation between maternal education and BMI which was explained in terms of prevalence of obesity.

In the present study, various ethnic groups showed no significant association in terms of weight, height, waist circumference and BMI. However, in a well-documented study among women from developed countries, ethnicity was found to show significant negative linearity with BMI. The finding was explained on the basis of certain sensitive psychosocial influence which vary from one ethnic group to another including social pressures on women to comply with certain body images (Sanchez-Vaznaugh *et al.,* 2009). Again, no significant differences were observed in the mean weight, height, waist circumference and BMI by maternal occupation. This may suggest that, maternal occupation could not have direct influence on the maternal anthropometry.

2.5.5 Comparison between Maternal Sociodemographic and Biometric indices

Maternal lipid levels change during pregnancy and this is a normal physiological process which is important because progressive increase of maternal circulating lipids enhances the provision of substrates needed for the development of the foetus (Misra *et al.,* 2011).

The current study analyzed the outcome of categories of maternal sociodemographic characteristics in relation to the biometric indices. The findings indicate that, at the various levels of maternal education, no significant association was observed between systolic and

diastolic blood pressures. Similarly, no association was found between maternal triglyceride and the levels of education. The same observations were made for high and low density lipoproteins and education level. However, significant association was observed between the levels of maternal education and total cholesterol. It was realized that, total cholesterol levels were high among mothers who attained primary, junior and senior high education, but was low for the no formal education and tertiary categories. Another finding of this study was that, with the exception of low density lipoproteins, the various ethnic groups did not show statistically significant association with the biometric indices. The study did not observe significant differences in the means of systolic and diastolic blood pressures, total cholesterol, triglycerides, high and low density lipoproteins in relation to the categories of maternal occupation.

This observation is consistent with a study which reported that, women with low education exhibited trend towards a worse (high) lipid profile as compared to their counterparts with high education levels although it lacked statistical significance (Lara and Amigo, 2018). During pregnancy, most of maternal physiological processes are increasingly influenced by the activities of placental hormones particularly in the third trimester. These changes in turn, affect glucose and lipid levels (Raghuram *et al.,* 2016). However, the findings in this current study could be explained in terms of relationship of education with the individual's health. Evidence suggests that, a highly educated individual is enlightened and practises healthy behaviour, enjoys better employment and income and is also aware of prevailing social and psychosocial factors which contribute to promotion of better health which also include the management of lipid profile (Egerter *et al.,* 2011). This could mean that, mothers with high level of education might encounter some degree of complications in the course of their pregnancies, since low TC levels are known to associate with adverse

pregnancy outcomes. It has been established that, low levels of total cholesterol in early pregnancy is associated with lower socioeconomic status which could contribute to deficiencies in micronutrient supply during pregnancy and has the potential adverse influence on the pregnancy (Oluwole *et al.,* 2014).

2.6 CONCLUSION

In conclusion, the study could not establish statistically significant relationship between maternal sociodemographic characteristics and anthropometric parameters. However, significant association between levels of maternal education and total cholesterol levels was observed. Also, there was significant association between maternal ethnicity and low density lipoprotein cholesterol levels.

CHAPTER THREE

ASSOCIATIONS BETWEEN PLACENTAL AND UMBILICAL CORD MORPHOMETRIC INDICES

3.1 LITERATURE REVIEW

3.1.1 Placental Development and Morphology

Characteristically, the placenta exhibits functional complexity in that, it performs immunological, respiratory, digestive, circulatory and excretory functions (Benirschke *et al*., 2006). Therefore, disorders which associate with the placenta show deleterious effects on the well-being of the foetus (Roberts, 2008). It is also known that, the growth of human foetus is limited by the inability of the mother and placenta to adequately supply nutrients and oxygen to the foetus and the consequence of foetal undernutrition is reduced growth and low birth weight (Ounsted, 1986; Harding, 2001).

Implantation is the first stage of placental development and consists of apposition, adhesion and invasion of the endometrium by the blastocyst. For implantation to be successful, a receptive endometrium with appropriate secretion of *oestrogen* and progesterone is needed. The *zona pellucida* surrounding the blastocyst is very important in that, it prevents premature implantation of the embryo in the oviduct. As the embryo arrived in the lumen of the uterus by the 6^{th} day after fertilization, localized enzymes lyse the *zona pellucida* creating an implantation window through which the blastocyst hatches out to undergo the implantation process. When the embryo is fully attached within the endometrium, implantation is described as interstitial (Larsen, 2001).

It has been observed that, the trophoblast cell's L–selectin and its carbohydrate receptors located on the epithelial cells lining the uterus modulates the blastocyst attachment to the

uterus. L-selectin allows the picking up of blastocyst out of the uterine cavity by epithelial cells of the uterus. Hence attachment and invasion by the trophoblast of the blastocyst is mediated by the integrins. Immediately after attachment, the trophoblast proliferates and differentiates into an inner mitotic cell layer of cytotrophoblast and an outer cell layer of polyploid nonmitotic syncytiotrophoblast. The syncytiotrophoblast appose to the walls of the uterus when the embryo emerges from the *zona pellucida* (Larsen, 2001; Keith *et al.*, 2011).

The normal site of implantation is the endometrial functional layer within the upper two-third region along the posterior wall of the uterus body. During this period, the blastocyst measures about 0.1 – 0.2 mm in diameter and is implanted in a 5 mm thick mucosa. Implantation sites other than the functional layer of the endometrium is described as ectopic pregnancy and could be life-threatening including tubal pregnancy and *placenta praevia* (Larsen, 2001).

The readiness of the endometrium for successful implantation is indicated by its secretion of certain biomarkers such as cytokines and leukaemia inhibitory factor (LIF). LIF is known to increase the endometrial expression of heparin-binding epidermal growth factor (HB-EGF) which also initiates the growth of trophoblast and hatching of blastocyst out of the *zona pellucida*. The endometrial luminal epithelium possesses non- adhesive and non-infective microvillous border which secretes mucin (MUC-1). This mucous layer is believed to serve as a barrier to inferior embryo implantation. Essentially, the endometrium needs to be protected from infections and blastocyst rejection during apposition and adhesion. This is achieved by the trophoblast secreting human leukocyte antigens-G (HLA-G); a subtype of major histocompatibility complex class I (MHC I) which is highly immunogenic capable of activating local cytotoxic T cells (Larsen, 2001;

Crocker and Burnett, 2005). The human placenta thus starts forming with the presence of trophectoderm that begins differentiation at the morula stage into trophoblast that forms the outer layer of the blastocyst (Cunningham *et al.,* 2005).

With the blastocyst firmly attached to the uterine epithelium, the differentiated polar trophoblast (syncytiotrophoblast) becomes invasive through secretion of metalloproteases and collagenases which lyse the extracellular matrix of the uterine endometrium, facilitating blastocyst invasion into the interstitium of the endometrium by day 8 post-conception (Coward and Wells, 2013). The embryo is considered fully implanted and implantation process completed by day 12 post conception with the embryo and its associated tissues being finally attached to the endometrium. The blastocyst at this stage is nourished with a nutritive material within the lacunar spaces and are secreted by the uterine glands till the time a link is formed with the maternal circulation (Larsen, 2001; Keith *et al.*, 2011; Huppertz, 2008).

The cytotrophoblast develops from the remaining mononucleate trophoblast and thus becomes the stem cell layer which quickly divides to undergo fusion to become syncytiotrophoblast. Beginning from day 12 post conception, the cytotrophoblast penetrates beyond syncytiotrophoblast to establish the extravillous cytotrophoblast (EVT) progenitors. These cells function to surround terminal branches of uterine arterial circulation (spiral arteries) as well as interacting with the maternal system through hormonal secretion to enhance blood flow to site of implantation and to facilitate the maternal adaptive responses in pregnancy (Potgens *et al.,* 2002; Chaddhaa *et al.,* 2004). Failure of cytotrophoblast to be completely invasive or its inability to change the spiral arteries into low resistance blood vessels leads to insufficient maternal blood flow to the

placenta that may cause the secretion of vasoactive substances leading to the development of hypertension and preeclampsia (Wilkin, 2002).

Placental vascularization is crucial for efficient materno-foetal exchange and also plays mechanical role in the establishment of complex placental arborization. It is estimated that, a term placenta develops a capillary network that measures approximately 550 km in length and a surface area of 15 m^2 (Burton *et al*., 2009). Placental vascularization experiences extensive and progressive remodeling in the course of gestation. In the first and early parts of second trimesters, volume, number and surface area of capillary network increase within the placental villi (te Velde *et al.*, 1997).

The development of placental vascular network occurs in three different stages: induction of haemangioblasts and angioblasts-initiated through fibroblast growth factor (FGF), which is followed by the assembly of primordial vessels – initiated through vascular endothelial growth factor/vascular endothelial growth factor receptor system (VEGF/VEGFR) and finally the transition from vasculogenesis to angiogenesis (Flamme *et al.*, 1997). The vasculature characteristically becomes adaptive to vasodilation, increased permeability and growth and development of new vessels to meet the increased demand of blood supply to the uterus and the developing foetus (Zygmunt *et al.*, 2003). Therefore, it is clear that, normal placental vasculature development will result in successful pregnancy outcomes. Mayhew *et al*. (2004) observed poor trophoblast invasion in foetal hypoxia and impaired growth associating with poor vasculature. Adequate placentation is known to be achieved through timely and coordinated differentiation and proliferation of cytotrophoblast stem cells stimulated by hypoxia (James *et al.*, 2006).

Inside the placenta, blood vessels form major part among other structures constituting the cotyledons which form a continuous circulation with the foetal circulatory system where

the vein transports oxygenated blood towards the foetal end while the arteries carry deoxygenated blood to the maternal end of the placenta. A term placenta therefore has chorionic arteries and veins which respectively develop from the umbilical cord arteries and vein (Wang and Zhao, 2010).

Aberrant vasculogenesis and angiogenesis are known to correlate with impaired placental and foetal development as has been observed in intrauterine growth restriction pregnancies. Specifically, abnormal angiogenesis is associated with a number of clinical conditions such as rheumatoid arthritis, chronic inflammation, cancer and diabetes (Folkman, 1995; Zygmunt *et al.,* 2003). Precise knowledge of placental morphogenesis and angiogenesis could provide evidence of correlation existing between histological structures of placenta and ultrasound applications in following up on pregnancy (Bancroft and Gamble, 2008).

The growing embryo is supported by a number of membranes and cavities. At the 8^{th} day post conception, tiny spaces filled with fluid appear among the syncytiotrophoblast which then fuse to become large lacunae. The patchy remains of the syncytiotrophoblast in between the lacunae are described as trabeculae which contribute to the placental villous tree development. With the lacunae fully formed, three distinct zones of the placenta become clearly defined: the chorionic plate pointing towards the embryo, the intervillous and villous tree that develop from lacunae and trabeculae systems and the primitive basal plate connected with the maternal endometrium (Huppertz, 2008).

After implantation, other extraembryonic tissues develop from the inner cell mass which differentiates into epiblast and hypoblast. The epiblast produces ectodermal derivative amnion which is a fluid-filled protective sac surrounding the yolk sac (embryo). The endodermal derivative allantois arises from the hypoblast and is known to be associated with the elimination of embryonic waste materials, the extraembryonic mesoderm that

constitutes a larger portion of the umbilical vesicles, the connective tissue support of the extraembryonic membranes and blood vessels (Sadler, 2012).

In an attempt to match the growing foetus, the amniotic cavity gradually distends to maximum fluid capacity of approximately one litre (1L) around 33 to 34 weeks of pregnancy. It has been observed that, as gestation progresses, most especially after 20 weeks, the source of amniotic fluid changes and is thought to come from foetal urine, filtration from maternal blood vessels and probably filtration from umbilical cord and chorionic plate. Although greater portion of the amniotic fluid is exchanged across the amniotic membrane, the foetus also swallows a lot of this fluid during late pregnancy at a rate of about 20 mL per hour. Quantitatively, 500-1000 mL of amniotic fluid at term of pregnancy is considered normal; however, an excess amount (> 2000 mL) is described as hydramnios which associates with multiple pregnancies and oesophageal atresia or anencephaly. Very little of amniotic fluid (< 500 mL) is described as oligohydramnios which has an association with bilateral renal agenesis and could result in premature rupture of the amniotic membranes in nearly 10% of pregnancies (Larsen, 2001).

According to Mihu *et al.* (2009), morphometric assessments of the placenta go through continuous process of development and improvement, and have become the choice for most studies since it eliminates subjectivity resulting from visual impression created by human factor. The subjectivity is superseded by the objectivity of the measurement process. Structural variations in placental morphology result in functional changes of the placenta. In this view, morphometry presents an interventional non-invasive approach to studying placental physiology and pathophysiology (Mitra *et al.,* 1997). The normal practice of placental examination following adverse pregnancy outcomes, such as, preterm labour,

severe intra uterine growth restriction (IUGR), still birth or poor birth outcome has being the measurement of placental and umbilical cord parameters (Salafia *et al.*, 2005; Coall *et al.*, 2009). Hence, placental morphology and morphometry are probable sources of information on perinatal outcome as well as predicting postnatal health status of both mother and the child (Sivarao *et al.*, 2002; Mayhew, 2005). Traditionally, placental shape is known to be round, oval, irregular, star-shaped or multi-lobar. Irregular placental shape has been associated with altered placental functions leading to poor pregnancy outcomes such as low birth weight and low birth weight to placental weight ratio (Yampolsky *et al.*, 2008). The placental weight alone does not express complete information on gestational adequacy encoded in the placenta. This is based on research findings in which it was observed that, placental diameter and thickness show significantly independent association with foetal growth. In this same study, neonatal size related to placental measurements and was independently and significantly associated with maternal body mass index (BMI) and diastolic pressure (Misra *et al.*, 2012).

Most often, the placental shape is described in morphological terms. The placenta is commonly round with centrally located umbilical cord (Jafari and Latifnejad, 2014). A study conducted in India observed that, majority of the placentae from the study population were oval and round (Agarwal *et al.*, 2015). However, another study found optimal number of average placentae being round with centrally inserted umbilical cord (Yampolsky *et al.*, 2009).

Although the causes of different placental shapes are not yet fully understood, it has been shown that, the directional growth of placental vasculature influences final shape of the placenta. The observation was that, when the uterine environment impedes the growth of placental vessels, the shape of the placenta then assumes that of the obstacle (Chang *et al.*,

2012). Other factors that influence the shape of the placenta are believed to include; where placenta is implanted in the uterus, regional variations in the decidua, changes in maternal vascular supply and probably the manner of its original implantation (Benirschke *et al.*, 2006). It is also assumed that, an irregular placental shape could be an indication of abnormal pattern of earlier trophoblastic invasion and placentation (Palomba *et al.,* 2013). Dimensional analysis has established that, the chorionic plate area is a measure of the space occupied by the placenta in the inner wall of the uterus, which in essence, determines the number of potential maternal spiral arteries that are capable of supplying materials to the placenta (Pathak *et al.*, 2010).

Findings from studies indicate possible association of shape of placental surface with neonatal birth weight and gestational age. There is evidence of statistically significant correlation of histopathology diagnoses with increased maternal utero-placental vascular pathology and foeto-placental vascularity. This implies that, deviation of placental shape from the mean may indicate an adverse effect of maternal utero-placental vascular pathology or foeto-placental vascular pathology on the foeto-placental outcome (Salafia *et al.*, 2010; Chang *et al.,* 2012).

During analysis of placental shape and developmental programming, the following observations were made; that the risk of developing hypertension in adult life was associated with reduced placental weight and surface area; pregnant women who experienced preeclampsia had reduced placental weight and more oval placentae; the short placental diameter strongly associated with the severity of preeclampsia (Barker *et al.*, 2010; Kajantie *et al.*, 2010).

The placenta is opaque at the maternal surface due to laminar degenerative processes located within the functional zone which separates placenta and uterine wall into basal plate that connects the placenta to become the maternal surface and the placental bed *in utero*. This basal surface is subdivided by a system of incomplete grooves into 10-40 distended regions referred to as the maternal cotyledons or lobes (Benirschke *et al.,* 2012). Each cotyledon is a blood filled chamber partially or completely separated from from one another by placental septae internally and contains one or more spiral arteries that eject blood into the chambers (Barker *et al.*, 2013).

The average number of cotyledons have been observed to be less numerous in hypertensive and preeclamptic placentae than in normotensive placentae (Londhe and Mane, 2011; Shevade1 *et al*., 2015). Similarly, reduced numbers of cotyledons was evident in placentae from pregnancy induced hypertensive mothers and were found to be associated with premature and low birth weight neonates (Kulandaivelu *et al.,* 2014). Indeed, it has been reported that, changes in the intracotyledon vasculature arrangement in hypertensive placentae lead to low birth weight (Salmani *et al.,* 2014). However, higher mean number of cotyledons in gestational diabetic placentae than in control group has been observed (Pankaj *et al.*, 2015).

Placental thickness and diameter (largest and smallest diameters) are gross structural features of the placenta that assess from different angles, placental growth and function. These are known to exhibit unique "critical periods of development" (Baptiste-Roberts1 *et al*., 2009). The diameter of the placenta is used to estimate the surface area which in turn characterizes the distribution of nutrient exchange tissues across the internal walls of the

uterus, while thickness also reflects the volume of endocrine and vascular nutrient exchange tissues (Barker *et al.*, 2010; Pathak *et al.*, 2010).

The thickness and diameter of placenta like other placental measurements are strongly associated with foetal development and perinatal outcomes. Adverse perinatal outcomes such as chronic foetal infections and intrauterine growth restriction have been observed in smaller placentae (Baghel *et al.*, 2015). Placental thickness is known to be used to differentiate normal from abnormal pregnancies as in the case of *diabetes mellitus* pregnancies which tend to have thick placentae (Kaushal1 *et al.*, 2015). The normal full term placenta for Nigerians is estimated to be 3 cm thick and 15 – 25 cm in diameter with 500 g – 600 g weight (Ohagwu *et al.*, 2009). Another Nigerian study also rated a normal full term placenta to have a diameter of 23 cm, thickness of 2.0 – 2.6 cm, weight of 470 g and an average volume of 500 mL (Kaushal1 *et al.*, 2015). The importance of establishing the relationship between placental thickness and neonatal growth trajectories is the observation of *foetal hydrops*, intrauterine foetal infections and maternal *diabetes mellitus* in very thick placentae (Ohagwu *et al.*, 2009; Afodun *et al.*, 2015; Kaushal1 *et al.*, 2015). Small placentae have also been found to impair foetal growth characteristics due to placental insufficient blood supply to the foetus with associated diseases and abnormalities including intrauterine growth restriction, chromosomal abnormalities, preeclampsia and severe maternal *diabetes mellitus* (Balla *et al.*, 2014).

Studies have shown a strong relationship between placental thickness and high risk of adverse perinatal outcome such as placental abruption, neonatal intensive care unit admission, perinatal deaths, foetal growth restriction, pregnancy induced hypertension, preterm birth, gestational age, birth weight and pH of umbilical cord blood. Placental dysfunction could result in thick placentae due to placental villi oedema and compensatory

proliferation (Raio *et al.,* 2004; Miwa *et al.,* 2014). Following these observations, a longitudinal study using ultrasound assessment has established a ‘‘warning limit’’ of placental thickness and diameter to be 2 cm and 18 cm respectively at 36 weeks of gestation as predictive of low birth weight in neonates. However, thickness exceeding 3 cm before 20 weeks, and more than 5 cm before 40 weeks are described as abnormal. These have proven to be predictive identification markers for foetal growth retardation (Balla *et al.,* 2014; Nagamani *et al.,* 2015).

Direct variation of placental thickness with gestational age has also been reported. In one of such studies, placental thickness was found to progressively increase with gestational age until 38 weeks after which the thickness decreases (Nagwani *et al.,* 2015). Another study observed mean placental thickness increment with advancing gestation age in the third trimester to be 3.581 cm (Karthikeyan *et al.,* 2012).

The weight of the placenta is known to play very important role in growth and development of foetal characteristics such as umbilical cord length, body length, head circumference and abdominal circumference (Afodun *et al.,* 2015). Placental measurement enhances the ability to carefully observe differences between individual dimensions in intrauterine experience as well as providing a biologically active method to detect the physiology of the foetal experience (Salafia *et al.,* 2005). Functionally, the placenta forms a barrier that filters physically harmful substances from entering into the foetus. Placental weight has been found to be an important source of information in the delivery room for the paediatrician on intrauterine wellbeing of the foetus (Adebami *et al.,* 2007).

Placental weight is known to be a reflection of placental development and functions in early intrauterine environment and correlates with maternal age, gestational age, parity, history of

maternal diabetes, preeclampsia, birth weight and the route of delivery. Placental weight also correlates with maternal height, weight and serum ferritin (Asgharnia *et al.,* 2008). Foetal development is regulated by the equation between foetal metabolic demand and maternal-placental supply which is strictly related to utero-placental blood flow, placental size and its transfer capabilities. Insufficient maternal placental supply than is needed would imply that, the foetus must adapt to the situation by the modification of its body composition and endocrine status, selective growth of specific organs and cardiovascular adaptations (Pardi *et al.,* 2002).

Placental weight is the gross summary measure of placental growth and aspects of functional capacity. It is observed that, placental weight in normal pregnancies relates to some functional capacities of the placenta such as the surface area of villous tissues, which is the primary nutrient transport determinant (Roland *et al.,* 2014). Placental weight therefore expresses the surface area available for mother to child nutrient exchange; this is because variation in the distribution, numbers, density and activity of the nutrient-specific transporter proteins located in the syncytio-endothelial membrane at the maternal surface of placenta brings about changes in the transport capacity of the placenta (Brett *et al.,* 2014). Similarly, it has been observed that, different phases of placental development varies with nutrient availability which in turn results in alterations in placental weight, vascular development, reduced angiogenic growth factor expression and diminished glucose, amino acid and lipid transport (Elangovan and Raviraj, 2016).

The weight of the placenta is considered to be a better identifiable marker of placental functional capacity than its size, although significant correlations have been observed between placental size and birth weight. In a study of over 24,000 placentae in the United States of America, it was realized that, the weight of placenta contributed to 36.5% of

variations in birth weight but only 13.9% of the variations in birth weight could be attributed to maternal factors including her age, parity, height, weight, cigarette smoking, ethnicity, social and economic characteristics. A positive correlation was observed between placental volume and weight in that study (Roland *et al.,* 2014).

Reduction in placental weight is found to be associated with low birth weight, premature and anaemic neonates of pregnancy-induced hypertensive mothers whereas significant increase in placental weight is observed in gestational *diabetes mellitus* mothers (Kulandaivelu *et al.,* 2014).

A consistently significant positive association of placental weight and volume with gestational age as well as birth weight has been observed (Afodun *et al.,* 2015). Other observations were the significant increase in placental weight and volume with parity. Multiparous mothers had large placental weight, volume, surface area and thickness and could be attributed to the fact that, anatomically, there is permanent variation in the structure of the spiral arteries after pregnancy which assists in remodeling vascular efficiency through effective trophoblastic migration in subsequent pregnancies (Roland *et al.,* 2014; Balihallimath *et al.,* 2015). According to Afodun *et al.* (2015), placental weight influences significantly foetal development as observed in various growth characteristics including umbilical cord length, body length and abdominal circumference.

3.1.2 Umbilical Cord Development and Morphology

In the early part of pregnancy, the primary yolk sac which develops between the hypoblast and the Heuser's membrane appears conspicuous, and as the pregnancy advances, it becomes smaller with a much longer connecting stalk derived from the extraembryonic

mesoderm. The connecting stalk suspends the embryonic disc and eventually develops into the umbilical cord while the degenerated primary yolk sac becomes the definitive or secondary yolk sac (Coward and Wells, 2013). Almost at the middle of the first trimester, the amnion continues to expand thereby obliterating the chorionic cavity to fuse with the chorion laeve. This covers the protruding placental disc and the lateral surface of the body pedicle which is the umbilical cord also known as funis (Cunningham *et al.,* 2005).

The distal portion of the umbilical cord contains yolk sac and umbilical cord vessels while the proximal region has some intestinal loops and remnant of the allantois. The embryonic disc and the amnion within the chorionic cavity are connected to the umbilical cord by the stalk. Almost at the end of the first trimester, the intestinal loop enters the embryo proper and the cavity within the cord becomes degenerated. When the allantois, vitelline duct and the vessels are degenerated, the only structures present in the cord at this moment are the umbilical cord vessels embedded within a specialized connective tissue extracellular matrix called Wharton's jelly rich in peptidoglycans to protect the cord blood vessels (Larsen, 2001).

Although the structure and functions of the umbilical cord appear to be relatively simple, it is indeed an amazing organ very necessary for intrauterine life and foetal well-being (Goynumer *et al.,* 2008). Normal term umbilical cord consists of two small arteries and one vein and connects at the foetal umbilicus to the foetal surface of the placenta. The outer region appears dull white, moist and measures 1 – 2 cm in diameter and a length of 20 – 120 cm which inserts centrally. Generally, umbilical cord length less than 30 cm is regarded as being abnormally short. The vessels are normally longer than the cord but are characteristically anastomosed. The anastomosis may occur in dextral (clockwise) or sinistral (anticlockwise) direction. The umbilical cord being a hollow cylindrical structure

could experience torsion, however, the spiraling help to prevent clamping (Cunningham *et al.*, 2005; Anjum *et al.*, 2015).

The knowledge on embryology, anatomy and physiology of the umbilical cord vessels results in better understanding of ultrasound imaging. The significant role played by the umbilical cord in foetal development also stimulates more studies into this foetal lifeline (Spurway *et al.*, 2012). The umbilical cord vessels lack *vasa vasorum* and therefore rely on themselves for their oxygen needs; this subjects the vessels to varied haemodynamic characteristics. Transverse sectioning of the umbilical cord reveals unique morphology of a vein and two arteries protected by Wharton's jelly. The umbilical cord vessels require special monitoring beginning from the first trimester since developmental abnormalities of the cord such as exceptionally short or long cord, insertion site and single artery, could result in cardiac and vascular anomalies of the neonate (Barnwal *et al.*, 2012; Anjum *et al.*, 2015).

Physiologically, the two umbilical cord arteries transport oxygen-poor blood under high pressure from the foetus to the placenta and the cord vein carries oxygen-rich blood from the placenta to the foetal heart. Histological studies of the umbilical cord vein and arteries show a single layer of smooth muscles within the *tunica media* and double layered smooth muscles in *tunica intima* (Kim *et al.*, 2008). The umbilical cord vessels function to maintain and protect blood flow to the foetus during grasping, normal movement, forces of labour and in situations of other umbilical cord abnormalities including knots and loops during term pregnancy. As a channel through which blood flows, the umbilical cord varies in its physical dimensions and extracellular matrix composition with maternal characteristics like gestational age, pregnancy disorders and genetic abnormalities of the foetus (Ferguson and Dodson, 2009).

The endothelia and smooth muscle layers of both umbilical cord arteries and vein exhibit differential mRNA gene expression of cytokines and cellular immunophenotypes which could be responsible for intrinsic anatomical variations observed in the cord artery and vein structures (Kim *et al.,* 2008). Histologically, both internal and external elastic laminae together with adventitia are absent in the walls of umbilical cord arteries but are substituted within the mucous connective tissue. However, the umbilical cord vein has thick interwoven muscularis layer made of circular, longitudinal and oblique smooth muscle fibres with internal elastic lamina (Spurway *et al.*, 2012). Umbilical cord vein has larger diameter with a thin single layer of circular smooth muscles while the cord arteries exhibit a two layered muscular wall with interlocking smooth muscle bundle, but lack elastic lamina in complicated pregnancy such as preeclamptic state (Barnwal *et al.,* 2012). A reduced vessel diameter and wall thickness in both cord artery and vein in preeclampsia as against normal pregnancies and pregnancies affected by chronic hypertension have been observed (Inan *et al.,* 2002). However, Koech *et al.* (2008) reported that, in preeclamptic cords, there was an increase in thickness of the *tunica media* and i*ntima* in the arteries and higher rate of internal elastic lamina duplication.

The cross-sectional areas of umbilical cord components are essential in evaluating foetal weight. A strong correlation between the cross-sectional areas of umbilical cord components and foetal anthropometric parameters has been established (Togni *et al.,* 2007). Sonographic determination of cross-sectional areas of umbilical cord vessels reported of the following averages and observations; umbilical cord diameter of 1.5 cm and umbilical circumference of 3.6 cm after birth (Patel *et al.,* 1989; Weissman *et al.,* 1994), umbilical cord vein diameter of 8 mm and artery diameter of 4 mm at term (Collins, 2002).

Sonographic umbilical cord diameter and area increase as a function of gestational age. The diameter of umbilical artery increases from 1.2 ± 0.4 mm at 16 weeks to 4.2 ± 0.4 mm at term of gestation and umbilical vein diameter varies from 2.0 ± 0.6 mm at 16 weeks of gestation to 8.2 ± 0.8 mm at term of gestation (Di Naro *et al.*, 2001). A successive increase in umbilical cord diameter and cross-sectional area up to 32 weeks of gestation with a subsequent reduction in umbilical cord size was observed in a study by Raio *et al.* (1999) in which a significant relationship between umbilical cord diameter, cross-sectional area and foetal anthropometric parameters were also observed. Barnwal *et al.* (2012) reported umbilical cord area of 51.56 ± 2.34 mm^2, Wharton's jelly area of 42.27 ± 2.12 mm^2, and total cord vessel area of 8.96 ± 0.82 mm^2 and concluded that, increase across the vessels could predict the presence of intrauterine growth restriction in term neonates of preeclamptic mothers.

Wharton's jelly is known to influence the composition of the umbilical cord tissue. Biochemical studies have shown that, a rise in the concentration of glycosaminoglycans in the extracellular matrix of Wharton's jelly coupled with large amount of proteoglycans renders the collagen fibres in the matrix insoluble, compact and gelatinous which influences the umbilical cord's mechanical and morphological characteristics (Barnwal *et al.*, 2012). Gestational progression stimulates the amount of Wharton's jelly to become most prominent in the umbilical cord during second and third trimesters. The differences in amount of Wharton's jelly content in normal pregnancies give indication of the circumstances that surround the macroscopic appearance of the umbilical cord (Ghezzi *et al.*, 2001).

Wharton's jelly is a derivative of the extraembryonic mesoblast. Its inclusion in the cord substance and subamnionic layers could explain their mucoid and compressible nature

(Kulkarni *et al.,* 2007). Wharton's jelly, made of collagen fibres forms a network of interconnected cavities, cavernous and perivascular spaces for storage of ground substance of the jelly (Vizza *et al.,* 1996). This ground substance has hyaluronic acid and proteoglycans in an aqueous solution of salts, metabolites and plasma proteins as its constituents (Skulstad *et al.,* 2006). The interconnected cavities within the Wharton's jelly functions in water storage and other substances in order to facilitate the exchange of nutrients, electrolytes and gases between the umbilical cord vessels and the amniotic fluid. For this reason, it has been observed that, quantitative increase in the amount of Wharton's jelly in normal pregnancies corresponds with the variations in the macroscopic morphology of the umbilical cord in the second and third trimesters (Rostamzadeh *et al.,* 2015).

Wharton's jelly appears to substitute adventitia for the umbilical blood vessels, which the umbilical cord vessels lack, binding and encasing them. Speculations are that, the cells of the Wharton's jelly may partake in the regulation of umbilical blood flow, and that, in some instances; the foetal growth could be affected by Wharton's jelly diminution leading to hypoplasia of the umbilical vessels (Gebrane-Younes *et al.,* 1986; Bruch *et al.,* 1997). According to Ghezzi *et al.* (2001), the ratio of the Wharton's jelly area to the total umbilical cord area decreases significantly with advancing gestation. This is because, the water content of the Wharton's jelly reduces towards the end of pregnancy.

The reduction in the amount of Wharton's jelly could result from an inherited disorder in the deposition of Wharton's jelly, making the umbilical circulation vulnerable to scornful abuse rather than the consequence of foetal disease (Raio *et al.,* 1999). Successive foetal deaths in the same family due to torsion of the umbilical cord resulting from primary absence of Wharton's jelly have been reported (Hersh and Buchino, 1988). However, the absence of Wharton's jelly around the umbilical cord vessels is an unusual cause of

perinatal mortality (Kulkarni *et al.,* 2007). The umbilical cord can be large (thick) enough exceeding an average of 4 cm in circumference with average weight of 15 g/10 cm at term (Casola *et al.,* 1985; Collins, 2002). Association between large umbilical cord and other foetal structural anomalies including umbilical cord tumours, urachal cysts, umbilical cord mucoid degeneration and omphalomesenteric cyst has been reported. Under such instances, morphological alterations occur at a limited portion of the umbilical cord (Iaccarino *et al.,* 1986; Benirschke and Kaufmann, 1995).

Di Naro *et al.* (2001) considered the possibility that, an abnormally large umbilical cord might be an additional parameter that can help to identify foetuses of mothers having some kind of glucose intolerance during pregnancy. In the same manner, the umbilical cord can be lean (thin), < 1cm in circumference and lack Wharton's jelly. Probably, lean cord could be determined by factors such as reduced amount of Wharton's jelly or reduced umbilical cord vessels' cross – sectional areas or by both (Ghezzi *et al.,* 2005). Di Naro *et al.* (2001) observed that, small umbilical cord vein area and low coiling index characterized large numbers of sonographically lean cords. Post – term (> 42 weeks) foetuses and intrauterine growth retardation (IUGR) foetuses are associated with lean cord, which could suggest both poor nutrition and lack of glycogen in the foetal tissues (Amiel – Tison and Stewart, 1994; Iffy and Varardi, 1994). In post-term pregnancies, the diameter of the umbilical cord is smaller in patients with oligohydramnios than in those with normal amniotic fluid (Silver *et al.,* 1987). In this regard, it is necessary to ensure normal amniotic fluid volume before assessment of abnormal cord can be made (Strong *et al.,*1992).

Differences in umbilical cord water and molecular contents could result as an independent risk factor for poor pregnancy outcome. The average cross-sectional area of the human umbilical cord is 14 cm^2. Lean (thin) umbilical cords may exhibit differences in blood flow

characteristics and are more vulnerable to compression. Consequently, abnormal assessment of the umbilical cord could be done when the amniotic fluid volume is normal (Silver *et al.*, 1987; Gill and Jarjoura, 1993; Collins, 2002). A highly significant relationship has been established between the presence of lean umbilical cord (cross-sectional area < 10^{th} percentile) and the delivery of small-for-gestational age (SGA) infants. Foetuses with lean umbilical cord after 20 weeks of gestation potentially, had 4.4-fold higher risk (95% confidence interval, 2.16 – 8.85) of having an SGA infant than those with a normal umbilical cord (Raio *et al.*, 1999).

Umbilical cord length indicates foetal motor function and the tensile force placed on it by foetal moves in the uterus. The factors that influence the growth of umbilical cord length are likely to imitate the mechanisms that regulate placental development and body length which may be environmental, genetic or socio-demographic in nature (Elarbah *et al.*, 2014). Physiological length of the umbilical cord has been variedly reported by several studies including Spurway *et al.* (2012) who stated that, the term umbilical cord measures averagely 50 – 60 cm in length but ranges from 30 to 100 cm and considered cords less than 30 cm as being short. Also, Elghazaly *et al.* (2016) reported on mean cord length as 47.42 ± 11.49 cm in males and 44.75 ± 11.29 cm in females with overall range of 24 – 90 cm. The average length of the umbilical cord of 56.2 ± 11.7 cm (range: 19 - 133 cm) was also reported by Suzuki and Fuse (2012). The umbilical cord length at term was reported to be 50 – 60 cm with extreme ranges from achordia (absence of cord) to about 300 cm (Elarbah *et al.*, 2014; Nandini *et al.*, 2015). Another study reported an average umbilical cord length of 60 cm with a range of 15 cm to 130 cm but actually observed mean cord

length of 56.5 cm for control group and 46 cm for the experimental group (Wright and Chan, 2009).

The normal umbilical cord length facilitates the passage of the foetus through the birth canal for a successful vaginal delivery without the pull of placenta. Umbilical cord length also associates with foetal bone strength. In such study, it was observed that, neonates with short umbilical cord showed lower bone speed of sound (SOS) than those who possessed longer cord. Again, motor dysfunction and reduced foetal movements which associate with short umbilical cords is found to correlate positively with decreased bone strength and mineralization of the foetus. It has been explained that, foetal movements generate mechanical strain on bones and influence bone cell migration from the extracellular spaces into the canalicular spaces (Wright and Chan, 2009; NuggedAlla, 2013).

Another study found statistically significant association of umbilical cord length with the development of childhood epilepsy. Multivariate analysis of the study showed 15% reduction in epileptic case incidence with every 10 cm increment in the umbilical cord length. One good reason being the observation that, a short umbilical cord is an effective marker of intrauterine activity that poses adverse future developmental risk to the foetus including mental and motor dysfunctions (Raisanen *et al.,* 2013). Umbilical cord length has been found to positively associate with males, uterine size, neurologic anomalies, growth and foetal activities and birth weight, maternal parity and age. Cord length is also correlated with body length, head circumference and placental weight (Petekkaya1 *et al.,* 2011; Collins, 2014; Elarbah *et al.,* 2014). Although umbilical cord length is a key morphologic character of the cord, it is indeed difficult to obtain accurate assessment antenatally by the use of the conventional ultrasound technique, but it has been observed that, various

pregnancy complications increase with increasing umbilical cord length (Sabnis *et al.,* 2012). Various abnormalities found to be associated with the umbilical cord include; an excessively long or short cord, improper umbilical cord insertion into the placenta and umbilical cord knots, all of which could result in complications in the course of pregnancy, labour or delivery (NuggedAlla, 2013).

Long umbilical cord is defined as a cord length that measures greater than 100 cm and short cord as measuring less than 30 cm (Balkawade and Shinde, 2012; Spurway *et al.,* 2012). However, other studies have defined long umbilical cord as measuring greater than 70 cm and short cord measuring less than 40 cm (Baergen *et al.,* 2001; Olumuyiwa and Ogunlaja, 2015). Mishra *et al.* (1987) also measured and defined long umbilical cord as measuring greater than 100 cm in length and short cord as having length of less than 20 cm.

Both Long and short umbilical cords are known to adversely affect the mother and the foetus. Studies have observed significant associations of long cords with maternal systemic diseases, pregnancy and delivery complications including cord prolapse, torsion, cord entanglement around the neck and body (NuggedAlla, 2013; Collins, 2014; Elarbah *et al.,* 2014). On the other hand, short umbilical cord has been associated with delayed second stage of labour, congenital malformation, foetal heart rate distress, placental abruption, umbilical cord rupture, uterine inversion, intrauterine growth restriction and foetal demise (Spurway *et al.,* 2012; Elarbah *et al.,* 2014).

The anatomy of umbilical cord insertion into the placenta is very unique and any deviation from the normal cord insertion into the placenta could adversely affect the foetus. The umbilical ring is fashioned to support foetal growth up to delivery without detachment. The

ring of the cord receives innervation from the vagus trunk, phrenic nerve and right adrenal gland nerve branches. This nervous arrangement presupposes an umbilical ring innervation of *ductus venosus* feedback mechanism that partially modulates blood flow into foetal circulatory system (Collins *et al.,* 2010).

The differences at the points of attachment of umbilical cord into the placenta could be explained by two distinct theories: the placental migration theory or trophotrophism, whereby the *chorion frondosum* follows advancing gestation to ensure adequate blood flow from a highly vascularized region so as to obtain maximum perfusion. The other theory is blastocyst polarity theory; in which there is abnormal positioning of the blastocyst during implantation resulting in the site of umbilical cord insertion into placenta deviating from normal (Jain *et al*., 2017). Placental implantation at the upper region of the uterus tends to insert the umbilical cord to the centre of the placenta because implantation to the lower portion of the uterus shows higher tendency of migrating upwards towards the uterine body or the base and this can push the umbilical cord towards a more marginal or even a velamentous insertion. It has been observed that, when the blastocyst fails to attach at the embryonic pole, the connecting stalk may attach at the margin or to the smooth adjacent chorion resulting in marginal or velamentous insertions respectively as pregnancy advances in age (Pathak *et al*., 2010). Another observation is that, marginal cord insertions commonly associate individuals with problems affecting specifically vascular supply and defects in the uterus (Antoniou *et al.,* 2011; Manikanta *et al.,* 2012).

The normal insertion site of the umbilical cord into placenta is at the centre away from the edge (central) or when the cord is inserted in the foetal surface of the placenta close to the centre (eccentric). Consequently, abnormal cord insertion can be described as any umbilical cord insertion not centrally placed into the placenta. Such insertions are classified as

marginal when the cord inserts 2 cm or less from the edge of the placenta; or velamentous cord insertion when the cord attaches to the placental membranes instead of the placental mass. Another abnormal cord insertion is furcated insertion whereby the umbilical cord branches before attaching to the placenta (Collins *et al.*, 2010; Manikanta *et al.,* 2012; Olaya and Bernal, 2014). Abnormal cord insertion makes a loose attachment into placenta and this potentially increases the risk of cord vessels being ruptured, resulting in reduced bloodflow and therefore decreased foetal growth (Elghazaly *et al.,* 2016).

Clinically, the distance of umbilical cord insertion from the centre of the placenta is known to indicate materno-placental insufficiency. The reason being that, maternal genetics, weight gain, medical disorders, environmental exposure and lifestyle including smoking and substance abuse alter placental growth leading to deviation from round or oval shape of the placenta and umbilical cord insertion at the centre. This deviation therefore adversely modifies the functional efficiency of the placenta (Whittle *et al.*, 2006; Yampolsky *et al.*, 2009).

Marginal cord insertion has been associated with abnormal pregnancy outcomes such as preterm labour, intrauterine growth restriction and can easily lead to velamentous insertion due to trophotrophism. The frequency of velamentous insertion increases with maternal risk factors such as maternal smoking habit, advanced age, *diabetes mellitus* and multiple births and associates with poor pregnancy outcomes (Pathak *et al*., 2010).

The prevalence of variations in umbilical cord attachment to the placenta has been studied. One study reported on 110 placentae with 75.45% having central and eccentric cord insertions, 16.36% marginal insertion, 7.27% furcated insertion and 0.90% velamentous insertion (Manikanta *et al.,* 2012). Sabnis *et al.* (2012) reported that, the incidence of marginal insertion ranges from 7.2% to 16.3% while furcated insertion ranges from 0.75%

to 7.27%. However, they observed incidence of marginal insertion to be 9.45% and 8.00% for furcated insertion. Another study also found the prevalence of central and eccentric insertions to be 69.5% and 30.5% respectively (NuggedAlla, 2013). The attachment of the umbilical cord to the placenta was found to be 58.3% central, 36.0% eccentric and 10.2% marginal with no velamentous insertion according to Petekkaya *et al.* (2011). 83.3% eccentric, 13.2% central and 3.5% marginal insertions of the umbilical cord into placentae were observed by Elghazaly *et al.* (2016). In a 216 incidence of abnormal cord insertions, 4.04% were velamentous, 0.43% furcated insertion and 19.14% marginal and paramarginal insertions (Olaya and Bernal, 2014).

3.2 AIM AND SPECIFIC OBJECTIVES

3.2.1 Aim

To investigate the relationships between morphological indices of the placenta and the umbilical cord.

3.2.2 Specific Objectives

- To determine mean morphometric indices of umbilical cord.
- To determine mean morphometric indices of the placenta.
- To investigate the association between morphological indices of the placenta among neonates with short and normal umbilical cord lengths.
- To determine correlation between morphological indices of the umbilical cord and placenta based on umbilical cord insertion.

3.3 MATERIALS AND METHODS

3.3.1 Study Design and Area

This descriptive cross-sectional study was conducted from March 2014 to October 2018 at Victory Maternity Home and Clinic in Ayigya – Kumasi, on delivered placentae and umbilical cords, foetal anthropometry and maternal socio-demographic characteristics.

3.3.2 Study Population

The study population consisted of pregnant women accessing antenatal care services and who delivered at the Victory Maternity Home and Clinic. Total number of 369 placentae delivered at the maternity unit were collected and washed under running tap water to clear away blood smear and clots. The umbilical cord was cut, leaving a stump length of 2.5 cm from its foetal site of insertion. The specimens were then placed in 50 litre plastic container filled with 25 litres of 10% neutral buffered formalin, sealed with an air-tight lid and kept at room temperature before transporting to the Department of Anatomy laboratory at the Kwame Nkrumah University of Science and Technology's School of Medicine and Dentistry. All the specimens were labeled with number sticker after washing for the purpose of identification.

3.3.3 Sample Size Determination

In order to generalize the study findings, a sample size that truly represented the entire population was calculated by the use of equation for cross-sectional study as shown below:

$$n = \frac{Z^2 qp}{d^2}$$ (Afodun *et al.*, 2015)

Where ***n*** is the minimum sample size, ***Z*** is the standard normal variant (at 5%) which is 1.96, ***p*** is the prevalence in the population based on previous study (Quantitative evaluation of placental and umbilical cord indices and perinatal outcome; *p*=50%), ***q*** = 1- ***p, d*** = relative precision and is usually 0.05. Therefore, $\boldsymbol{n} = : \frac{(1.96)^2(1-0.50)*0.50}{0.05^2} = \frac{0.960}{0.0025} = 384$

However, after the samples were audited for complete information on maternal socio-demographic characteristics, placental and umbilical cord morphometric and foetal indices, the total number of the sample became 364 since those with incomplete information were excluded.

3.3.4 Inclusion and Exclusion Criteria

Factors considered for inclusion in this study are; placentae and umbilical cords from mothers with uncomplicated pregnancy and normal vaginal delivery, complete information on their socio-demographic characteristics, known gestational age, singleton pregnancy, live birth neonate, availability of mother's ANC card and samples with identification tags. However, pregnancies with complications, multiple pregnancies, incomplete information on socio-demographic characteristics, unknown gestational age, stillbirth, unavailability of ANC card and sample without identification tags were excluded from the study.

3.3.5 Sample Preparation

Soon after delivery, the freshly collected placenta was thoroughly rinsed under running tap water to remove blood clots. The washed placenta together with the membranes and umbilical cord were placed in 10% neutral buffered formalin in a 50 litre plastic container

with the attached number sticker that corresponded with the number indicated in the pre-designed register for neonatal and maternal indices. At the Anatomy laboratory, the samples were further processed in a buffer solution of 0.5% formaldehyde in saline for detailed examination and measurements of the placenta's gross structure in accordance with standard methods used in placenta examinations (Benirschke *et al.*, 2006).

3.3.6 Placental Morphometry Computation

After preparation of each placenta, the following placental indices were computed from the gross structure:

1. **Weight of placenta**: It was measured using an electronic weighing scale (OIML Electronic Waterproof Weighing Scale – AIPI-SS2) and recorded after the umbilical cord was cut and placental membranes trimmed. The placenta was then placed on the scale. The measurement was repeated and the average taken as the weight of placenta.
2. **Volume of placenta**: This was obtained using water displacement method and recorded. The placenta after being trimmed and the cord cut was gently lowered into transparent graduated beaker (1000 litres capacity) containing water; the initial water volume V_1 was noted and final volume V_2 after putting in the placenta was also recorded. The difference between V_2 and V_1 then gave the volume of water displaced and that also became the volume of the placenta.
3. **Diameter of Placenta**: This was measured with a non-elastic measuring tape. The average of maximum (D1) and minimum (D2) diameters gave the diameter (D) of the placenta.

4. **Surface Area**: The maternal surface area of the placenta was computed using the formula:

   Surface area = $\frac{\pi D1 \times D2}{4}$, where D1 is the largest diameter and D2 is the smallest diameter).

5. **Placental Thickness**: The placenta was placed on a flat surface and a thin long graduated needle was inserted into the placenta, at the centre, at the margin and midway between the centre and the margin. The average of the three recordings was taken as the thickness of the placenta.

6. **Shape of Placenta**: The shape of each placenta was qualitatively assessed after thorough inspection. The placentae were then grouped as being round (R), oval (O) or irregular (I) as shown below.

Round Oval Irregular

Figure 2: Photographs showing different placenta shapes.

7. **Number of Cotyledons**: The counting of placental cotyledons follows a method by Kumari *et al.* (2016). In this method, gentle pressure was applied at the central part of the foetal surface using the two thumbs of the hands while holding in place the periphery of the placenta with other fingers, consequently the cotyledons on maternal surface become prominent. The placenta was then placed in a flat tray

with the maternal side facing up. The cotyledons were counted from the left towards right in a loop pattern and the total number of cotyledons recorded as shown below.

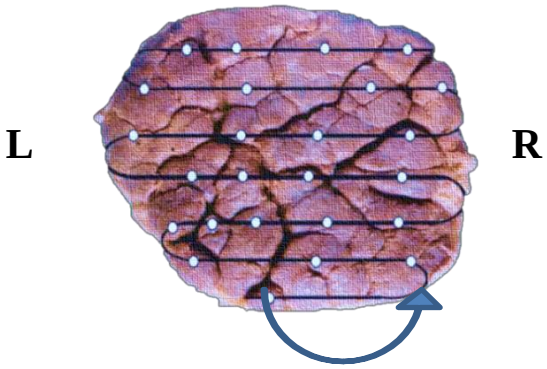


Figure 3: Method of counting placental cotyledons from left to right in a looped pattern

8. **Umbilical Cord Insertion**: The sites of umbilical cord insertion into the placenta were recorded only after proper inspection. They were categorized into Central insertion when the cord inserts at or near the centre usually less than 3 cm from the centre; Eccentric insertion when the cord inserts more than 3 cm from the centre and more than 2 cm from the closest margin. The third category was the marginal insertion, defined as umbilical cord inserting within 2 cm from the placental disc edge.

3.3.7 Umbilical Cord Morphometry

1. **Umbilical Cord Length**: The umbilical cord was immediately clamped at delivery and in all cases; 2.5 cm umbilical cord stump was left on the neonate. Umbilical cord measurements were made with the umbilical cord still attached to the placenta in its entirety using a standard non – elastic measuring tape from the

foetal end to its point of insertion on the placenta. The 2.5 cm stump was added to each measurement made. The umbilical cord lengths were categorized into short, when the measured length was < 40 cm, normal, when the measurement was within 40 and 70 cm and long cord if the measurement was > 70 cm (Baergen *et al.*, 2001).

2. **Umbilical Cord and Vessel Diameter**: Umbilical cord diameter (UCD) was measured using a pair of electronic vennier calipers placed outer-to-outer at three different points, precisely at the foetal end (D1), mid–portion (D2) and at the placental surface (D3) with the average being the diameter of the cord. The foetal end of the umbilical cord was sliced with a surgical blade before the diameters of the umbilical cord vessels were measured with the electronic vennier calipers and the result recorded.
3. **Umbilical Cord Weight:** The cord weight was measured using an electronic weighing scale after the umbilical cord excised from the placenta. The umbilical cord was then placed on the scale. The weighing was repeated twice and the average of the three weight measurements was taken as the weight of the umbilical cord.
4 **Umbilical Cord Volume**: This was obtained by the use of water displacement method and recorded. The umbilical cord after being cut from the placenta was gently lowered into a transparent graduated beaker (500 mL capacity) containing water, the initial water volume V_1 was noted, and the final volume V_2 after placing in the cord was also recorded. The difference between V_2 and V_1 then gave the volume of water displaced and that became the volume of the umbilical cord.

5. **Umbilical Cord Area**: The cross-sectional areas of the umbilical cord, umbilical arteries and umbilical vein in a free loop of the umbilical cord were computed using the formula for calculating the surface area of a cylinder with the assumption that, the umbilical cord takes the shape of a cylinder. That is:

   $A = 2\pi r^2 L$ Where ***r*** is the radius and ***L*** is the length of umbilical cord.

6. **Area of Wharton's jelly**: The cross-sectional area of the Wharton jelly was estimated by subtracting the total vessel area from the cross-sectional area of the umbilical cord. That is: $AWJ = UCA - (UCVA + A1A + A2A)$,

   where ***AWJ*** is the area of Whartons jelly, ***UCA*** is the cross sectional area of the cord, ***UCVA*** is the area of umbilical cord vein, ***A1A*** and ***A2A*** are the cross sectional areas of cord arteries 1 and 2 respectively.

3.4 RESULTS

Table 6 below shows the descriptive statistics of the umbilical cord indices. The mean umbilical cord length was 36.31 ± 8.75 cm (range: 13.83 – 68.83 cm), umbilical cord diameter was 1.03 ± 0.18 cm (range: 0.44 – 2.07 cm), and umbilical cord area was 61.80 ± 24.76 cm^2 (range: 5.96 – 231.60 cm^2) with cord volume of 34.91 ± 10.39 cm^3 (range: 12.50 – 65.00 cm^3) respectively. The mean umbilical cord weight was 62.75 ± 17.65 g (range: 21.54 – 131.00 g).

Table 6: Descriptive statistics of the umbilical cord indices

Variable	Mean ± SD	Range
UCL (cm)	36.31 ± 8.75	13.83 – 68.83
UCD (cm)	1.03 ± 0.18	0.44 – 2.07
UCA (cm^2)	61.80 ± 24.76	5.96 – 231.60
UCV (cm^3)	34.91±10.39	12.50 – 65.00
UCW (g)	62.75 ± 17.65	21.54 – 131.0

UCL= Umbilical Cord Length, UCD = Umbilical Cord Diameter, UCA = Umbilical Cord Area, UCV = Umbilical Cord Volume, UCW = Umbilical Cord Weight, cm =centimeter, cm^2 = centimeter square, cm^3 = centimeter cube, g = gramme

The distribution of umbilical cord insertions into placenta is shown in Fig. 4. The patterns of cord insertions observed were central, eccentric and marginal. Out of the total 368 placenta samples, 115(31.25%) had central cord insertion, 182(49.46%) with eccentric cord insertion and 71(19.29%) had marginal cord insertion.

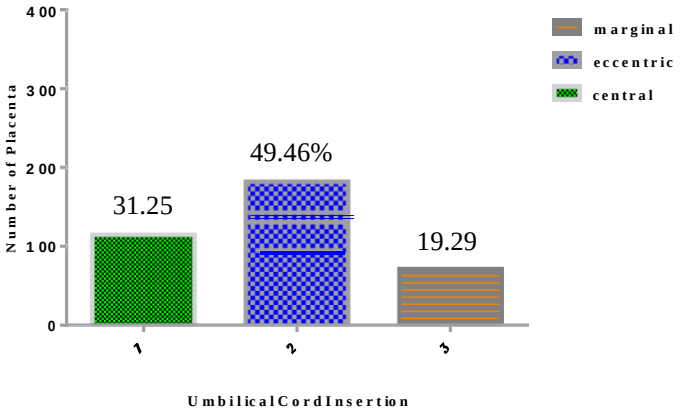


Figure 4: Distribution of Placentae by Umbilical Cord Insertion

The mean of placental indices are shown in Table 7. Mean placental weight was 510.30 ± 104.00 g (range: 274.20 – 809.00 g). Placental diameter had a mean of 19.43 ± 2.37 cm

(range: 13.50 - 27.50 cm), while mean placental thickness was 2.80 ± 0.46 cm (1.80 – 4.05 cm). Placental area and volume had mean values of 299.70 ± 73.30 cm^2 (range: 133.60 - 592.4 cm^2) and 619.60 ± 105.80 cm^3 (range: 275.30 - 834.8 cm^3) respectively. The mean number of cotyledons was 17.49 ± 3.18 (range: 9.00 - 27.00).

Table 7: Descriptive statistics of the Placental indices

Variable	Mean ± SD	Range
PW (g)	510.30 ±104.00	274.20 – 809.00
PD (cm)	19.43 ± 2.37	13.50 – 27.50
PT(cm)	2.80 ± 0.46	1.80 – 4.05
PA(cm^2)	299.70 ± 73.30	133.60 – 592.4
PV (cm^3)	619.60 ±105.80	275.30 – 834.8
No. of COTYL	17.49 ±3.18	9.00 – 27.00

PW – Placental Weight, PD – Placental Diameter, PT – Placental Thickness, PA - Area of Placenta, PV – Placental Volume, No. of COTYL- Number of Cotyledons of the placenta, SD – Standard Deviation, cm =centimeter, cm^2 = centimeter square, cm^3 = centimeter cube, g = gramme

The morphologic indices of the placenta were compared between neonates with normal and short umbilical cords, using paired t-test as shown in Table 8. Mean placental weight was significantly higher (518.60 ± 6.32 g) for neonates with normal umbilical cord length than those with short umbilical cords (486.50 ± 10.22 g) (p = 0.0090). Normal cord length neonates recorded a significantly larger mean placental diameter (19.67 ± 0.13 cm) compared to that of short cord neonates (18.75 ± 0.26 cm) (p = 0.0009). Mean placental area differed significantly (p = 0.0018) between normal and short cord neonates recording means of 306.80 ± 4.20 cm^2 and 279.90 ± 8.17 cm^2 respectively. The mean placental thickness was 2.78 ± 0.03 cm for normal cord length neonates and 2.86 ± 0.05 cm for short cord neonates. Similarly, the placental volumes for normal cord length and short

cord length neonates was 621.10 ± 6.41 cm^3 and 615.10 ± 10.78 cm^3 respectively. The differences observed for both placental thickness and volume were not statistically significant ($p > 0.05$). However, significant differences ($p < 0.0001$) were observed between the mean number of placental cotyledons in normal cord length neonates (18.21 ± 0.16) and short cord neonates (15.47 ± 0.38).

Table 8: Comparison of Placental Indices between Neonates with Short and Normal Umbilical Cord Lengths

	Short Cord (N=96)	**Normal Cord (N=272)**	
Variable	**Mean ± SD**	**Mean ± SD**	**p-Value**
PW(g)	486.50 ± 10.22	518.60 ± 6.32	0.0090
PD (cm)	18.75 ± 0.26	19.67 ± 0.13	0.0009
PA(cm^2)	279.9 ± 8.17	306.80 ± 4.20	0.0018
PT(cm)	2.86 ± 0.51	2.78 ± 0.26	0.1574
PV (cm^3)	615.10 ± 10.78	621.10 ± 6.41	0.6327
No. of COTYL	15.47 ± 0.38	18.21 ± 0.16	< 0.0001

PW = Placental Weight, PD = Placental Diameter, PA = Area of Placenta, PT = Placental Thickness, PV = Volume of Placenta, No. of COTYL = Number of Placental Cotyledons, SD = Standard Deviation, p – Value < 0.05, cm = centimeter, cm^2 = centimeter square, cm^3 = centimeter cube, g = gramme

The relationship between umbilical cord and placental indices with reference to the type of umbilical cord insertion into the placenta were studied using Pearson correlation. The results of umbilical cord and placental indices for central and marginal cord insertions are shown in Table 9. In the case of the central cord insertion, placental weight positively correlated with the following other indices of the placenta; diameter ($r = 0.486$, $p < 0.0001$), area ($r = 0.483$, $p < 0.00010$) and volume ($r = 0.880$, $p < 0.0001$). However, there was no significant correlation between placental weight, thickness and number of placental

cotyledons. Also, no statistically significant correlation was observed between placental weight and the umbilical cord morphometric indices ($p > 0.05$).

Placental diameter positively correlated with other placental indices such as the area ($r = 0.996$, $p < 0.001$), the volume ($r = 0.399$, $p < 0.001$) and number of cotyledons ($r = 0.202$, $p < 0.05$). There was no significant correlation between placental diameter and thickness as well as the umbilical cord indices ($p > 0.05$). Placental area showed significant correlation with the volume ($r = 0.388$, $p < 0.001$) and number of cotyledons ($r = 0.191$, $p < 0.05$), but the area showed no significant correlation with placental thickness and the umbilical cord indices ($p > 0.05$). The placental thickness did not significantly correlate with the number of cotyledons, and other umbilical cord indices ($p > 0.05$) except a negative correlation ($r = -0.186$, $p < 0.05$) with the umbilical cord volume.

There was no correlation between placental volume and number of cotyledons or any of the umbilical cord indices. The umbilical cord length showed no significant correlation with cord diameter ($r = 0.089$, $p > 0.05$), but positively correlated with cord area ($r = 0.519$, $p < 0.0001$), cord volume ($r = 0.454$, $p < 0.0001$) and cord weight ($r = 0.457$, $p < 0.0001$). Umbilical cord diameter only showed positive correlation with cord area ($r = 0.785$, $p < 0.0001$), but not with cord volume ($r = 0.064$, $p > 0.05$) or weight ($r = 0.126$, $p > 0.05$). The umbilical cord area positively correlated with cord volume ($r = 0.300$, $p < 0.001$) and cord weight ($r = 0.361$, $p < 0.0001$). Umbilical cord volume showed significant positive correlation with cord weight ($r = 0.395$, $p < 0.0001$).

When placental and umbilical cord morphometric indices were correlated with respect to marginal cord insertion, the observations were that, placental diameter positively correlated with placental weight ($r = 0.670$, $p < 0.0001$). Placental area showed significant positive correlation with weight ($r = 0.671$, $p < 0.0001$) and diameter ($r = 0.997$,

$p < 0.001$).

Placental thickness did not show any significant correlation with weight ($r = 0.036$, $p > 0.05$), diameter ($r = 0.027$, $p > 0.05$) and area ($r = 0.020$, $p > 0.05$). Whereas placental volume showed significant positive correlations with the weight ($r = 0.850$, $p < 0.0001$), diameter ($r = 0.575$, $p < 0.0001$) and area ($r = 0.562$, $p < 0.0001$), it was not so for thickness ($r = 0.035$, $p > 0.05$). The number of cotyledons in this case showed no significant correlation with the weight ($r = 0.091$, $p > 0.05$), diameter ($r = 0.134$, $p > 0.05$), area ($r = 0.126$, $p > 0.05$), thickness ($r = 0.134$, $p > 0.05$) and volume ($r = 0.094$, $p > 0.05$).

The negative correlations observed between umbilical cord length and placental indices such as weight ($r = -0.103$, $p > 0.05$), diameter ($r = -0.048$, $p > 0.05$), area ($r = -0.064$, $p > 0.05$), thickness ($r = -0.058$, $p > 0.05$), volume ($r = -0.037$, $p > 0.05$) and number of cotyledons ($r = -0.130$, $p > 0.05$) were all not statistically significant. Similarly, no significant correlations were found between umbilical cord diameter and placental indices. However, significant correlation was observed between cord diameter and cord length ($r = 0.327$, $p < 0.001$). Both cord area and volume respectively did not show any significant association with placental indices but correlated positively with cord length ($r = 0.722$. $p < 0.0001$; $r = 0.412$, $p < 0.0001$) and diameter ($r = 0.843$, $p < 0.0001$; $r = 0.285$, $p < 0.001$). The cord volume and area also correlated significantly with each other ($r = 0.377$, $p < 0.001$). Again umbilical cord weight did not correlate significantly with any of the placental indices and also the cord volume. It significantly correlated positively with the cord length ($r = 0.294$, $p < 0.05$), cord diameter ($r = 0.445$, $p < 0.0001$) and cord area ($r = 0.409$, $p < 0.0001$).

Table 9: Pearson Correlation of Placental and Umbilical Cord Indices of Centrally (not bold upper right corner) and Marginally (Bold lower left corner) Inserted Umbilical Cord

Variable	PW (g)	PD (cm)	PA (cm^2)	PT (mm)	PV (cm^3)	P COTYL	UCL (cm)	UCD (cm)	UCA (cm^2)	UCV (cm^3)	UCW (g)
PW		0.496^{q}	0.483^{q}	-0.061^{n}	0.880^{q}	0.116^{n}	-0.050^{n}	-0.090^{n}	-0.103^{n}	-0.062^{n}	-0.169^{n}
PD	**0.670^{q}**		0.996^{p}	-0.089^{n}	0.399^{p}	0.202*	-0.062^{n}	-0.039^{n}	-0.078^{n}	0.085^{n}	0.013^{n}
PA	**0.671^{q}**	**0.997^{p}**		-0.085^{n}	0.388^{p}	0.191*	-0.063^{n}	-0.033^{n}	-0.074^{n}	0.083^{n}	0.007^{n}
PT	**0.036^{n}**	**0.027^{n}**	**0.020^{n}**		0.035^{n}	0.032^{n}	-0.079^{n}	0.048^{n}	-0.014^{n}	-0.186*	0.002^{n}
PV	**0.850^{q}**	**0.575^{q}**	**0.562^{q}**	**0.035^{n}**		0.055^{n}	-0.001^{n}	-0.054^{n}	-0.042^{n}	-0.063^{n}	-0.128^{n}
P COTYL	**0.091^{n}**	**0.134^{n}**	**0.126^{n}**	**0.134 ^{n}**	**0.094 ^{n}**		-0.156^{n}	-0.018^{n}	-0.095^{n}	-0.036^{n}	-0.148^{n}
UCL (cm)	**-0.103^{n}**	**-0.048^{n}**	**-0.064^{n}**	**-0.058 ^{n}**	**-0.037 ^{n}**	**-0.130^{n}**		-0.089^{n}	0.519^{q}	0.454^{q}	0.457^{q}
UCD (cm)	**0.196^{n}**	**0.177^{n}**	**0.163^{n}**	**0.030 ^{n}**	**0.183 ^{n}**	**0.111^{n}**	**0.327^{p}**		0.785^{q}	0.064^{n}	0.126^{n}
UCA (cm^{2})	**0.063^{n}**	**0.079^{n}**	**0.065^{n}**	**-0.001 ^{n}**	**0.080 ^{n}**	**-0.084^{n}**	**0.722^{q}**	**0.843^{q}**		0.300^{p}	0.361^{q}
UCV (cm^3)	**-0.056^{n}**	**0.003^{n}**	**-0.010^{n}**	**-0.181 ^{n}**	**-0.117 ^{n}**	**0.226^{n}**	**0.412^{q}**	**0.285^{p}**	**0.377^{p}**		0.395^{q}
UCW (g)	**0.112^{n}**	**0.079^{n}**	**0.062^{n}**	**0.090 ^{n}**	**0.169 ^{n}**	**0.196^{n}**	**0.294***	**0.445^{q}**	**0.409^{q}**	**0.201^{n}**	

*Bold figures are correlation coefficients (r) obtained from marginally inserted umbilical cord. Unbold figures are correlation coefficients (r) obtained from Centrally inserted UC. q <0.00001, p<0.001, *<0.05, n > 0.05. PW = Placental Weight, PD = Placental Diameter, PA = Placental Area, PT = placental thickness, PV = placental volume, P COTYL = placental cotyledon, UCL = umbilical cord length, UCD = umbilical cord diameter, UCA = umbilical cord area, UCV = umbilical cord volume, UCW = umbilical cord weight, cm =centimeter, cm^2 = centimeter square, cm^3 = centimeter cube, g = gramme, mm =millimetre*

Placentae with eccentric umbilical cord insertions were studied using Pearson correlation to determine the association between placental and umbilical cord indices as shown in Table 10 below.

With the exception of the umbilical cord volume, none of the placental index correlated significantly with the umbilical cord indices. The umbilical cord volume significantly showed positive correlation with the placental weight although it was weak ($r = 0.15$, $p = 0.0394$)

Table 10: Pearson Correlation of Placental and Umbilical Cord Indices of Eccentrically inserted Umbilical cords.

Variable	PW(g)	PD(cm)	PA(cm^2)	PT(mm)	PV(cm^3)	P COTYL
UCL(cm)	0.09(0.223)	0.09(0.213)	0.10(0.169)	0.02(0.766)	0.04(0.565)	-0.14(0.064)
UCD(cm)	0.08(0.292)	0.01(0.880)	0.01(0.903)	0.00(0.954)	0.07(0.366)	0.04(0.576)
UCA(cm^2)	0.10(0.183)	0.06(0.393)	0.07(0.367)	0.01(0.893)	0.07(0.350)	-0.04(0.582)
UCV(cm^3)	0.15(0.0394)*	0.09(0.200)	0.09(0.213)	0.01(0.910)	0.12(0.102)	-0.05(0.464)
UCW(g)	0.00(0.994)	-0.10(0.164)	-0.11(0.154)	0.04(0.557)	0.04(0.552)	-0.05(0.527)

*Correlation coefficients (r) is outside the parenthesis and p – values are inside the parenthesis, * = $p < 0.05$, UCL = umbilical cord length, UCD = umbilical cord diameter, UCA – umbilical cord area, UCV – umbilical cord volume, UCW = umbilical cord weight, cm = centimeter, cm^2 = centimeter square, cm^3 = centimeter cube, g = gramme, mm = millimetre*

3.5 DISCUSSION

3.5.1 Umbilical cord and Placental Indices

Exploring the role of umbilical cord and placental indices in determining foetal health and well-being has become very relevant in the field of medicine. The mean of the umbilical cord parameters according to this study were 36.31 ± 8.75 cm in length, 1.03 ± 0.18 cm in diameter, 61.80 ± 24.76 cm^2 in area, 34.91 ± 10.39 cm^3 in volume and 62.75 ± 17.65 g umbilical cord weight. Similarly, a mean placental weight of 510.30 ± 104.00 g, a mean diameter of 19.43 ± 2.37 cm, mean thickness of 2.80 ± 0.46 cm and mean number of cotyledons of 17.49 ± 3.18 were observed in the present study. The mean of 299.70 ± 73.30 cm^2 and 619.60 ± 105.80 cm^3 were also recorded for the area and volume of the placenta respectively.

Variations in the morphometric parameters of umbilical cord and placental measurements are common among research studies. Nevertheless, information on these differences are very crucial to the sonologist, obstetrician and the paediatrician as alterations in cord length, diameter and placental parameters pose potential dangers including foetal demise and abnormalities such as aplasia, chromosomal abnormalities, congenital tracheo-oesophageal fistula to the foetus (Kulshreshtha and Saxena, 2018). A number of studies have reported that, umbilical cord length ranges from a complete absence of umbilical cord (achordia) to about 300 cm in length with a diameter of 1–3 cm (Spurway *et al.,* 2012; Ogunlaja and Ogunlaja, 2015; Olumuyiwa and Ogunlaja, 2015; Rohinidev *et al.,* 2016). These studies also reported that, a normal term umbilical cord length ranges from 40 cm to 60 cm.

In an earlier study at the Victory Maternity Home and Clinic, Kumasi, the umbilical cord measurements observed were; cord length of 42.91 ± 9.17 cm, diameter of 1.31 ± 0.23 cm,

umbilical cord area of 180.40 ± 51.14 cm^2 and a cord volume of 60.22 ± 26.18 cm^3. Also, placental weight of 608.40 ± 102.60 g, placental diameter of 18.37 ± 2.16 cm and area of 133.00 ± 48.80 cm^2 were recorded (Bimpong, 2012). Abaidoo *et al.* (2008) in studying the morphological variations in the baby's supply line at University of Science and Technology hospital in Kumasi reported a mean umbilical cord length of 47.04 ± 12.80 cm and observed that, 69.60% of cord lengths were within the range of 41.50 to 55.00 cm. Some other studies within the Kumasi metropolis have also reported mean cord length of 44.80 ± 12.00 cm (Appiah, 2009) and 41.74 ± 12.09 cm (Tetteh, 2015). Similar studies including Olumuyiwa and Ogunlaja (2015) and Rohinidev *et al.* (2016) reported mean umbilical cord length values of 51.50 ± 6.67 cm and 54.30 ± 7.29 cm respectively. Mean umbilical cord length of 58.20 ± 8.70 cm for normal pregnant women has also been observed (Sabnis *et al.,* 2012). However, Baergen *et al.* (2001), reported a mean umbilical cord length of 37 cm while a mean cord length of 38.7 cm has been reported (Kulshreshtha and Saxena, 2018). Comparing the previous and current findings from the Victory Maternity Home and Clinic and the findings reported by Abaidoo *et al.* (2008), Appiah (2009) and Tetteh (2015), it presupposes that, the mean umbilical cord length values in the Kumasi Metropolis are lower than the reported findings from other studies conducted outside Kumasi in Ghana. The reported figures for cord lengths in the Kumasi Metropolis were slightly higher than the cord length classified as short cord (Collins, 1992; Flamm, 1999; Benirschke and Kaufmann, 2000; Balkawade and Shinde, 2012). It could therefore be assumed that, normal cord length among neonates in the Kumasi metropolis fell between 36 cm and 48 cm, since all these findings were reported from studies of normal maternal singleton foetuses.

The umbilical cord diameter recorded in the present study (1.03 ± 0.18 cm) is lower than observed in previous study (1.31 ± 0.23 cm) at same the facility. Tetteh (2015) also found a mean cord

diameter of 1.19 ± 0.21 cm. However, these findings were lower than the 2.10 ± 0.04 cm observed by Abaidoo *et al.* (2008). These variations in cord diameter is possible due to a number of factors including differences in Wharton's jelly water content, glycosaminoglycans, extracellular matrix (Afroze *et al.*, 2017), cord vessel area especially the areas of artery and Wharton's jelly, pathologic state of the umbilical cord such as cord oedema, polyhydramnios as well as foetal hydrops. Diseased state of the placenta is also known to influence cord diameter. In studying umbilical cord diameter percentile curves and their relationship to birth weight and placental pathology, it was reported that, there is association between cord diameter, vessel area and placental weight, where it was observed that, significant increase in cord artery area led to large umbilical cord diameter, while a decrease in Wharton's jelly area resulted in low umbilical cord diameter. There was also, an association between smaller cord diameters and low placental weight (Proctor *et al.*, 2013).

The umbilical cord area and volume in the present study were lower than that observed in an earlier study at the same facility. The difference is expected since the cord area was mathematically estimated from cord length and diameter with low mean values. In the first study, cord volume was estimated using formula for calculating the volume of a cylinder; while water displacement by immersion method was used in the current study. The variations in cord volumes could result from differences in approach in the volume determination and also the cord morphology. Water displacement by immersion has been found to have greater accuracy and precision, justifying its use in the present study (Hughes and Lau, 2008).

The prevalence of various forms of umbilical cord insertion into the placenta observed in this study was 31.25% central, 49.46% eccentric and 19.29% marginal with no velamentous insertions. The pattern of the current findings is similar to observations of several studies. For example, 32.4%

central, 67.2% eccentric, 0.3% marginal and 0.1% velamentous insertions were found by Balkawade and Shinde (2012). A study conducted on 40 placentae at the Cape Coat Teaching Hospital in the Central region of Ghana showed cord insertion distribution of 57.5% eccentric, 27.5% central and 15% marginal with no velamentous insertion (Tsegah and Asante, 2018). Also, Anjum *et al.* (2015) recorded 38% central, 54% eccentric, 6% marginal and 2% velamentous insertions. Another study also recorded the major cord insertions into the placenta as 66% eccentric, 27% central and 7% marginal (Elangovan and Raviraj, 2016). However, these observations contradict the 53.8% central, 36.0% eccentric and 10.2% marginal insertions reported by Petekkaya *et al.* (2011). Although these studies vary in the percentage distribution of central and eccentric insertions, it could be derived by deduction tha,t the total percentage of normal cord insertions (both central and eccentric) ranges from 80 to 99%. This appears to correspond to the frequently reported ranges of 5 – 7% marginal and 1 – 2% velamentous insertions in all pregnancies by sonologists (Moshiri *et al.,* 2014).

The placenta could be likened to the "black box flight recorder" of aeroplanes which records all flight data and conversations and as such any information relating to the flight at any moment could be traced from the black box recorder. The placenta as "black box" records all prenatal experiences of the foetus and therefore placental measurements significantly predict perinatal outcomes (Afodun *et al.,* 2015). The placental morphometric characteristics in the current study showed mean weight of 510.30 ± 104.00 g, mean diameter of 19.43 ± 2.37 cm and a mean thickness of 2.80 ± 0.46 cm. The mean values for the area, volume and number of cotyledons found were 299.70 ± 73.30 cm^2, 619.60 ± 105.80 cm^3 and 17.49 ± 3.18 respectively. Placental mean values reported by two other studies in the Kumasi metropolis included weight of 578.81 ± 121.60 g, diameter of 17.40 ± 1.83 cm, thickness of 2.04 ± 0.45 cm,with area and volume

measurements being 240.29 ± 50.04 cm^2 and 486.91 ± 135.15 cm^3 respectively (Tetteh, 2015). The second study recorded a mean weight of 563.47 ± 132.00 g, mean diameter of 18.69 ± 2.05 cm, and thickness of 2.68 ± 0.55 cm but did not report on area and volume (Appiah, 2009).

The mean values recorded in the present study are similar, but higher than the results of a study in India which found placental measurements of normal population to include a weight of 397.50 ± 42.29 g, diameter of 15.40 ± 1.34 cm, thickness of 1.96 ± 0.23 cm, the mean number of cotyledons was 16.93 ± 2.49 and placental surface area of 187.61 ± 32.73 cm^2 (Agarwal *et al.*, 2015; Anjum *et al*., 2015). Elangovan and Raviraj (2016) recorded an average of 20 cotyledons per placenta in normal pregnancy. The other finding was 466.6 ± 20.6 g weight, 398.8 ± 14.1 cm^3 volume, 18.56 ± 1.7 cm in diameter, 1.79 ± 0.10 cm thickness, 266.03 ± 22.40 cm^2 area and 17.46 ± 0.10 number of cotyledons. Tsegah and Asante (2018) also recorded mean values of placenta as; 474.10 g (SE = 14.23) in weight, 409.83 cm^3 (SE = 14.60) in volume 19.48 cm (SE = 0.31) in diameter and 1.96 cm (SE = 0.06) in thickness. The term placenta has been estimated to measure about 23 cm in diameter, thickness of 2.0 to 2.6 cm, a weight of 470 g and volume of 500 mL (Cunningham *et al.*, 2005). These observed variations in placental measurements could be attributed to genetics, regional and racial differences, quality of antenatal care services and nutritional status of mothers as reported by Afodun *et al.* (2015). This makes standardization of values of placental indices practically impossible globally.

3.5.2 Placental Characteristics of Neonates with Short and Normal Umbilical Cord Length

Placenta is derived from the Latin "Plakons" as its Greek equivalent means "flat cake on a plate'' functions in many ways to support pregnancy and the developing foetus (Anjum *et al.*, 2015). The

umbilical cord connects the foetus to the placenta and serves as the conduit of nutrient and waste material transport (Wright and Chan, 2009; Sabnis *et al.,* 2012). The length of umbilical cord is known to indicate level of intrauterine foetal activeness (Baergen *et al.,* 2001). The foetal activity has been reported to depend on the quality of placental morphology; a reflection in placental sufficiency of nutrient supply (Anjum *et al.,* 2015). The present study compared the placental measurements of neonates with short and normal umbilical cord lengths.

The placental weight, diameter, area and number of cotyledons of normal umbilical cord length neonates were significantly higher than that of short–cord neonates. However, differences in placental volume and thickness between the short and normal cord neonates did not show statistical significance. Bimpong (2012) observed significantly higher placental weight in normal than in short–cord neonates and suggested that, the growth and development of cord length and placenta could be influenced by similar control mechanisms. Significant positive correlation has been reported between normal umbilical cord length and placental weight where an increase in the length of umbilical cord corresponded with an increase in placental weight (Petekkaya1 *et al.,* 2011). The placental weight has been found to be heavy in normal cord than short cord length neonates and even heavier in long-cord neonates (Algreis *et al.,* 2016). Olumuyiwa and Ogunlaja (2015) observed significant positive correlation between normal umbilical cord length and placental weight.

These reported findings presuppose that, as the umbilical cord length increases, the chorionic plate also enlarges which is in line with the significantly larger placental diameter, area and number of cotyledons observed in neonates with normal than those with short cord in the current study. As morphologically and functionally important parameter, placental growth in weight reflects efficiency in its supply of nutrients and oxygen which are crucial in foetal metabolism (Agarwal *et*

al., 2015). This could explain to some extent the abnormalities associated with short cord and neonatal outcomes. However, placental thickness and volume showed no significant difference between normal and short cord neonates. This observation supports findings of other studies in which placental thickness did not show statistical significance with umbilical cord length but gestational age (Ohagwu *et al.,* 2009; Elangovan and Raviraj, 2016).

3.5.3 Pearson Correlation between Placental and Umbilical cord Indices According to Type of Cord Insertion

The use of human placental and umbilical cord parameters in monitoring the progress and development of the foetus and maternal health in pregnancy has necessitated both real-time and long term bio-monitoring of these all important but transient organs which provide the developing foetus with its needs (Zadroina *et al.,* 2012). Umbilical cord insertions into the placenta have been variedly reported. Some studies found no significant relationship between umbilical cord insertion and placental or neonatal indices (Adesina *et al.,* 2016; Tsegah and Asante, 2018), although other studies have reported some association between umbilical cord insertion and placental or neonatal variables (Pathak *et al.,* 2010; Anjum *et al.,* 2015). In all these observations, it is not the point of attachment which exerts influence on the relationship, rather the functional interactions between the umbilical cord and placental variables as the cord inserts centrally or marginally. The present study therefore based on the type of umbilical cord insertion into the placenta to examine possible correlations existing within and between umbilical cord and placental indices.

In studying correlations of placental and umbilical cord parameters in centrally inserted umbilical cords, it was found that, significant positive correlations ($p < 0.05$) existed within the placental parameters, except placental thickness which did not show any statistically significant relationship

with any of the placental parameters ($p > 0.05$). Also, the number of placental cotyledons only correlated significantly with placental diameter and area of the placenta. These placental indices showed little or no correlation with other placental parameters. Similarly, majority of the umbilical cord indices showed significant positive correlations among themselves. However, umbilical cord diameter only correlated significantly with cord area ($p < 0.05$), while umbilical cord volume showed positive correlations with cord length and weight. Umbilical cord area was the only index that exhibited significant positive correlation with all other umbilical cord indices.

In the marginally inserted cord placentae, the results indicated that, both placental thickness and number of cotyledons did not correlate with other placental parameters ($p > 0.05$). However, all other placental indices showed significant positive ($p < 0.05$) relationships among themselves. In the case of umbilical cord indices, there were significant positive correlations within almost all the cord indices. However, umbilical cord length did not correlate with cord diameter and weight, while cord weight also showed no significant correlation with cord volume. The umbilical cord indices again correlated positively with one another.

These findings of the current study clearly lead to the speculations that, placental thickness has no influence on other placental parameters whether umbilical cord inserts centrally or marginally. However, the number of cotyledons positively correlates with placental diameter and area when cord inserts centrally. This observation is contrary to a study finding which indicated that, the number of placental cotyledons does not independently associate with other placental parameters (Barker *et al.,* 2013). Also, the umbilical cord area's relationship with other cord indices is not influenced by the type of umbilical cord insertion into the placenta. Similarly, the umbilical cord diameter correlates positively with volume and weight when cord inserts marginally.

Both the placenta and umbilical cord provide functional intermediation between the mother and

foetus during pregnancy. As a result of this interaction or association existing among placental and umbilical cord indices are of great importance in understanding the role of these organs in pregnancy. Several studies focus on relationships existing between either placental indices or umbilical cord parameters and neonatal outcome (Ohagwu *et al.,* 2009; Londhe and Mane, 2011; Petekkaya1 *et al.,* 2011; Nagamani *et al.,* 2015). The current study therefore used Pearson correlation to establish relationship between placental and umbilical cord variables for placentae with central, eccentric and marginal cord insertions.

Pearson correlation performed to analyse relationship between placental and umbilical cord indices of centrally inserted cord placentae showed that, the umbilical cord length, diameter, area and weight had no significant correlation with the placental parameters. Nonetheless, the cord volume exhibited significant negative correlation with placental thickness ($p < 0.05$). This implies that, as the placental thickness increases, the volume of umbilical cord decreases.

Also, in eccentrically inserted cord placentae, the umbilical cord volume was found to correlate positively with placental weight, which means that, the weight of the placenta increases with umbilical cord volume. The Pearson correlation between umbilical cord and placental indices in marginally inserted cord placentae did not show statistically significant correlations. In a similar study conducted to assess the relationship between placental and umbilical cord morphologies, it was observed that, significant relationship existed between umbilical cord artery and vein diameters with placental weight (Petekkaya1 *et al.,* 2011). Another study by Tsegah and Asante (2018) found that, only placental index showed significant positive correlation with umbilical cord length as well as birth and placental weight in eccentrically inserted cord placentae and concluded that, where the umbilical cord inserts into the placenta may not exert significant influence on neonatal or placental indices.

3.6 ONCLUSION

The study observed majority of umbilical cord insertions to be eccentric and was followed by the centric and then marginal ones. Statistically significant difference was observed between placental weight, diameter, area and number of cotyledons of short and normal umbilical cord length neonates when placental parameters of the two groups were compared.

In placentae with central cord insertions, a significant positive relationship was observed between number of cotyledons and placental diameter and area. However, placental thickness exhibited no correlation with any of the placental parameters. Similarly, umbilical cord diameter showed no relationship with other cord parameters except a positive correlation with cord area. The umbilical cord volume and weight also related positively.

In both central and marginal cord insertions, the umbilical cord area positively correlated with all other cord indices, which presupposes that, the type of cord insertion has no adverse effect on umbilical cord area relationship with other measurements.

More importantly, the umbilical cord volume correlated negatively with placental thickness when cord inserts centrally while it showed positive correlation with placental weight in eccentric cord insertions**.**

CHAPTER FOUR

MODELING OF NEONATAL AND MATERNAL BOOKING BIOMETRIC INDICES

4.1 LITERATURE REVIEW

4.1.1 Birth Weight

Neonatal birth weight is a crucial determinant of the child's future health index including the possibility of surviving, probable medical complications and the probability of attaining good health in adulthood. According to the Centre for Disease Control and Prevention (CDC), adverse health consequences associated with birth weight is dependent on one of the following indicators; extremely low birth weight (< 1.0 kg), very low birth weight (< 1.5 kg), low birth weight (< 2.5 kg), normal birth weight (2.5 – 4.0 kg) and high birth weight (> 4.0 kg) **(**Gill *et al.,* 2013). Extremely low birth weight, very low birth weight or low birth weight neonates are known to suffer complications such as hypothermia, hypoglycaemia, perinatal asphyxia, respiratory distress, anaemia, malnutrition, infections, neurological disorders and hearing deficits. This implies that, neonatal health outcomes vary directly with a defined class of birth weight; the lower the birth weight, the higher the probability of experiencing adverse health outcomes (Martin *et al.,* 2011; Gill *et al.,* 2013).

In statistical terms, normal birth weight is defined to fall within the range around the central tendency such as the centile range (Malin *et al.,* 2013). However, in clinical terms, neonates with low birth weight fall into one of four categories:

1. The intrauterine growth restriction group who do not realize their growth potential due to environmental influences such as placental insufficiency and maternal medico-social conditions (Brodsky *et al.,* 2004).

2. Those who have structural or chromosomal abnormality and cannot reach their full growth.

3. Those who are small at birth but attain their growth potential later in life and suffer various degrees of pathological conditions.

4. The low birth weight neonates who achieve their growth potential but are delivered prematurely (Malin *et al.*, 2013).

Birth weight is a potential neonatal variable capable of predicting pre- and postnatal development which probably influences both short and long term consequences on the health and survival of the neonate. Several factors have influenced research interest in birth weight over decades making it a popular topic among neonatal indices (Wilcox, 2001). One of such factors is the precise recordings, free and readily available large volumes of birth weight data. The other factor is that, birth weight indicates the chances of neonatal survival or otherwise; hence, it has been found to be a strong predictor of infant mortality. The third factor looks at birth weight at population level where mean birth weight associates with the risk of neonatal mortality (Wilcox and Rusell, 1990). Finally, birth weight is known to influence health outcomes of the individual later in life. Adulthood chronic diseases such as asthma, low intelligent quotient and hypertension have been linked to birth weight (Richards *et al.,* 2001).

Birth weight has been found to associate with pathological conditions such as obesity, cardiovascular diseases, cancer and diabetes later in adult life. Additionally, low birth weight is known to relate with foetal growth restriction or prematurity and high risk of infant morbidity and mortality. High birth weight has also been linked with the risk of developing obstetric complications including dystocia, postpartum haemorrhage and infections (Wang *et al.,* 2017). Notwithstanding, biological determinants linking birth weight to infant mortality or development of diseases in adulthood have been attributed to either the genetic constitution or metabolic

variability of the individual (Wilcox, 2001). While variations in maternal circulating lipid levels are assumed physiologically to be normal response to pregnancy, steady rising levels of maternal lipids enhance necessary substrate availability to foetus for growth and well-being (Herrera,2002). It has been reported that, second trimester maternal serum triglycerides positively associated with birth weight and reduced levels of total cholesterol and low – density lipoprotein cholesterol associated with intrauterine growth restriction (Misra *et al.,* 2011).

Other predisposing factors which affect birth weight include socio-economic status, cultural, demographic characteristics, booking body mass index (BMI), pregnancy weight gain and certain behavioural characteristics (Upadhyay *et al.*, 2011).

The concept of "foetal programming" also known as "foetal origin hypothesis" is defined as the programming or influence on pregnancy and foetal outcomes together with the future adult life health and development resulting from the intrauterine environment activities. The concept presupposes that, variations in nutrient supply to the foetus lead to developmental adaptations in which long term changes in structure, physiology and metabolism are observed and which also predispose such individuals to the risk of becoming overweight or obese in adult life (Yu *et al.,* 2013). Most often than not, birth weight is used as an acceptable parameter to indicate intrauterine life experiences such as micro-nutrient deficiencies resulting probably from placental transfer problems or insufficiency, infections like malaria and syphilis as well as maternal malnutrition leading to low birth weight. However, sufficient placental transfer, adequate maternal nutrition and infection free intrauterine environment produce normal birth weight neonates (Amosu and Degun, 2014). It has also been observed that, intrauterine growth restriction is associated with stillbirth and one key method of conducting successful population-based screening to identify foetuses at risk of stillbirth is the use of foetal weight assessment. Increase in birth weight is a recommended strategy

to improve on neonatal mortality in the United States of America (Wilcox, 2001; Moraitis *et al.,* 2014).

Birth weight is known to associate positively with maternal characteristics such as being unmarried, less than 20 years of age, multiple pregnancies, less than 2 years birth spacing, the sex and birth order of the neonates. It is also found to be significantly related with maternal age, height, parity and obesity (Qaiser and Omair, 2016).

4.1.2 Body Length

Unlike birth weight, body length is not a straight forward predictor of neonatal mortality and morbidity. However, body length is a relevant prognostic and aetiologic factor in assessing the quality of intrauterine life and any additional information necessary for monitoring the up keep of the foetus. Body length is also used in diagnosing pathological state as well as body proportion abnormalities including hydrocephalus, microcephalus and achondroplasia (Kierans *et al.,* 2007). Growing in length expresses differential growth of head, trunk and long bones in the lower limbs. Neonatal body length is better identified with the gestational age especially for the growth restricted neonates with chromosomal or congenital Rubella (Qaiser and Omair, 2016).

Body length is found to be influenced by maternal pregnancy weight and occupation. Several studies have found statistically significant association between maternal weight and occupational status with body length but not with other maternal characteristics and associated these observations with adequate maternal nutrition and better antenatal care (Phaneendra *et al.,* 2001; Elshibly and Schmalisch, 2008; Dwivedi and Verma, 2015). Occupational status has been found to relate positively with body length and this could be predictive of the importance of rest in

pregnancy and inadequate maternal nutrition resulting from work place pressures (Casas *et al.,* 2015; Dwivedi and Verma, 2015).

The sex of the neonate has also been reported to influence body length. In one study, it was observed that, male neonates were 100 g heavier and 0.53 cm longer than the female counterparts (Muslimatun *et al.,* 2002). A second study which tracked body size from birth to adolescence after adjusting for gestational age using birth length and weight reported that, every centimetre in birth length corresponded with 0.9 cm height increase in adolescence while a kilogramme weight at birth corresponded with 4 cm increase in height and BMI by 0.5 kg/m^2 at adolescence (Strauss and Dietz, 1998). According to the percentile classifications of birth length and weight in another study, neonates who were short and light at birth were short and light at the adolescent age while long and heavy neonates were found to be tall and heavy at adolescence. Similarly, neonates in the shortest category but had tall parents were found to be tall at adolescence and those who were in the longest percentile group but were born to short parents were also tall at adolescence. The study therefore concluded that, after adjusting for gestational age, birth length becomes predictor of adolescence height and weight but birth weight predicts adolescent weight, height and BMI (Pietiläinen *et al.,* 2001).

These findings seem to support the foetal origin hypothesis which proposes that, favourable (or unfavourable) foetal growth conditions (FFGC) have life-long health consequences for outcomes such as adult blood pressure and diabetes risk. The FFGC is an indirect variable which takes into consideration all the environmental, genetic and epigenetic factors involved in the programming of the foetus *in vivo* (Camerota and Bollen, 2016).

4.1.3 Ponderal Index

At birth, Ponderal index (PI) serves as an estimate of neonatal nutritional status as well as an agent of intrauterine environment that possibly affect gene expression linking associated phenotypes with diseases (Labayen *et al.,* 2011). This index probably is the only neonatal proportionality index that cuts across international boundaries independent of race, sex, birth order and sometimes gestational age (Nili *et al.,* 2003). Ponderal index according to Rohrer's formula is expressed mathematically as:

$$PI = \frac{Birth\ weight\ (g)\ x\ 100}{(birth\ length(cm))^3};$$ (Aderinsola and Joseph, 2007).

Clinicians have over the years expressed concerns about the assessment of foetal nutritional status as this poses various episodes of harmful effects of malnutrition on different organ systems. As a result, different approaches have been used to as early as possible identify foetal malnutrition (Georgieff and Sasanow, 1986). Birth weight to length ratio, ponderal index, placental weight, birth weight /placental weight ratio have been found to relate positively with perinatal mortality and morbidity (Fayyaz, 2005). Indeed, among the different indices of body proportionalities, Rohrer's Ponderal index has been found to be very useful in grouping neonates into proportionate and disproportionate classes. This approach has a number of advantages as it takes into account all information relating to the timing of growth retardation and neonatal nutritional status. Also, it predicts the consequences of small – for – gestational age neonates, especially when information relating to gestation is not reliable (Onyiriuka and Okolo, 2005). Another usefulness of Ponderal index lies in its ability to quantify weight loss as well as sub-categorizing small-for-gestational age neonates on the basis of proportionality of growth restriction into symmetric and asymmetric forms. Symmetric small – for – gestational age has been found to exhibit high risk of developing

more morbidities whereas asymmetric small-for-gestational are known to associate with increased incidence of perinatal mortality (Oluwafemi *et al.,* 2013). Accordingly, PI is categorized into three as low when its value is less than 2.32 g/cm^3; normal when it is between 2.32 to 2.85 g/cm^3 and PI value greater than 2.85 g/cm^3 as high (Aderinsola and Adebami, 2006).

The Ponderal index which is a measure of the relative weight at birth and associates positively with early infancy dietary habit and BMI in later life (Pietilainen *et al.,* 2001). One study in Norway observed that, infants with high PI at birth were exclusively breastfed for a short period and introduced to solid foods earlier than infants with normal PI at birth. The study also found that, high PI infants consumed meat with vegetables/potatoes, yoghurt, commercial baby drink/sweetened squash and higher daily intake of commercial infant porridge. Another finding was that, high PI at birth corresponds with significant increase in BMI at sixth to twelfth months of neonatal growth. These findings from the study could be a guide of what parents of high PI infants would expect in terms of exclusive breastfeeding and time and type of complimentary foods to be introduced (Lande *et al.,* 2005).

In fact, the use of PI to identify varied patterns of growth retardation has huge clinical and epidemiological significance as this brings to bear the dangers associated with disproportionate intrauterine growth retarded infants than proportionate infants. Also, disproportionate growth retarded infants after birth experience early extreme increase in weight gain, body length and head circumference which indicate the potentiality to match the growth of their normal counterparts. These not only influence their treatment at the hospital, but also necessitate their postnatal follow-ups (Onyiriuka and Okolo, 2005).

4.1.4 Abdominal and Head Circumferences

The abdominal and head circumferences are among the routine measurements performed at the obstetric and neonatal units in hospitals. The relevance of abdominal circumference measurement lies in its ability to project the size of abdominal viscera in healthy neonates and to ascertain any pathological state in the abdominal cavity (Meldere *et al.,* 2015). Head circumference measurement on the other hand is a global tool for monitoring the growth and development of neonatal brains. Head circumference measuring more than 2 standard deviation scores either above or below a reference population value relative to the age and sex is considered an abnormality and is described as macrocephaly or microcephaly respectively (Geraedts *et al.,* 2011).

In broader context, these anthropometric parameters are applied in the clinical assessment of physical development. Abdominal circumference is known to be affected by factors such as resistance offered by the anterior abdominal wall, time of feeding and defecation, breathing phase and fat deposition (Meldere *et al.,* 2015).

4.2 AIM AND SPECIFIC OBJECTIVES

4.2.1 Aim

To establish a mathematical model that predicts neonatal outcome using maternal booking biometric indices.

4.2.2 Specific Objectives

- To determine the mean values of maternal booking biometric indices and neonatal anthropometry.
- To investigate correlations between maternal booking biometric and neonatal anthropometric indices.
- To develop mathematical models for the relationship between maternal booking biometric and neonatal anthropometric parameters.

4.3 MATERIALS AND METHODS

4.3.1 Study Design and Area

An analytical descriptive cross sectional study was conducted on 240 pregnant women who attended antenatal care (ANC) at the Victory Maternity Home and Clinic in the Kumasi Metropolis, between March 2014 and October 2018.

4.3.2 Inclusion and Exclusion Criteria

Included in this study were pregnant women who consented to the collection of their fasting blood samples, gave to singleton live births without pregnancy or delivery complications and whose neonates anthropometric records were complete.

Excluded in the study were pregnant women who gave multiple births, had pregnancy or delivery complications; whose neonates‘ anthropometric records were incomplete.

4.3.3 Study Variables

Neonatal anthropometry including birth weight, body length, head and abdominal circumferences were measured with support from a trained nurse within 24 hours after delivery. Maternal booking biometric indices including; total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL-C), low density lipoprotein (LDL-C), systolic and diastolic blood pressures were taken on their first ANC visit.

Birth weight was measured using a Salter spring balance (Salter Abbey, Suffolk, UK) with the baby being naked. Body length was measured using Harpenden infantometer with the baby in a relatively quiet position. The occipito-frontal head circumference and abdominal circumference were measured at the level of umbilicus during expiration using a flexible non-elastic tape measure.

The maternal fasting blood samples were analysed using standard enzymatic kits for the following: total cholesterol (TC), triglyceride (TG) and high density lipoprotein (HDL-C) on Automated Chemistry Analyzer (Flexor junior, Vital Scientific N.V., The Netherland) with reagents from ELITech Group company, (SEPPIM S.A.S, France). Low density lipoprotein cholesterol (LDL-C) was estimated using the Friedewald equation incorporated in the auto – analyzer.

4.3.4 Statistical Analysis

The present study used multivariate analysis of variance (MANOVA) to model association between maternal booking biometric and foetal anthropometric indices.

First, cross correlations were performed to establish relationships within and between the neonatal and maternal data sets. The models were developed using step by step approach of multivariate

analysis of variance. Here, four foetal indices were modelled jointly with six predictors of maternal biometric indices using multivariate test (Type II MANOVA): p – value < 0.05 was considered statistically significance. The final refitted model was assessed using Type II MANOVA, Pillai's test statistics. The model was presented with coefficients, standard error (SE), value and model – value for each predictor. In this study, all statistical analyses were performed with IBM SPSS Version 22.0 (SPSS Inc., Chicago, IL).

4.4 RESULTS

4.4.1 Neonatal and Maternal Descriptive Characteristics

The descriptive statistics of neonatal indices is shown in Table 11 below. The mean values of the neonatal indices were: birth weight 3.17 ± 0.48 kg (range: 1.20 – 4.00 kg). Mean body length was 40.95 ± 7.38 cm (range: 14.20 –55.00 cm). Head and abdominal circumferences respectively had mean values and ranges of 32.13 ± 5.57cm (range: 12.20 –55.00 cm) and 32.57 ± 5.07 cm (range: 11.00 – 46. 00 cm).

Table 11: Descriptive Statistics of Neonatal Indices

Variable	Mean ± SD	Range
BW (kg)	3.17 ± 0.48	1.20 – 4.00
BL (cm)	40.95 ± 7.38	14.20 – 54.00
HC (cm)	32.13 ± 5.57	12.20 – 55.00
AC (cm)	32.57 ± 5.07	11.00 – 46.00

BW= birth weight, BL = body length, HC = head circumference, AC = abdominal circumference; SD = standard deviation, cm = centimeter, kg = kilogramme

Table 12 shows the mean values and ranges of maternal characteristics of the 240 mothers who consented to the lipid profile test. The mean age of the mothers was 27.21 ± 6.01years ranging from 15 to 42 years. Mean parity was 2.65 ± 1.56 and ranged from 1 – 8 children. The mean Gestational age was 36.40 ± 2.03, with range (30 – 42 weeks). Mean maternal weight was 66.70 ± 11.27 kg with a range of 37 – 95 kg and mean height was 1.60 ± 0.08m ranging from 1.20 to 1.80 m. The mean BMI was 25.89 ± 4.47 kg/m^2, with range (14.81 – 41.42) kg/m^2. The systolic blood pressure had mean of 119.29 ± 28.10 mmHg and ranged from 90 – 250 mmHg. Mean diastolic blood pressure and its range were respectively 73.84 ± 13.65 mmHg and 50 – 120 mmHg. The mean value of the concentration of TC, TG, HDL-C and LDL-C according to maternal lipid profile was 4.03 ± 1.10 mmol/L; 1.48 ± 0.77 mmol/L; 1.11 ± 0.47 mmol/L and 2.24 ± 0.84 mmol/L respectively.

Table 12: Descriptive Statistics of maternal Characteristics

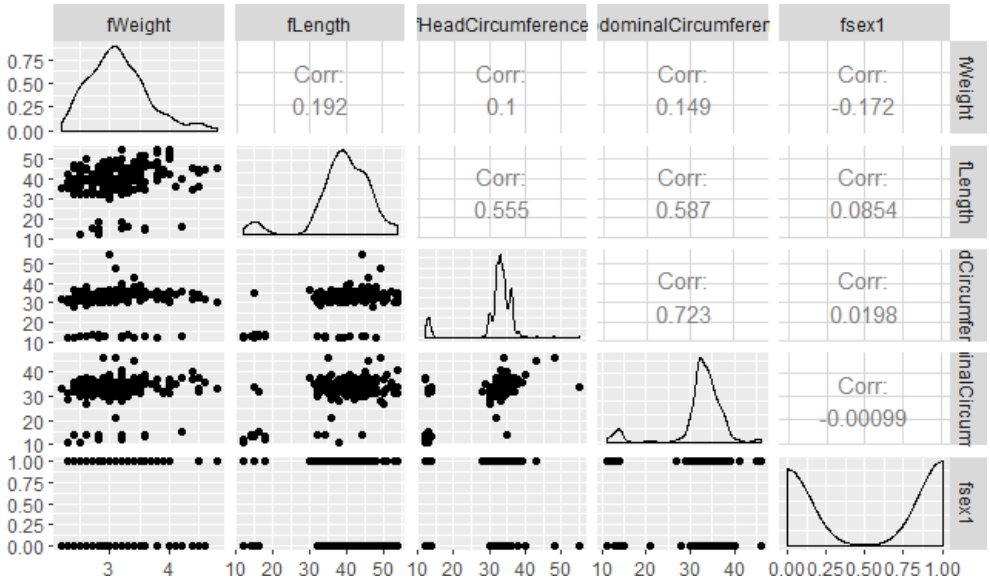
Characteristics	Mean ± SD	Range
Age (years)	27.21 ± 6.01	15 – 42
Parity	2.65 ± 1.56	1 – 8
GA (weeks)	36.40 ± 2.03	30 – 42
MWt (kg)	66.70 ± 11.27	37 – 95
MHt (m)	1.60 ± 0.08	1.20 – 1.80
BMI (kg/m^2)	25.89 ± 4.47	14.81 – 41.42
SBP (mmHg)	119.29 ± 28.31	90 – 250
DBP (mmHg)	73.84 ± 13.65	50 – 120
TC (mmol/L)	4.03 ± 1.10	1.40 – 9.15
TG (mmol/L)	1.48 ± 0.77	0.38 – 6.92
HDL-C (mmol/L)	1.11 ± 0.47	0.05 – 2.98
LDL-C (mmol/L)	2.24 ± 0.84	0.36 – 5.68

GA = gestational age, MWt = maternal weight, MHt = maternal height, BMI = body mass index, SBP = systolic blood pressure, DBS = diastolic blood pressure, TC = total cholesterol, TG = triglycerides, HDL-C = high density lipoprotein, LDL-C = low density lipoprotein, kg = kilogramme, m = metre, mmHg = mllimetre mercury, mmol/L =

millimole per litre, kg/m^2 = kilometer per metre square.

4.4.2 Pearson correlation between Neonatal Anthropometric and Maternal booking Biometric Indices

Correlation structure within the anthropometric indices of the neonates observed strong positive correlations as presented in Figure 5. Head circumference and body length showed a moderate positive correlation with coefficient of 0.555. Also, abdominal circumference and body length showed moderate correlation with coefficient of 0.587 while head and abdominal circumferences correlated positively with coefficient of 0.723. However, birth weight and neonatal sex showed weak correlations with other neonatal indices.

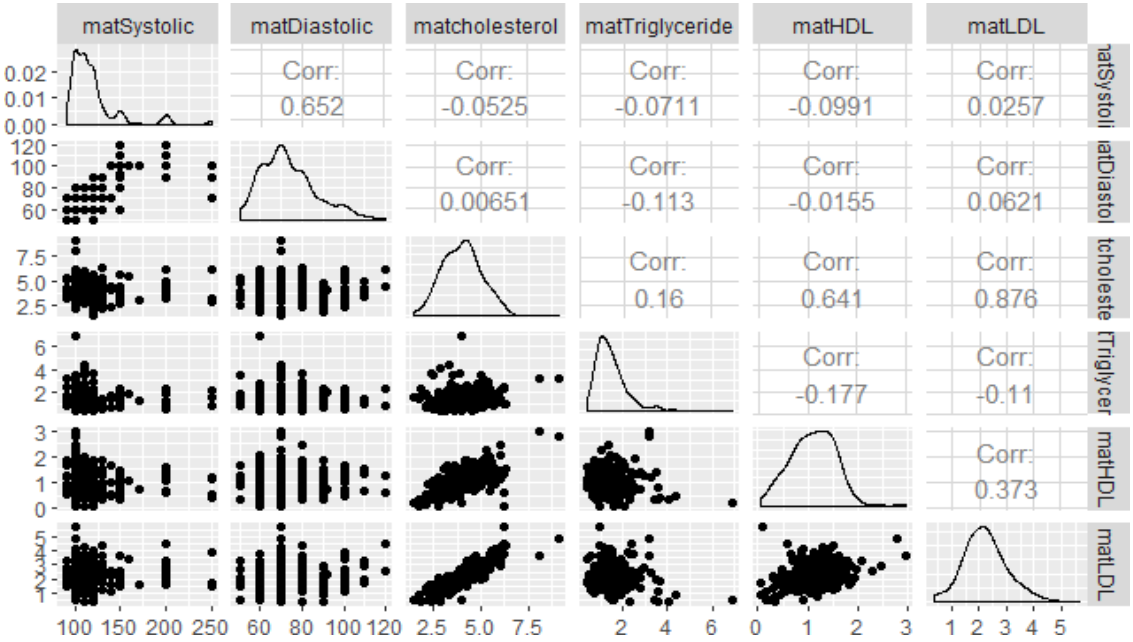


fWeight = birth weight, fLength = Neonatal body length, dCircumfer = neonatal head circumference, finalCircum = neonatal abdominal circumference, fsex1 = neonatal sex

Figure 5: Pearson Correlation Structure for Foetal Indices

Figure 6 below illustrates the correlation structure of maternal biometric indices. Strong correlations within the indices are depicted by the correlation coefficients (r). There was a strong positive correlation between systolic and diastolic blood pressures with coefficient of r = 0.652.

A weak negative correlation was observed between diastolic blood pressure and total cholesterol (r = - 0.113). The correlation found between triglycerides and total cholesterol was weak but positive (r = 0.160). Correlations between HDL-C and LDL-C with total cholesterol were moderate (r = 0.641) and strong (r = 0.876) respectively. However, triglyceride showed weak negative correlations with both HDL-C and LDL-C in the order of r = -0.117 and -0.110, while correlation between HDL-C and LDL-C was positive with r = 0.373.



matSystolic = Maternal booking systolic blood pressure, matDiastolic = Maternal booking diastolic blood pressure matcholesterol = Maternal booking total cholesterol, matTriglyceride = Maternal booking triglyceride, matHDL = Maternal booking high density lipoprotein, matLDL = Maternal booking low density lipoprotein

Figure 6: Pearson Correlation Structure for Maternal Biometric Indices

In Table 13, maternal booking biometric indices were cross correlated with foetal parameters. The Pearson's cross correlation revealed weak relationship between maternal biometric indices and foetal parameters. Maternal booking diastolic blood pressure and HDL-C showed positive relationship with all neonatal indices, although these relations were weak. Both booking total

cholesterol and LDL-C exhibited weak negative relations with neonatal birth weight, body length and sex, but related positively with head and abdominal circumferences. Also, booking systolic blood pressure and triglyceride related negatively with birth weight, head and abdominal circumferences while positively relating with body length.

Table 13: Cross Correlation between Maternal Biometric Parameters and Neonatal Indices

Variable	MSBP	MDBP	MTC	MTG	MHDL-C	MLDL-C
BW	-0.007	0.035	-0.047	-0.067	0.032	-0.06
BL	0.109	0.069	-0.005	0.031	0.015	-0.039
HC	0.052	0.094	0.037	-0.117	0.171	0.002
AC	-0.039	0.037	0.083	-0.057	0.138	0.060

BW = body weight, BL = body length, HC = head circumference, AC = abdominal circumference, MSBP = maternal systolic pressure, MDBP = maternal diastolic pressure, MTC = maternal total cholesterol, MTG = maternal triglyceride, MHDL-C = maternal high density lipoprotein, MLDL-C = maternal low density lipoprotein.

4.4.3 Neonatal Anthropometric and Maternal booking Biometric Indices Modelling

With regards to the four models fitted, none of the maternal biometric parameters was significant; as all the models fitted had p – value > 0.05 as shown in Table 14 below. However, the multivariate regression model for neonatal weight, length, head and abdominal circumferences could respectively be represented as:

$$\mathbf{y_{weight} = 3.173 - 0.001M_{systolic} - 0.002M_{diastolic} + 0.119MT_C - 0.094MT_G - 0.060M_{HDL\text{-}C} - 0.170M_{LDL\text{-}C}}$$

$$\mathbf{y_{length} = 34.280 + 0.035M_{systolic} - 0.002M_{diastolic} + 3.230MT_C - 1.011MT_G - 2.141M_{HDL\text{-}C} - 3.756M_{LDL\text{-}C}}$$

$$\mathbf{y_{HCir.} = 27.853 + 0.003M_{systolic} + 0.040M_{diastolic} + 0.300MT_C - 0.846MT_G + 2.375M_{HDL\text{-}C} - 0.964M_{LDL\text{-}C}}$$

$$\mathbf{y_{ACir.} = 30.192 - 0.019M_{systolic} + 0.041M_{diastolic} - 0.774MT_C + 0.112MT_G + 2.278M_{HDL\text{-}C} + 0.825M_{LDL\text{-}C}}$$

where;

y_{weight} is the predicted neonatal birth weight, y_{length} is the predicted neonatal body length, $y_{HCir.}$ and $y_{ACir.}$ are the predicted neonatal head and abdominal circumferences respectively.

$M_{systolic}$ and $M_{diastolic}$ are the maternal systolic and diastolic blood pressures respectively.

MT_C is maternal total cholesterol; MT_G is maternal Triglyceride, M_{HDL-C} is the maternal high density lipoprotein and M_{LDL-C} is maternal low density lipoprotein.

Table 14: Multivariate regression Analyses between Neonatal and Maternal booking Biometric Indices

Neonatal Response Variable	Maternal Predictive Variables	Standard Coefficients	Standard Error	t-value	Model p-value
BW	*Intercept*	3.173	0.222	14.28	<0.0001
	Msystolic	-0.001	0.002	-0.49	0.624
	Mdiastolic	0.002	0.003	0.721	0.472
	Mtcholesterol	0.119	0.201	0.592	0.554
	Mttriglyceride	-0.094	0.100	-0.945	0.345
	MHDL-C	-0.060	0.206	-0.292	0.770
	MLDL-C	-0.170	0.203	-0.840	0.402
BL	*Intercept*	34.280	0.222	9.528	<0.0001
	Msystolic	0.035	0.024	1.462	0.145
	Mdiastolic	-0.002	0.050	-0.034	0.973
	Mtcholesterol	3.230	3.246	0.995	0.321
	Mttriglyceride	-1.011	1.615	-0.626	0.532
	MHDL-C	-2.140	3.328	-0.643	0.521
	MLDL-C	-3.756	3.282	-1.144	0.254
HC	*Intercept*	27.853	2.932	9.499	<0.0001
	Msystolic	0.003	0.020	0.164	0.870
	Mdiastolic	0.040	0.040	0.997	0.320
	Mtcholesterol	0.310	2.646	0.117	0.907
	Mttriglyceride	-0.846	1.316	-0.643	0.521
	MHDL-C	2.375	2.712	0.876	0.382
	MLDL-C	-0.964	2.674	-0.360	0.719
AC	*Intercept*	30.192	2.676	11.284	<0.0001
	Msystolic	-0.019	0.018	-1.081	0.281
	Mdiastolic	0.041	0.037	1.121	0.263
	Mtcholesterol	-0.774	2.414	-0.321	0.749
	Mttriglyceride	0.112	1.201	0.094	0.926
	MHDL-C	2.278	2.475	0.920	0.358
	MLDL-C	0.825	2.440	0.338	0.736

BWt = birth weight, BL = body length, HC = neonatal head circumference, AC = abdominal circumference, Msystolic = maternal systolic blood pressure, Mdiastolic = maternal diastolic blood pressure, Mtcholesterol = maternal total cholesterol, Mttriglyceride = maternal triglyceride, MHDL-C = maternal high density lipoprotein, MLDL-C = maternal low density lipoprotein.

With the results of multivariate regression analysis showing the relationships, it became necessary to perform a Type II MANOVA test – Pillai's test statistic to reveal differences not discovered by the individual regressions. From Table 15, maternal systolic blood pressure was shown to be jointly statistically significant in at least the four models irrespective of what was observed in Table 14. This implies that, among the six maternal biometric predictors, it was only systolic blood pressure that had influence on the neonatal response variables.

Table 15: Type II MANOVA Tests: Pillai's test statistic of Maternal Biometric and Foetal Indices

Characteristic	Df	test stat	approx F	num Df	den Df	Pr(>F)
Msystolic	1	0.037376	2.29083	4	236	0.04941
Mdiastolic	1	0.011659	0.69600	4	236	0.59539
Mtcholesterol	1	0.010661	0.63576	4	236	0.63746
Mttriglyceride	1	0.009595	0.57159	4	236	0.68351
MHDL-C	1	0.014853	0.88956	4	236	0.47083
MLDL-C	1	0.015416	0.92377	4	236	0.45076

Msystolic = maternal systolic blood pressure, Mdistolic = maternal diastolic blood pressure, Mtcholesterol = maternal total cholesterol, Mttriglyceride = maternal triglyceride, MHDL-C = maternal high density lipoprotein, MLDL-C = maternal low density lipoprotein, Df = degree of freedom, test stat = test statistic, approx. F = approximation based on F – distribution, num Df = numerator degree of freedom, den Df = denominator degree of freedom, Pr(> F) = Significance level of F-ratio

In a post hoc manner, the models were refitted to establish mathematical function(s) which distinguish the maternal explanatory variables from one another on the neonatal response variables. Table 16 below shows the results of refitted models in which it was observed that, systolic blood pressure significantly predicted neonatal body length. Therefore the equation means that, for every

1 standard deviation increase in booking systolic blood pressure, body length is predicted to increase by 0.03 standard deviation if all other variables remain constant. However, no changes in the remaining maternal biometric indices could significantly result in changes in other neonatal response variables. Given the results in Table 16, the modelled function for calculating body length could therefore be expressed as:

$\mathbf{Y_{length} = 35.385 + 0.031M_{systolic}}$, ($p = 0.0341$). Where Y_{length} is the neonatal body length and $M_{systolic}$ is the maternal systolic blood pressure.

Table 16: Refitted Models between Maternal Systolic Blood Pressure and Foetal Indices

Neonatal Response Variable	Maternal Predictive Variables	Standard Coefficient	Standard Error	t-value	Model p-value
BW	*Intercept*	3.154	0.136	23.25	<0.0001
	Msystolic	-0.001	0.001	-0.110	0.912
BL	*Intercept*	35.385	2.191	16.152	<0.0001
	Msystolic	0.031	0.011	2.702	0.0341
HC	*Intercept*	30.219	1.821	16.596	<0.0001
	Msystolic	0.012	0.015	0.821	0.412
AC	*Intercept*	33.332	1.642	20.303	<0.0001
	Msystolic	-0.008	0.013	-0.602	0.548

BW = birth weight, BL = body length, HC = head circumference, AC = abdominal circumference, Msystolic = maternal systolic blood pressure, t-value = test value, p-value = significance level

4.5 DISCUSSION

4.5.1 Neonatal and Maternal Descriptive Statistics

The mean values of birth weight, body length, head and abdominal circumferences observed in the current study were slightly lower than the values reported by the International Foetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH – 21ST) project, which established for routine clinical practice and accurate estimation of prevalence of small-for-age babies across the world, an international anthropometric standards to closely relate clinical and population assessment of foetuses, neonatal babies and infants. The INTERGROWTH – 21ST reference mean values recorded were 3.3 ± 0.5 kg for birth weight, 49.3 ± 1.8 cm for body length and 33.9 ± 1.3 cm for head circumference and have been adopted by over 125 countries worldwide including Ghana (Villar *et al.*, 2014). The slight changes in mean anthropometric values observed between the present study and the INTERGROWTH – 21ST project, although not statistically significant. The differences could be attributed to the different sample sizes, methodological limitations and diet pattern of study participants in both studies.

Similar studies in the Kumasi Metropolis have recorded birth weights of 3.07 ± 0.51 kg, 3.23 ± 0.47 kg and 3.24 ± 0.51 kg with head circumferences of 34.43 ± 2.97 cm, 32.90 ± 2.89 cm and 34.27 ± 1.95 cm while body lengths were; 48.79 ± 2.70 cm, 45.11 ± 4.56 cm and 50.64 ± 3.43 cm. These mean neonatal anthropometric values of current study and the previous studies slightly vary but are not significantly different. The anthropometric parameters of the neonate can serve several purposes for the clinician, as these can be used in assessing physical, neurological and mental state of the neonate. These parameters are also cost-effective and easy to obtain (Appiah, 2009; Bimpong, 2012; Tetteh, 2015; Bimpong *et al.*, 2019).

The mean of maternal age, parity and BMI recorded by the present study are similar to the finding of a study conducted by Ephraim *et al.* (2014) in the Cape Coast Municipality which observed mean maternal age of 28.0 ± 5.2 years, parity of 1.60 ± 1.3 and BMI of 27.0 ± 2.1 kg/m^2 among the control groups. An earlier study at Victory Maternity Home and Clinic also recorded maternal age of 27.14 ± 5.95 years, weight of 63.12 ± 8.61 kg, parity of 2.68 ± 1.71 (Bimpong, 2012). The studied mean booking BMI indicates that, the mothers were overweight and could experience a total weight gain of 11.5 – 16.0 kg.

These maternal anthropometric indices clearly reflect in maternal nutritional status which determines nutrient availability to the foeto-placental unit. The influences of these anthropometric indices are exhibited when expressed at the lower or higher levels. Mosha and Napendaeli (2010) reported maternal age range of 20 – 35 years as appropriate for giving birth without any obstetric related problems. However, below or above of this range, could result adverse perinatal outcomes. This mean weight also presupposes that, more mothers enter into pregnancy already overweight (WHO, 2000; Addo, 2010; Ephraim *et al.,* 2014). The mean booking weight in this current study is also higher than the cut-off point of less than 40 kg, below which the mothers are three times susceptible to delivering a low birth weight neonate relative to mothers with booking weight greater than 40 kg (Nahar *et al.,* 2005). These measured maternal variables though showed differences in values when compared with other studies; they however, did not vary significantly among the populations in these studies.

The height recorded in the present study is well above the various height cut – off points reported to predict or associate with adverse pregnancy outcomes which included a range of 150 – 153 cm in Ghana (Kwawukume *et al.,* 1993), < 155 cm in Burkina Faso (Sokal *et al.,* 1991), < 156 cm in Denmark (Kappel *et al,* 1987), ≤ 150 cm in Kenya (Mati, 1983), <146 cm in Tanzania (Essex,

1977), < 140 cm in India (Bhatt *et al.,* 1967), < 160 cm in Zimbabwe (Tsu, 1992) and ≤ 157 cm in the United States of America (Witter *et al.,* 1995). The mean maternal height observed in the present study is higher than the World Health Organization's recommended reference of 145 cm which defines whether a person's stature is short or not (Rudman *et al.,* 1998). These observations imply that, maternal height in the current study is normal and not short statured. Maternal height as an essential anthropometric index indicates status of maternal health and nutrition from infancy and is influenced by the individual's genetic history (Kotingo *et al.,* 2015).

The booking lipid measurements in this study were found to be within the normal reference ranges. Also, these mean values were closer to the upper limits of the recommended lipid concentration levels for non-pregnant women which indicate the initiation of rising level of lipids as pregnancy commences (Geraghty *et al.,* 2016).

Generally, the importance of high levels of maternal circulating lipids during pregnancy is seen in the: high cellular proliferation leading to uterine enlargement, blood volume expansion, implantation of the foetus, blood vessel formation in the utero-placental region and healthier foeto-placental growth and development (Omorogiuwa and Ozor, 2015). The determination of maternal booking blood lipid levels may serve as a guide in predicting the health status of the mother, foetus and placenta as pregnancy progresses.

The elevated booking cholesterol and triglyceride levels could indicate risk of developing gestational diabetes. An elevated level of HDL-C may play a protective function for the maternal vascular endothelium in the course of pregnancy. Increased level of high density lipoprotein facilitates the transport of total cholesterol across the placenta (Geraghty *et al.,* 2016). It has been observed that, booking lipid levels relate to having a single lifetime pregnancy and that, women having higher than normal levels of TG, LDL-C and lower than normal level of HDL-C before

conception are at high risk of conceiving only once in their lifetime. Similarly, higher booking levels of LDL-C and TC could associate with not having pregnancy at all (Pirnat *et al.,* 2018). This could stem from the fact that, high levels of maternal circulating lipids are indications of potential development of coronary artery disease which is very detrimental to pregnancy development and foetal health.

The systolic and diastolic blood pressures recorded in the present study were similar to 120.1 ± 11.3 mmHg and 77.2 ± 10.1 mmHg, observed in a study conducted in Nigeria (Omorogiuwa and Ozor, 2015). An initial high booking BMI observed at the first antenatal visit has been associated with increased risks of pregnancy hypertensive disorders while entering into pregnancy with overweight or obese BMI classification has between three to five fold higher risk of developing preeclampsia. Also, the effect exerted by booking BMI on the rising levels of systolic and diastolic blood pressures continues throughout pregnancy (Savitri *et al.,* 2016). However, rising levels of systolic and diastolic blood pressure together with higher booking BMI in the first and third trimesters of pregnancy have been reported in a Brazilian cohort study on the blood pressure variations throughout pregnancy according to early gestational BMI, which found mean systolic blood pressure values of 109.7 mmHg (95% CI = 108.4 – 111.1 mmHg), 107.8 mmHg (95% CI = 106.4 – 109.2 mmHg), 111.0 mmHg (95% CI = 109.5 – 112.5 mmHg) for first, second and third trimesters respectively. The corresponding mean diastolic blood pressure values for the first, second and third trimesters were respectively 66.7 mmHg (95% CI = 65.6 – 67.8 mmHg), 64.4 mmHg (95% CI = 63.3 – 65.4 mmHg) and 67.0 mmHg (95% CI = 65.8 – 68.1 mmHg) (Rebelo *et al.,* 2015). The linkage between booking BMI and the increasing levels of systolic and diastolic blood pressures with increasing gestation is seen in two ways; first, higher booking BMI is associated with increased maternal abdominal adiposity which in turn influences cardiovascular

risks. Secondly, the pregnancy itself enhances secretion of relaxin which through upregulation of matrix metalloproteinases and tissue inhibitors of metalloproteinases remodels or softens vessel collagens to vary the compliance and capacitance of the vessel walls (Savitri *et al.*, 2016; Ngene and Moodley, 2019).

This supposes that, mothers included in the current study were not chronic hypertensive which otherwise could have affected the outcome of their pregnancies. Notwithstanding, since the mean BMI for the mothers of the present study fell within overweight category, there is the potential of systolic and diastolic blood pressures also increasing as the gestation progresses.

4.5.2 Pearson's correlations between maternal booking biometric indices and neonatal anthropometric parameters

Pearson correlation performed among the neonatal anthropometric parameters in the present study observed strong positive association between neonatal body length with head and abdominal circumferences. There was also strong correlation between head circumference and abdominal circumference. However, birth weight in the current study showed weak correlation with body length, head and abdominal circumferences. The strong positive correlation between body length and body circumference observed is in line with Qaiser and Omair (2016) definition of body length as an expression of differential growth in head, trunk and long bones in the leg. This implies that, increase in body length results in corresponding increase in head circumference and long bones of the leg. The weak correlation between birth weight and other anthropometric indices in this study is in agreement with similar observation in which the Pearson's correlation coefficient of birth weight exhibited weak relationship with other neonatal anthropometric indices (Pankaj and Kanchan, 2017). In following up the body size from birth to adolescence, it was found that, body

length exhibited strong positive correlation with adolescent height and weight while birth weight correlated with adolescent height, weight and BMI (Strauss and Dietz, 1998; Pietiläinen *et al.*, 2001). These results are clear indications that, the strength of neonatal anthropometric indices varies in correlating with one another.

Pearson's correlation among maternal booking biometric indices in the current study showed that, there was strong positive relationship between maternal systolic and diastolic blood pressures. However, the systolic blood pressure exhibited negative weak correlation with maternal total cholesterol, triglyceride and high density lipoproteins (HDL-C) but was positive with the low density lipoproteins (LDL-C). The diastolic blood pressure also showed weak negative correlation with triglycerides and high density lipoproteins but positive relationship with total cholesterol and low density lipoproteins. The correlations observed for the total cholesterol with HDL-C and LDL-C were strong and positive but weak with triglycerides. Triglyceride showed weak negative relationship with HDL-C and LDL-C. Correlation between HDL-C and LDL-C was positive. The observed association between total cholesterol and LDL-C as well as HDL-C is physiologically accepted. This is because, the LDL-C facilitates the supply of total cholesterol to cells with LDL-C receptors. In fact, the amount of total cholesterol freed by the LDL-C is said to regulate cholesterol metabolism. This is because, elevated levels of LDL-C in the cell result in:

1. reduction in the synthesis of 3 – hydroxyl – 3 – methylglutaryl coenzyme A reductase which modulates the intracellular synthesis of cholesterol,
2. enhanced storage of cholesterol within the cell by activating other enzymes and
3. reduced level of synthesis of LDL-C receptors by the negative feedback mechanism (Cox and García-Palmieri, 1990).

In this regard, TC and LDL-C are always strongly and directly related, leading to increased risk of coronary heart disease (CHD). Also, increased level of HDL-C has been found to serve as a cardio-protective factor to the development of coronary heart diseases. Therefore, decreasing levels of HDL-C with increased TC and LDL-C could be very risky. The weak association of TG with other lipids is ideal as elevated level of TG is linked to the development of atherosclerotic heart disease (Cox and García-Palmieri, 1990). It could therefore be speculated that, elevated levels of TC, LDL-C and HDL-C and reduced level of TG at the start of pregnancy can be regarded as useful to the developing pregnancy.

The maternal booking biometric indices and neonatal anthropometric indices were cross correlated; the observations were weak correlations between biometric and neonatal anthropometric indices whose correlation coefficients ranged from 0.109 to 0.171. Maternal booking systolic blood pressure showed weak positive relationship with neonatal body length while the HDL-C weakly correlated positively with all neonatal anthropometric parameters. Triglyceride exhibited weak negative correlation with neonatal head circumference. Booking diastolic blood pressure, total cholesterol and LDL-C showed very weak correlations with the neonatal anthropometric parameters with correlation coefficients ranging from 0.002 to 0.094. In this case, both total cholesterol and LDL-C showed negative relationship with the neonatal birth weight and body length but positively correlated with head and abdominal circumferences. These observations of the present study contradicted the findings of Clausen *et al.* (2005) which reported positive correlation of first trimester triglycerides with birth weight and a negative correlation between HDL-C and birth weight. Also, a negative correlation of HDL – C with birth weight, body length and chest circumference and a positive relationship of TG and LDL – C with body length, head and abdominal circumferences except birth weight have been reported (Mitra *et al.*,

2012). Another study observed positive correlation of first antenatal visit triglyceride level with birth weight, head and shoulder circumferences while head circumference has been found to correlate negatively with LDL – C. Neonatal body length here showed no significant correlation with any of the maternal circulating lipids (Liu *et al.*, 2016).

4.5.3 Maternal booking Biometric Indices and Neonatal Anthropometric Indices Modelling

This current study used multivariate analysis of variance (MANOVA) modeling to examine possible influence of maternal booking biometric indices (systolic and diastolic blood pressures, TC, TG, HDL-C, LDL-C) on neonatal anthropometric parameters (birth weight, body length, head and abdominal circumferences). The first phase consisted of analyzing individually four neonatal indices (birth weight, body length, head and abdominal circumferences) which constituted the response variable against the six maternal booking biometric parameters (explanatory variables) using multivariate regression as shown in Table 12. The basic multiple regression model containing standard partial regression coefficients in predicting the corresponding outcome of the response variable is expressed by:

$\hat{\boldsymbol{\gamma}} = \hat{\boldsymbol{\beta}}0 + \hat{\boldsymbol{\beta}}1x1 + \hat{\boldsymbol{\beta}}2x2 + \hat{\boldsymbol{\beta}}3x3 + ……..+\hat{\boldsymbol{\beta}}kxk.$, where ;$\hat{y}$ is the predicted response variable. $\hat{\beta}1$'s are the estimated regression coefficients, $\hat{\beta}0$ is the intercept when all of the explanatory variables are equal to zero xi (i = 1, ……k) is the estimated explanatory variable. is the estimated explanatory variable. Thereafter, other models were developed using Pillai's test statistics, in which it was found that, booking systolic blood pressure appeared to be jointly significant in at least the four models. This implies that, among the six maternal predictors, booking systolic blood pressure seemed to have influence on the neonatal response variables. Following this observation, he models were refitted to obtain relationship between the systolic blood pressure

and the specific neonatal response which was found to be the body length ($p < 0.05$). From the current study findings, an average of one unit increase in maternal systolic blood pressure leads to 0.03 unit increase in neonatal body length. This finding is contrary to the "Growing Up in Singapore Towards Healthy Outcomes" (GUSTO) study which reported an inverse relationship between central systolic blood pressure and neonatal birth parameters after adjusting for maternal and neonatal covariates. The GUSTO study observed that, 1 – SD increase in central systolic blood pressure resulted in a decrease of 40.52 g in birth weight, 0.19 cm in body length, 0.12 cm in head circumference and 11.16 g in placental weight , but did not find same for the peripheral systolic blood pressure except birth weight (Lim et al., 2014). A similar study conducted among residence in Salisbury hospital district also observed inverse association of systolic blood pressure with head circumference and body length, and reported that, 1 - SD decrease in head to length ratio resulted in an increase of 1.2 mmHg in systolic blood pressure. In relating systolic blood pressure to birth weight and body length through ponderal index, it was found that, systolic blood pressure decreased as ponderal index increased and that, 1-SD increase in ponderal index was associated with 1.1 mmHg decrease in systolic blood pressure (Law et al., 1991). The conflicting results between the present and other studies could arise from the conditions surrounding the collection of systolic blood pressure information. Whereas in this current study, the systolic blood pressure information were taken under clinical setting according to standard protocol, in the other studies systolic blood information were taken by field investigators. In the present study, blood pressures were measured using standard mercury sphygmomanometer while other studies used automated oscillometric and Spacelab devices. The varying use of different blood pressure devices which are likely to generate different Korotkoff phases could also be responsible for these varied results (Lim et al., 2014). One cannot rule out

the contribution of differences in race, socioeconomic, geographical and healthcare of study populations in the observed varied results.

4.6 CONCLUSION

The anthropometric parameters of neonates at birth and that of their mothers were found to be in the normal reference ranges, but not statistically significant when compared with other studies and internationally documented standards.

Strong positive correlations were observed between neonatal body length, head and abdominal circumferences. Maternal diastolic and systolic blood pressures strongly correlated but showed weak negative association with TG and HDL-C and positively with LDL-C.

A weak but positive correlation was observed between systolic blood pressure and neonatal body length and head circumference. However, negative relationship was observed between systolic blood pressure and birth weight. HDL-C and diastolic blood pressure correlated positively with all neonatal anthropometric parameters, although the relationships were weak. TC and LDL-C negatively correlated with birth weight and body length and related positively with head and abdominal circumferences. TG showed positive relationship with body length and related negatively with birth weight, head and abdominal circumferences.

Although other maternal booking biometric indices related with neonatal anthropometry, it was systolic blood pressure that was found to be significantly related with body length at birth, and that, a unit increase in systolic blood pressure leads to 0.031 cm increase in body length.

CHAPTER FIVE

MODELLING OF MATERNAL BOOKING BIOMETRIC PARAMETERS WITH PLACENTAL AND UMBILICAL CORD INDICES

5.1 LITERATURE REVIEW

5.1.1 Maternal Booking Visit Biometry

Normal pregnancy is characterized by rising levels of maternal serum total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglyceride (TG) (Sales *et al.,* 2015). Physiologically, cholesterol is an essential structural component of plasma membranes, modulates metabolism and serves as a precursors for steroid hormones. Cholesterol is delivered to the materno-foetal transport system via LDL receptors across the placental border to support foetal growth and development through activation and propagation of hedgehog signalling (Zhang *et al.,* 2017). The transfer of cholesterol from maternal LDL and HDL across the placenta requires the use of LDL receptors and scavenger receptor B1 (SR-B1) respectively and reaches the foetal HDL by the use of ATP binding cassette (ABC) G1 and ABCA1 (Huda *et al*., 2009).

The flowing out of cholesterol from the apical side (maternal end) of the placenta proceeds through three common routes. The first one occurs down a concentration gradient to phospholipid or HDL using processes independent of proteins. The second involves the use of scavenger receptor class B type 1 (SR-B1) to mediate the flow of cholesterol down a concentration gradient to phospholipid disc or HDL, and thirdly, cholesterol can flow to lipid – deficient apolipoproteins through ATP- binding cassette transporter A1 (ABCA1). These three

effluxes are made possible by the presence of SR-B1 and ABCA1 in the placenta (Woollett, 2005).

Low or high maternal serum cholesterol concentrations during pregnancy are known to associate with certain disease states or conditions. For instance, pregnant women with abetalipoproteinaemia, hypobetalipoproteinaemia or those who take in low cholesterol diet possess extreme to moderate low plasma cholesterol concentrations during pregnancy. Similarly, women with high maternal circulating cholesterol concentrations during pregnancy develop hypercholesterolaemia in the third trimester (Salameh and Matrogiannis, 1994).

5.1.2 Relationship between maternal booking lipids and Placental indices

The significance of studying mechanisms involved in the transport of cholesterol to foetus is as important in first trimester embryogenesis as the full complementary growth and development of organ systems of the foetus observed in the third trimester (Kallol *et al.,* 2018). Averagely, about half of the total fatty acid demand by the foetus in the third trimester is met by the placental transfer as the placental membrane lipoprotein lipase degrades triglycerides and lipoproteins. The reported high levels of HDL-C and LDL-C in umbilical cord venous plasma is attributed to increase in placental permeability leading to efflux of cholesterol into foetal circulation (Frantz *et al.,* 2012).

Transport of maternal triglycerides present in plasma lipoproteins to the placenta involves hydrolysis and re-esterification to release abundance of fatty acid which then diffuse to the foetal plasma and becomes bound to α – foeto-proteins. These fatty acids are then transported to the

foetal liver where re-esterification occurs again and are released into circulation as triglycerides (Herrera, 2002).

The transport of maternal cholesterol across the placenta to the foetus passes from the trophoblast layer closer to the maternal circulation to the endothelial layer in contact with foetal circulation. The secretion of maternal cholesterol by the membrane trophoblast at the basal end seems to occur by diffusion or is mediated by ATP-binding cassette transporter A1 (ABCA1), as the ABCA1 is restricted to the basal side of the trophoblast layer and SR-B1 is also localized on the apical side (Woollett, 2011). The cholesterol efflux from the basal end of trophoblast reaches the endothelial cells of the foeto-placental vasculature before entering the foetal circulation by a process highly and tightly controlled by the liver – X – receptors (LXRs) (Stefulj *et al.*, 2009).

The transfer capacity of the placenta could be modulated by several mechanisms including placental morphometry (surface area, thickness, weight, abundance of transporter activity and expressions, substrate availability and establishment of concentration gradient between maternal and foetal circulations. Increased cholesterol and triglyceride concentrations in both maternal and foetal compartments result in high levels of placental fatty acid transporters in the cotyledons while expression and activities of some nutrient transporters such as glucose transporters, become affected by maternal metabolism. The system A which regulates neutral amino acid transport is also quite reduced in placentae of foetuses who develop foetal growth restriction (Tarrade *et al.*, 2015).

Placental morphometry as a reflection of structural and functional efficiency also enhances transfer of cholesterols. In an animal model experiment using rabbit, it was reported that, placental transfer of cholesterol related positively with rising levels of plasma lipoproteins, while

the increased levels of plasma lipoproteins varied directly with the presence of collagen. Collagen in its physiological concentration is essential in providing tensile strength in blood vessels, thereby facilitating exchange of materials between maternal circulation and the placenta. However, deposition of large quantities of collagen could influence certain physical characteristics of the placenta. In the said experiment, it was found that, intake of a 0.5% cholesterol diet produced atherosclerotic lesion in the placenta (Frantz *et al.,* 2012). Another study has also reported on association between rising levels of maternal hypercholesterolaemia and endothelial dysfunction of human placental microvasculature (Fuenzalida *et al.*, 2018).

5.1.3 Relationship between Maternal Booking Blood Pressure and Placental Indices

It is estimated that, about 30% of pregnancy-associated complications are as a result of chronic changes in maternal blood pressure, out of which 70% occur in early part of pregnancy. The potential pathophysiological attributes to these observations seem to come from immunologic or placental origin (Oshvandi *et al.,* 2018). The physiological observation of reduced vascular resistance, increased blood volume, variations in hormonal and other metabolic levels signify gradual adaptation of the maternal circulatory system as gestation progresses. However, no agreement has been reached with reference to the effects of these changes as normal variation in a normal uncomplicated pregnancy (Rebelo *et al.,* 2015). Pregnancy is characterized by susceptibility of developing blood pressure-related pathological conditions such as hypertension, diabetes, preeclampsia and eclampsia that, can possibly alter both macroscopic and microscopic structural features of the placenta with the potential of risking the well-being of the mother, foetus and neonate (Prieto *et al.*, 2018).

In uncomplicated pregnancy, blood pressure levels decrease up to about the 18 – 20 weeks of gestation after which the level rises until delivery. A study has reported on a significant reduction in systolic and diastolic blood pressures until mid – gestation (That is 22 – 24 weeks) and then increasing up to delivery (Grindheim *et al.,* 2012). Higher booking blood pressure levels have been linked to a higher risk of gestational hypertension and preeclampsia development (Macdonald-Wallis *et al.,* 2011). The trend of average changes in blood pressure levels across pregnancies categorized by hypertensive disorders of pregnancy (HDP) in a joint model have observed higher systolic and diastolic blood pressure levels in women with either essential hypertension, gestational hypertension or preeclampsia than normotensive women (Macdonald-Wallis *et al.,* 2012). Also, problems of HDP have been associated with deformities in the placenta. In this regard, reporting on the normal values and variations of systolic and diastolic blood pressures in healthy pregnancies should be considered relevant by the obstetrician, anatomist and paediatrician in order to identify abnormal changes likely to influence the onset of a disorder (Macdonald-Wallis *et al.,* 2014). Following inconsistencies and complexity of placental morphology studies, quantitative assessment of the placenta has become the way to understand the range of functions in relation to the structure of this haemochorial organ. A significant reduction in surface area, volume and weight of the placenta results in slow transfer of essential nutrients to the developing foetus which most often than not leads to stillbirth, a characteristic common in hypertensive pregnant women (Akshara *et al.,* 2018).

The mechanism by which maternal blood pressure levels influence adverse pregnancy outcome can be seen first as a cause of placental dysfunction and secondly a consequence on adaptation of maternal cardiovascular system to pregnancy. High blood pressure level in pregnancy is postulated to compensate for insufficient placental perfusion since this affects placental villous

tree development and subsequent decrease in placental functional capacity (Bakker *et al.,* 2011). The early stages of pregnancy are critical for epigenetic reprogramming. Hence, specific relationship of blood pressures in the initial stages of gestation is also likely to be influenced by epigenetic mechanisms during this crucial period of foetal development. One evidence of this observation reported on variations in DNA methylation patterns between placentae of preeclamptic and normal pregnancies which presupposes the role of epigenetic in trophoblastic invasion and placental development (Choudhury and Friedman, 2012; Staley *et al.,* 2015). In the course of normal pregnancy, interference in the chorionic villi maturation may occur either to slow or enhance the process. Mature normal placenta has immature intermediate villi at the centre of each placental lobule and it is the prevalence of these villi, villi vessels, and high levels of cytotrophoblast and absence of syncytial bridges at the intervillous space that determine immaturity of villi during the first trimester. Therefore, variations in blood pressure levels at an early gestation may alter this process of villi maturation with adverse consequences of uteroplacental microcirculation (Prieto *et al.,* 2018).

5.1.4 Maternal booking Lipids and Umbilical Cord Indices Relationship

The perinatal triad of mother, placenta and foetus becomes functionally complete with a functional umbilical cord which offers a smooth passage of blood from the placenta to the foetus or foetus to placenta. The umbilical cord is morphologically composed of two arteries and a vein embedded in a nutrient – rich substance referred to as Wharton's jelly. As a result of its special function, variations in the umbilical cord morphometry is often attributed to the Wharton's jelly content other than the cord vessels (Bimpong *et al.,* 2019).

The Wharton's jelly has few cells capable of producing large quantity of extracellular matrix (ECM) that serves as a reservoir of growth factors including peptide growth factor (PGF), insulin-like growth factor (IGF), fibroblast growth factor and transforming growth factor. Certain products of lipid metabolism such as cholesteryl esters and free cholesterol are part of Wharton's jelly and any change in the lipids could result in up or down regulation of cellular functions (Romanowicz and Bankowski, 2010). Owing to the important role played by serum cholesterols in the Wharton's jelly, it functions as energy requirement and its influence on plasma membrane of cells of the developing foetus. It is imperative that, endogenous cholesterol synthesised by the foetal tissues alone may not be enough and thus maternal-foetal cholesterol transfer is necessary in order to meet the cholesterol demand of the foetus. This is evident by the positive correlation observed between maternal and umbilical cord cholesterols in term pregnancies (Herrera and Ortega-Senovilla, 2010).

Maternal circulating cholesterol levels are known to physiologically increase from prenatal stage referred to as maternal physiological hypercholesterolaemia (MPH) and is related to changes in umbilical cord vein functions (Leiva *et al.,* 2013). Indeed, the functions of umbilical cord arteries and the vein are similar to the pulmonary artery and vein, but not like other arteries and veins in the rest of the foetal body. The umbilical cord vein transports oxygenated blood to foetal heart while cord arteries return deoxygenated blood to the placenta. This practically implies that, all essential nutrient substrates from the mother across the placenta are conveyed to the foetus by the umbilical cord vein (Spurway *et al.,* 2012). This umbilical circulation is described as ―closed system‖ since the volume of blood transported to the placenta equals the volume of blood returned to the foetus. Also, volume of blood flow (Q) is a function of blood velocity and cross sectional area of vessels (Acharya *et al.,* 2016). Hence, structural abnormalities of the

umbilical cord vessels may associate with vascular resistance and in turn lead to hypoperfusion, poor transfer of nutrient-rich blood to the foetus and deficiencies in eliminating metabolic waste products.

5.1.5 Maternal booking Blood Pressure and Umbilical Cord Indices Relationship

Systemic arterial blood pressure, commonly called blood pressure (BP) is measured and recorded as systolic over diastolic pressures. The systolic pressure as the numerator is larger and corresponds to arterial pressure due to ejection of blood during ventricular contraction (systole), while diastolic pressure is the denominator which corresponds to arterial pressure due to ventricular relaxation (diastole). Blood pressure is affected by cardiac output, compliance, blood volume and resistance, and any factor that influences these parameters is likely to affect blood pressure. Resistance for instance, normally relates directly to vessel length and inversely to luminal diameter of the vessel (Biga *et al.,* 2016). Blood pressure is therefore a mirror reflection of these haemodynamic factors.

Studies have found that, blood pressure development varies among uncomplicated pregnancies and pregnancies complicated by gestational hypertensive disorders. Although weakly, first and second trimester systolic and diastolic blood pressures directly relate to the development of preeclampsia (Hermida *et al.,* 2000; Gaillard *et al.,* 2011). It is known that, cord vessels undergo morphologic modifications characterized by widening of the media, large numbers and thickening of elastic lamella, reduced cellularity and increased collagen content during foetal development and that, umbilical cord perfusion decreases in preeclamptic mothers. Also, preeclampsia is associated with decreased total cord and Wharton's jelly areas, while chronic

hypertension associates with a rise in vascular resistance and changes in mechanical properties of the cord vessels (Inan *et al.*, 2002). It has been explained that, failure of the trophoblast to invade maternal vessels at any of the placental ends results in continuous vasoconstrictive capabilities of the vessels which decreases foeto-placental circulation and maternal blood pressure increases in compensation (Borges *et al.*, 2013). Changes in diastolic blood pressure levels are thought to influence preeclampsia development rather than altered systolic blood pressure levels. However, both diastolic and systolic blood pressure levels may indicate cardiovascular adaptation variations which probably influence foetal growth (Bakker *et al.*, 2011).

5.2 AIM AND SPECIFIC OBJECTIVES

5.2.1 Aim

To establish mathematical models to predict the outcome of placental and umbilical cord indices using maternal booking biometric parameters.

5.2.2 Specific Objectives

- To investigate correlations between maternal booking biometric and umbilical cord indices.
- To investigate correlations between maternal booking biometric and placental indices.
- To establish a mathematical model to predict the outcome of umbilical cord indices using maternal booking biometric indices.

- To establish a mathematical model to predict the outcome of placental indices using maternal booking biometric indices.

5.3 MATERIALS AND METHODS

5.3.1 Study Design and Area

This analytical descriptive cross-sectional study was conducted between March 2014 and October 2018 on placenta, umbilical cord, neonates and maternal booking biometric indices. A total of 240 pregnant women who attended antenatal care at the Victory Maternity Home and Clinic in Kumasi for the first time and consented to participate were enrolled into the study.

5.3.2 Inclusion and Exclusion Criteria

Included in the study were mothers who consented to the collection of their blood samples, had singleton pregnancy with no pregnancy or delivery complication, and from whom the records about her and the neonate were complete. Exclusion criteria included mothers who did not consent to the blood sample collection, multiple pregnancies, pregnancy or delivery complication, incomplete records about mother and the neonate.

5.3.3 Study Variables

The study variables were categorized into placenta, umbilical cord and maternal booking biometric indices. After sample preparations, the listed parameters below were measured. Detailed description of sample preparation is shown in **Section 3.3.6**.

5.3.3.1 Placental Indices

The following placental measurements were made on the gross structure:

1. **Weight of placenta**: It was measured using an electronic weighing scale and recorded after the umbilical cord was cut and the placental membranes trimmed. The placenta was then placed on the scale. The weighing was repeated and the average of the two weights determined as the weight of placenta.
2. **Volume of placenta**: This was obtained by the use of water displacement method and recorded. The placenta was gently lowered into transparent graduated beaker (1000 litres capacity) containing water. The initial water volume V_1 was noted, and final volume V_2 after putting in the placenta was also recorded. The difference between V_2 and V_1 then gave the volume of water displaced and that also became the volume of the placenta.
3. **Diameter of Placenta**: This was measured with a non-elastic measuring tape. The average of maximum (D1) and minimum (D2) diameters was taken as the diameter (D) of the placenta.
4. **Surface Area**: The maternal surface area of the placenta was computed using the formula:

   Surface area $= \frac{\pi D1 \times D2}{4}$, (where D1 is the largest diameter and D2 is the smallest diameter).

5. **Placental Thickness**: The placenta was placed on a flat surface and a thin long graduated needle was inserted into the placenta, at the centre, at the margin and midway between the centre and margin. The average of the three recordings was taken as the thickness of the placenta.

5.3.3.2 Umbilical Cord Indices

1. **Umbilical Cord Length**: The umbilical cord was immediately clamped at delivery and in all cases; 2.5 cm umbilical cord stump was left on the neonate. Umbilical cord measurements were made with the umbilical cord still attached to the placenta in its entirety using a standard non – elastic measuring tape from the foetal end to its point of insertion into the placenta. The 2.5 cm stump was added to each measurement made.
2. **Umbilical Cord Diameter**: Umbilical cord diameter (UCD) was measured with the use of a pair of electronic Vennier calipers placed outer - to-outer at three different points, precisely at the foetal end (D1), mid portion (D2) and at the placental surface (D3); with the average being the diameter of the cord.
3. **Umbilical Cord Weight:** The cord weight was measured using an electronic weighing scale and recorded after the umbilical cord was excised from the placenta. The umbilical cord was then placed on the scale. The measurement was repeated twice and the average of the three weights was taken as the weight of the umbilical cord.

5 **Umbilical Cord Volume**: This was obtained by the use of water displacement method and recorded. The umbilical cord after being cut from the placenta was gently lowered into a transparent graduated beaker (500 mL capacity) containing reasonable initial water volume V_1 was noted, and the volume V_2 after placing in the cord was also recorded. The difference between V_2 and V_1 then gave the volume of water displaced and that became the volume of the umbilical cord according to Archimedes principle.

6. Umbilical Cord Area: The area of the umbilical cord in a free loop of the umbilical cord was computed using formula for surface area of a cylinder with the assumption that, the

umbilical cord takes the shape of a cylinder. That is: $A = 2\pi r^2 L$; where r is the radius and L, the length of umbilical cord.

5.3.3.3 Maternal Booking Biometric Indices

Maternal booking biometric indices included; total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL-C), low density lipoprotein (LDL-C), systolic and diastolic blood pressures which were obtained on their first ANC visit. Method of sample collection and measurements are detailed in **Section 2.3.5.**

5.3.4 Statistical Analysis

In this study, mean ± SD was used for the descriptive characteristics of the study variables. Multivariate analysis of variance (MANOVA) was employed to model association between maternal booking biometric and placental and umbilical cord measurements.

First, correlation structure and cross correlations were developed to establish relationships within and between the maternal and placental and umbilical cord data sets. The correlations between the variables were described as weak or strong with regards to the correlation coefficient value. The models were then developed using step by step approach of multivariate analysis of variance. Six placental indices were modelled jointly with six predictors of maternal biometric indices using multivariate regression analysis. Statistical significance was pegged at $p < 0.05$. The final refitted model was developed using Type II MANOVA tests: Pillai's test statistic and a post hoc MANOVA procedure called descriptive discriminant analysis (DDA). Similarly, five umbilical cord indices were modelled jointly with six predictors of maternal biometric indices

using multivariate test (Type II MANOVA). The final refitted model was assessed using Type II MANOVA, Pillai's test statistic and DDA. The models were presented with coefficients of estimation, standard error (SE), t -value and model p -value for each predictor. In this study, all statistical analyses were performed with IBM SPSS Version 22.0 (SPSS Inc., Chicago, IL).

5.4 RESULTS

5.4.1 Descriptive Statistics of Placental Indices for Modelling

The mean value for placental weight in this current study was 502.40 ± 103.70 g (95% CI of 489.20 - 515.60 g). Mean values of placental diameter and thickness were 19.01 ± 2.41 cm (95% CI of 18.71 - 19.32 cm) and 2.85 ± 0.53 cm (95% CI of 2.78 – 2.92 cm) respectively. Placental area and volume recorded mean values of 287.40 ± 74.28 cm^2 (95% CI of 278.00 - 296.90 cm^2) and 623.20 ± 109.80 cm^3 (95% CI = 609.20 - 637.10 cm^3) respectively. The mean number of cotyledons was 16.99 ± 3.47 (95% CI of 16.55 - 17.43) as shown in Table 17 below.

Table 17: Descriptive Statistics of Placental Measurements

Variable	Mean ± SD	Range	95% CI of Mean Lower - Upper 95% CI
PW (g)	502.40 ± 103.70	274.20 – 781.70	489.20 – 515.60
PD (cm)	19.01 ± 2.41	13.50 – 27.50	18.71 – 19.32
PT (cm)	2.85 ± 0.53	1.80 – 4.05	2.78 – 2.92
PA (cm^2)	287.40 ± 74.28	133.60 – 592.40	278. 00 – 296.90
PV (cm^3)	623.20 ± 109.80	275.30 – 834.80	609.20 – 637.10
P COTYL	16.99 ± 3.47	9.00 – 27.00	16.55 – 17.43

PW= Placental Weight, PD = Placental Diameter, PT = Placental Thickness, PA = Area of Placenta, PV = Volume of Placenta, PCOTYL = Number of Placental Cotyledons, 95% CI = 95% Confidence Interval of Mean, g = gramme, cm = centimeter, cm^2 = centimeter square, cm^3 = centimeter cube

The umbilical cord measurements are presented in Table 18 below. The mean umbilical cord length was 38.10 ± 7.86 cm (95% CI of 37.11- 39.10 cm). Mean value of umbilical cord was 1.04 ± 0.17 cm (95% CI of 1.01 - 1.06 cm). Umbilical cord area and volume had mean of 66.10 ± 24.49 cm^2 (95% CI = 62.99 - 69.22 cm^2) and 34.02 ± 11.16 cm^3 (95% CI = 32.60 - 35.44 cm^3) respectively. The mean umbilical cord weight was 65.01 ± 21.35 g (95% CI of 62.30 - 67.73 g).

Table 18: Descriptive Statistics of Umbilical Cord Indices

Variable	Mean ± SD	Range	Lower - Upper (95% CI)
UCL (cm)	38.10 ± 7.86	19.17 – 59.83	37.11 – 39.10
UCD (cm)	1.04 ± 0.17	0.44 – 2.07	1.01 – 1.06
UCA (cm^2)	66.10 ± 24.49	5.96 – 231.60	62.99 – 69.22
UCV(cm^3)	34.02 ± 11.16	12.50 – 65.00	32.60 – 35.44
UCW(g)	65.01 ± 21.35	21.54 – 131.00	62.30 – 67.73

UCL = Umbilical cord length, UCD = Umbilical cord diameter, UCA = Umbilical cord area, UCV = umbilical cord volume, UCW = Umbilical cord weigh, SD - Standard deviation, 95% CI = 95% confidence interval, g = gramme, cm = centimeter, cm^2 = centimeter square, cm^3 = centimeter cube

The descriptive statistics of maternal booking biometric indices are displayed in Table 19. Mean of systolic blood pressure was 119.29 ± 28.31 mmHg and had 95% CI of 115.70 – 122.90 mmHg. The corresponding mean diastolic blood pressure was 73.84 ± 13.65 mmHg (95% CI = 72.11 – 75.58 mmHg). The mean total cholesterol was 4.03 ± 1.10 mmol/L (95% CI = 3.89 – 4.17 mmol/L) while mean value for triglyceride was 1.48 ± 0.77 mmol /L (95% CI = 1.38 -1.58 mmol/L). The respective mean for high density lipoprotein (HDL –C) and low density lipoprotein (LDL-C) was 1.11 ± 0.47 mmol/L (95% CI = 1.05 – 1.17 mmol/L) and 2.24 ± 0.84 mmol/L (95% CI = 2.14 – 2.35 mmol/L).

Table 19: Descriptive Statistics of Maternal Booking Biometric Indices

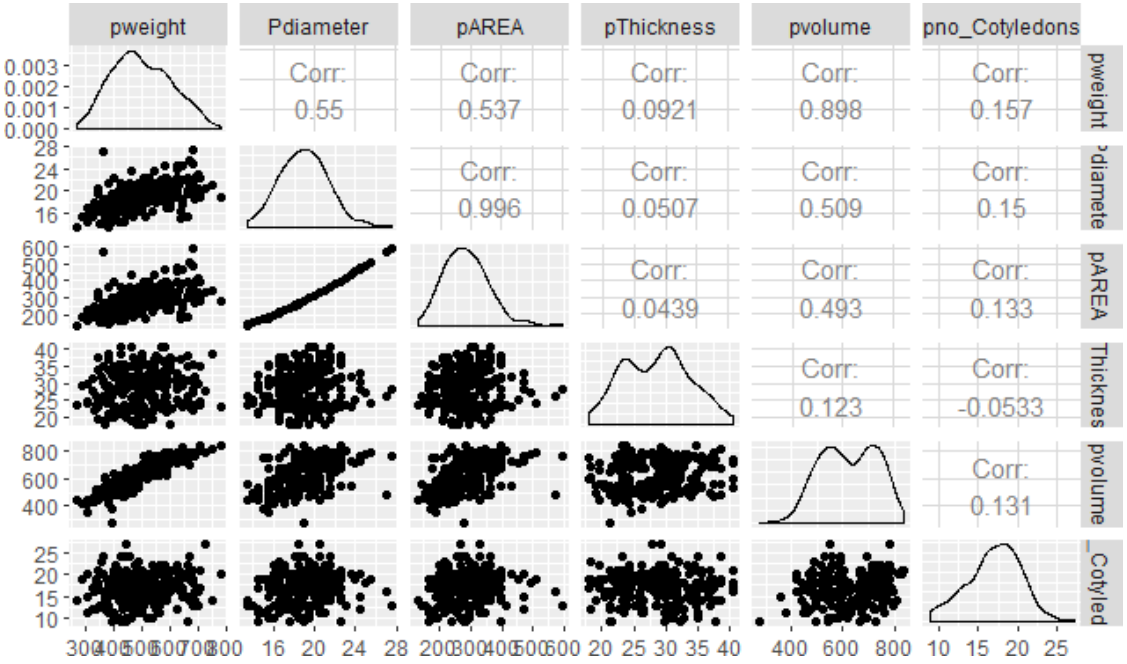
Characteristic	Mean ± SD	Range	95% CI of Mean Lower - Upper 95% CI
SP (mmHg)	119.29 ± 28.31	90 – 250	115.70 – 122.90
DP (mmHg)	73.84 ± 13.65	50 – 120	72.11 – 75.58
TC (mmol/L)	4.03 ± 1.10	1.40 – 9.15	3.89 – 4.17
TG (mmol/L)	1.48 ± 0.77	0.38 – 6.92	1.38 – 1.58
HDL (mmol/L)	1.11 ± 0.47	0.05 – 2.98	1.05 – 1.17
LDL (mmol/L)	2.24 ± 0.84	0.36 – 5.68	2.14 – 2.35

SP= Systolic blood pressure, DP = Diastolic blood pressure, TC = total cholesterol, TG = Triglyceride, HDL = High density lipoprotein, LDL = Low density lipoprotein, SD - Standard deviation, 95% CI = 95% confidence interval, mmHg = millimeter mercury, mmol/L = millimole per litre

5.4.2 Pearson correlation between Placental and Maternal booking Biometric Indices

Correlation structure of placental parameters shows strong positive correlations within as presented in Figure 7. Strong positive correlation existed between placental weight and area (r = 0.537), placental weight and diameter had r of 0.550, placenta weight and volume recorded r = 0.898. Similarly, placental area strongly correlated with the diameter (r = 0.996). Placental area

positively correlated with volume (r = 0.493). However, very weak correlations were observed between both placental thickness and number of cotyledons with weight, diameter, area and volume.



pweight = placenta weight, Pdiameter = placenta diameter, pAREA = placenta area, pThickness = placenta thickness, pvolume = placenta volume, pno.cotyledons = number of placental cotyledons, Cotyled = number of placental cotyledons. Corr = correlation coefficient

Figure 7: Pearson's Correlation Structure of Placental Measurements

Pearson's cross correlation between placental and maternal booking measurements showed very weak correlations. From Table 20, it was observed that, both systolic and diastolic blood pressures related negatively with the placental indices, although the correlations were very weak. While maternal booking HDL showed a weak positive correlation with all the placental measurements. Maternal total cholesterol showed negative correlation with only the number of placental cotyledons.

Maternal booking triglyceride correlated negatively with placental diameter, thickness, volume and number of cotyledons, but related positively with placental weight and area. Also, LDL exhibited negative correlations with placental area and number of cotyledons while showing positive relationship with placental weight, diameter, thickness and volume.

Table 20: Pearson's Cross Correlation between Placental Indices and Maternal booking Biometric Parameters

Variable	Msystolic	Mdiastolic	Mcholesterol	Mtriglyceride	MHDL	MLDL
Pweight	-0.054	-0.040	0.052	0.022	0.029	0.026
Pdiameter	-0.095	-0.041	0.020	-0.002	0.027	0.003
Parea	-0.088	-0.037	0.005	0.001	0.013	-0.010
Pthickness	-0.044	-0.060	0.064	-0.039	0.081	0.054
Pvolume	-0.047	-0.069	0.053	-0.007	0.029	0.032
Ncotyledon	-0.086	0.030	-0.025	-0.168	0.142	-0.052

Pweight = placental weight, Pdiameter = Placental diameter, Parea = Area of Placenta, Pthickness = Placental thickness, Pvolume = Placental volume, Ncotyledon = Number of cotyledons, Msystolic = Maternal booking systolic blood pressure, Mdiastolic = Maternal booking diastolic blood pressure, Mcholesterol = Maternal booking cholesterol, Mtriglyderide = Maternal booking triglyceride, MHDL = Maternal booking high density lipoprotein, MLDL = Maternal booking low density lipoprotein

5.4.3 Placental and Maternal booking Biometric Indices Modeling

Six maternal explanatory variables were fitted with the placental response variables (Table 21); it was found that, there were significant effects of maternal cholesterol, triglyceride, HDL and LDL on placental volume; as these models fitted had p – value < 0.05. In general, the fitted models

for placental weight, diameter, thickness, area, volume and number of cotyledons were respectively represented as:

$\mathbf{P_W}$ = 505.591 – 0.128M_{SBP} – 0.125M_{DBP} + 61.911M_{TC} – 24.725 – 54.944M_{HDL} – 58.471 $M_{LDL.}$

$\mathbf{P_D}$ = 19.600 – 0.010M_{SBP} – 0.006M_{DBP} + 0.670M_{TC} – 0.314M_{TG} – 0.560M_{HDL} – 0 .669M_{LDL}

$\mathbf{P_T}$ = 29.465 + 0.001M_{SBP} – 0.028M_{DBP} + 0.647M_{TC} – 0.510M_{TG} + 0.088M_{HDL} – 0.446 M_{LDL}

$\mathbf{P_A}$ = 306.906 – 0.280M_{SBP} + 0.179M_{DBP} + 19.363M_{TC} – 9.023M_{TG} – 17.420M_{HDL} – 20.302M_{LDL}

$\mathbf{P_V}$ = 647.179 + 0.061M_{SBP} – 0.677M_{DBP} + 96.270M_{TC} - 44.755M_{TG} - 88.662M_{HDL} - 91.394M_{LDL}

$\mathbf{P_{COT}}$ = 17.904 – 0.019M_{SBP} + 0.031M_{DBP} + 1.067M_{TC} – 1.172M_{TG} + 0.071M_{HDL} – 1.589M_{LDL}

Where;

P_W is the predicted placental weight, P_D is the predicted placental diameter, P_T is the predicted placental thickness, P_A is the predicted placental area, P_V is predicted placental volume and P_{COT} is the predicted number of placental cotyledons. M_{SBP} and M_{DBP} are the maternal systolic and diastolic blood pressures respectively. M_{TC} is maternal total cholesterol; M_{TG} is maternal Triglyceride, M_{HDL} is the maternal high density lipoproteins and M_{LDL} is maternal low density lipoprotein.

Table 21: Multivariate regression Models for Placental and Maternal Booking Biometric Indices

Predictor	P_W EST(SE)	P_D EST(SE)	P_A EST(SE)	P_T EST(SE)	P_V EST(SE)	P_{COT} EST(SE)
Intercept	505.591(46.999)	19.600(1.095)	306.906(33.689)	29.465(2.340)	647.179(49.725)	17.904(1.519)
$\mathbf{M_{SBP}}$	-0.128(0.314)	-0.010(0.007)	-0.280(0.225)	0.001(0.016)	0.061(0.333)	-0.019(0.010)
$\mathbf{M_{DBP}}$	-0.125(0.648)	0.006(0.015)	0.179(0.465)	-0.028(0.033)	-0.677(0.686)	0.031(0.021)
$\mathbf{M_{TC}}$	61.911(42.397)	0.670(0.988)	19.363(30.396)	0.647(2.165)	96.270(44.864)*	1.067(1.370)
$\mathbf{M_{TG}}$	-24.725(21.090)	-0.314(0.492)	-9.023(15.120)	-0.510(1.077)	-44.755(22.317)*	-1.172(0.682)
$\mathbf{M_{HDL}}$	-54.944(43.467)	-0.560(1.013)	-17.420(31.163)	0.088(2.220)	-88.662(45.996)*	0.071(1.405)
$\mathbf{M_{LDL}}$	-58.471(42.858)	-0.669(0.999)	-20.302(30.727)	-0.446(2.189)	-91.394(45.352)*	-1.589(1.385)

M_{SBP} = Maternal booking visit systolic blood pressure, M_{DBP} = Maternal booking visit Diastolic blood pressure, M_{TC} = Maternal booking visit total cholesterol, M_{TG} = Maternal booking visit triglyceride, M_{HDL} = Maternal booking visit high density lipoprotein, M_{LDL} = Maternal booking visit low density lipoprotein, EST = Estimation, SE = Standard error, P_W = Placental weight, P_D = Placental diameter, P_A = Area of placenta, P_T = Placental thickness, P_V = Placental volume, P_{COT} = Number of cotyledons

From Table 21, the size of joint effects of the maternal booking lipids on placental volume in the multivariate regression models can be expressed mathematically as:

$$\mathbf{P_V = 647.179 + 96.270M_{TC} - 44.755M_{TG} - 88.662M_{HDL} - 91.394M_{LDL}}$$

In order to evaluate the performance of the multivariate regression models in predicting the outcome of the placental indices, a robust Type II MANOVA test – Pillai's test statistic was used. The result of the Pillai's test statistic is presented in Table 22. There were significant joint effects of maternal total cholesterol, triglyceride, HDL-C and LDL-C on placental variables as observed in Table 21. The Pillai's test statistic performed showed that, none of the maternal biometric variables could independently predict the outcome of any of the placental variables.

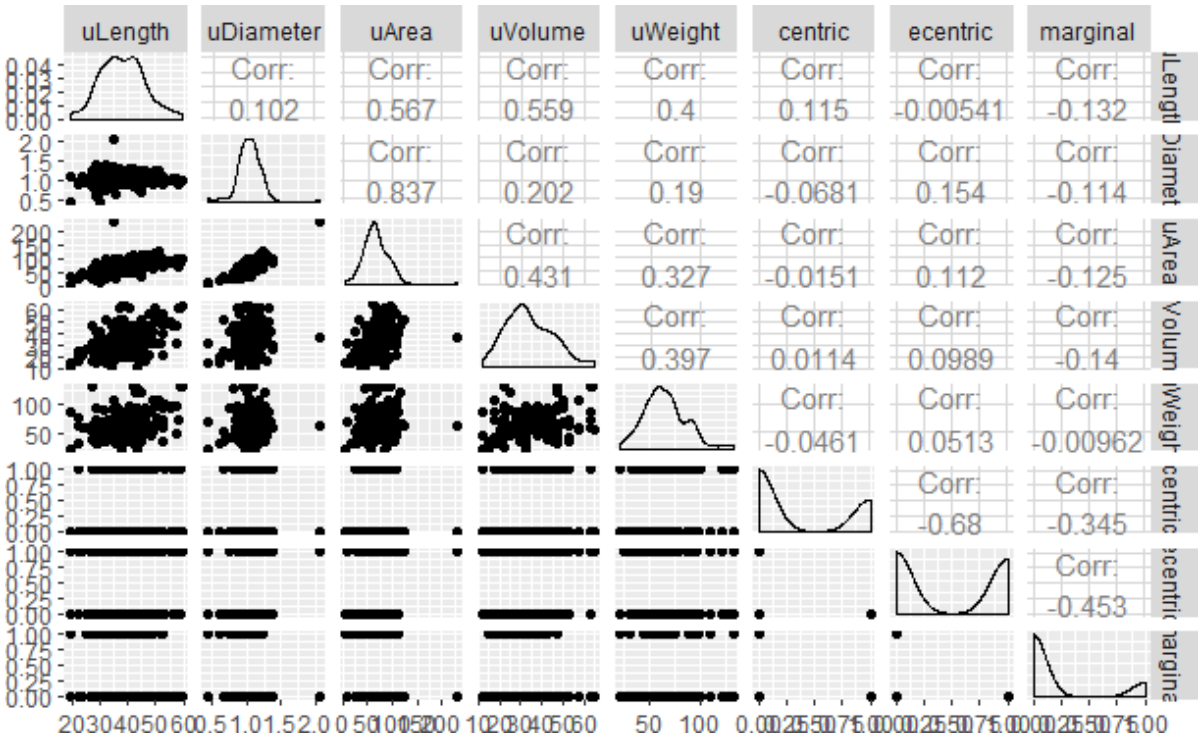
Table 22: Type II MANOVA Tests: Pillai's test statistic on Maternal booking Biometrics and Placental Parameters

Predictor	Df	test stat	approx F	num Df	den Df	Pr(>F)
Msystolic	1	0.027773	1.11410	6	234	0.3547
Mdiastolic	1	0.025800	1.03283	6	234	0.4046
Mtcholesterol	1	0.025206	1.00845	6	234	0.4204
Mtriglyceride	1	0.035737	1.44538	6	234	0.1981
MHDL	1	0.021250	0.84672	6	234	0.5350
MLDL	1	0.025771	1.03167	6	234	0.4053

Msystolic = Maternal systolic blood pressure, Mdiastolic = Maternal diastolic blood pressure, Mtcholesterol = Maternal total cholesterol, Mtriglyceride = Maternal triglyceride, MHDL = Maternal high density lipoprotein, MLDL = Maternal low density lipoprotein, Df = Degree of freedom, test stat = Test statistic, approx. F = Approximation based on F – distribution, num Df = Numerator degree of freedom, den Df = denominator degree of freedom, Pr(>F) = Significance level of F – ratio

5.4.4 Pearson correlation between Umbilical Cord and Maternal booking Biometric Parameters

Correlation structure was developed to establish the relationships within the umbilical cord measurements (Figure 8). Umbilical cord length showed strong positive correlation with cord weight, diameter, area and volume as indicated by the high r values. However, negative correlations of cord length with eccentric and marginal insertions were observed. The correlations between the umbilical cord weight, diameter, area and volume were all strong and positive. In respect of cord insertion, it was found that, marginal cord insertion exhibited weak negative correlations with length, diameter, area, volume and weight. Centric insertion also negatively correlated with umbilical cord diameter, area and weight.



uLength = umbilical cord length, uDiameter = umbilical cord diameter, uArea = umbilical cord area, uWeight = umbilical cord weight, centric = central cord insertion, eccentric = eccentric cord insertion, marginal = marginal cord insertion, Volum = umbilical cord volume

Figure 8: Correlation Structure of Umbilical Cord Indices

Pearson's cross correlation between umbilical cord and maternal booking biometric parameters is presented in Table 23 below. Most of the correlations between cord and the booking biometric parameters were weak comprising both positive and negative relations. Notwithstanding, significant strong positive correlations were also observed. Maternal diastolic blood pressure positively correlated with umbilical cord length, volume and weight. Maternal HDL – C also showed positive correlations with umbilical cord area and eccentric insertion.

Table 23: Cross Correlation between Maternal Biometric and Umbilical Cord Indices

Maternal Biometric Index	UC Length	UC Weight	UC Diameter	UC Area	UC Volume	Centric Insertion	Eccentric Insertion	Marginal Insertion
M systolic	0.054	0.057	-0.031	-0.007	0.064	0.026	0.045	-0.090
M diastolic	0.126*	0.121*	0.007	0.068	0.101*	-0.001	0.058	-0.073
M cholesterol	0.022	-0.073	0.044	0.058	-0.009	-0.039	0.064	-0.035
M triglyceride	0.085	-0.082	-0.031	0.026	-0.053	-0.045	0.017	0.033
M HDL	0.086	0.015	0.101	0.132*	0.070	-0.098	0.145*	-0.067
M LDL	-0.064	-0.059	0.040	0.014	-0.031	0.010	0.007	-0.020

UC = Umbilical Cord, M = Maternal, HDL = High density lipoprotein, LDL = Low density lipoprotein, ***** *= p < 0.05*

5.4.5 Maternal booking Biometric and Umbilical Cord Indices Modeling

In Table 24, five multivariate regression models were fitted with the umbilical cord response variables (umbilical cord length, diameter, area, volume and weight) against the six maternal booking biometric indices. The results showed that, maternal diastolic blood pressure, total cholesterol, triglyceride, HDL-C and LDL-C had similar significant linear effects on predicting the outcome of umbilical cord length, diameter and area (p – v alue < 0.05). In general, the fitted models for umbilical cord length, weight, diameter, area and volume could respectively be represented as:

$$Y_{len} = 29.479 – 0.007M_{SBP} + 0.095M_{DBP} + 2.390M_{TC} + 0.124M_{TG} + 0.242M_{HDL} – 3.476M_{LDL}$$

$$Y_{WET} = 58.727 – 0.031M_{SBP} + 0.227M_{DBP} – 8.218M_{TC} + 1.705M_{TG} + 9.370M_{HDL} +5.924M_{LDL}$$

$$Y_{DIA} = 1.012 + 0.001M_{DBP} – 0.135M_{TC} + 0.058M_{TG} + 0.162M_{HDL} + 0.134M_{LDL}$$

$$Y_{AREA} = 49.056 - 0.071M_{SBP} + 0.241M_{DBP} - 18.032M_{TC} + 9.993M_{TG} + 25.340M_{HDL} + 16.571M_{LDL}$$

$$Y_{VOL} = 28.175 + 0.005M_{SBP} + 0.077M_{DBP} + 1.441M_{TC} - 1.119M_{TG} + 0.899M_{HDL} - 2.419M_{LDL}$$

Where; Y_{len} is the predicted umbilical cord length; M_{SBP} is maternal systolic blood pressure; M_{DBP} is maternal diastolic blood pressure; M_{TC} is maternal total cholesterol, M_{TG} is maternal triglyceride; M_{HDL} is maternal high density lipoprotein; M_{LDL} is maternal low density lipoprotein; Y_{DIA} is predicted umbilical cord diameter; Y_{AREA} is predicted cord area; Y_{VOL} is predicted cord volume.

The multivariate regression models can be used to calculate a score for each of the respective umbilical cord response variable. However, by considering the level of statistical significance in Table 21 below, the multivariate multiple regression models for umbilical cord length, diameter and area can be expressed respectively as:

$$\mathbf{Y_{Length} = 29.479 + 0.095M_{DBP}}$$

$$\mathbf{Y_{Diameter} = 1.012 - 0.135M_{TC} + 0.162M_{HDL} + 0.134M_{LDL}}$$

$$\mathbf{Y_{Area} = 49.056 + 9.993M_{TG} + 25.340M_{HDL}}$$

Table 24: Multivariate Regression Models for Maternal Biometrics and Umbilical Cord Indices

Maternal Variable	UC Length EST(SE)	UC Weight EST(SE)	UC Diameter EST(SE)	UC Area EST(SE)	UC Volume EST(SE)
Intercept	29.479(3.540)	58.727(9.503)	1.012(0.075)	49.056(11.032)	28.175(5.021)
Msystolic	-0.007(0.024)	-0.031(0.064)	-0.000(0.001)	-0.071(0.074)	0.005(0.034)
Mdiastolic	0.095(0.049)*	0.227(0.131)	0.001(0.001)	0.241(0.152)	0.077(0.069)
Mtcholesterol	2.390(3.194)	-8.218(8.574)	-0.135(0.067)*	-18.032(9.953)	1.411(4.530)
Mtriglyceride	0.124(1.589)	1.705(4.265)	0.058(0.033)	9.993(4.951)*	-1.119(2.254)
MHDL	0.242(3.274)	9.370(8.790)	0.162(0.069)*	25.340(10.204)*	0.899(4.645)
MLDL	-3.476(3.229)	5.924(8.667)	0.134(0.068)*	16.571(10.060)	-2.419(4.80)

Msystolic =Maternal systolic blood pressure, Mdiastolic = Maternal diastolic blood pressure, Mtcholesterol = Maternal total cholesterol, Mtriglyceride = Maternal triglyceride, MHDL = Maternal high density lipoprotein, MLDL = Maternal low density lipoprotein, UC = Umbilical cord, *** =** *$p < 0.05$*

In order to agree with the multivariate multiple regression analysis, a Type II MANOVA test: Pillai's test statistic was conducted to determine which of the six maternal explanatory variables had joint effect on the umbilical cord response variables. The results of the MANOVA test: Pillai's test statistic is shown in Table 25 below. It was observed that, maternal total cholesterol, HDL and LDL had joint significant effect on the umbilical cord indices.

Table 25: Type II MANOVA Tests: Pillai test statistic of Maternal Lipids with Umbilical Cord Indices

Maternal Lipids	Df	test stat	approx F	num Df	den Df	Pr(>F)
Msystolic	1	0.008109	0.38423	5	235	0.85935
Mdiastolic	1	0.023009	1.10687	5	235	0.35740
Mtcholesterol	1	0.048776	2.41002	5	235	0.03725
Mtriglyceride	1	0.040691	1.9936	5	235	0.08037
MHDL	1	0.048381	2.38953	5	235	0.03871
MLDL	1	0.051264	2.53959	5	235	0.02917

Msystolic = Maternal systolic blood pressure, Mdiastolic = Maternal diastolic blood pressure, Mtcholesterol = Maternal total cholesterol, Mtriglyceride = Maternal triglyceride, MHDL = Maternal high density lipoprotein, MLDL = Maternal low density lipoprotein, Df = Degree of freedom, test stat = Test statistic, approx. F = Approximation based on F – distribution, num Df = Numerator degree of freedom, den Df = denominator degree of freedom, Pr(>F) = Significance level of F – ratio

A post hoc MANOVA procedure; descriptive discriminant analysis (DDA) was further conducted to establish a set of linear equations that together model the differences among the response variable. Therefore, the models were refitted with only the significant predictors from the joint effect test (Table 26).

Table 26: Refitted Models for Maternal booking TC, HDL and LDL with Umbilical Cord Length and Diameter

Maternal Variable	UC Length EST(SE)	UC Diameter EST(SE)
Intercept	35.814(2.035)	1.022(0.043)
TC	2.326(1.134)*	-0.028(0.028)
HDL	0.192(1.623)	0.059(0.028)*
LDL	-3.314(1.460)*	0.028(0.031)

*EST = Estimated value, SE = Standard Error, UC = Umbilical cord,TC = Total cholesterol, HDL = High density lipoprotein, LDL = Low density lipoprotein, EST = Estimation, SE = Standard error, * = $p < 0.05$*

From Table 26, the mathematical functions that could predict the umbilical cord length and area using maternal booking lipids are respectively given as:

$Y_{length} = 35.814 + 2.326M_{Cholesterol} - 3.314M_{LDL.}$

Where; Y_{Length} is the predicted umbilical cord length.

$Y_{Area} = 1.022 + 0.059M_{HDL}.$

Where Y_{Area} is the predicted umbilical cord area

5.5 DISCUSSION

5.5.1 Descriptive Statistics of Placental and Maternal booking Biometric Indices

The present study found the mean placental weight, diameter and thickness to be 502.40 ± 103.70 g, 19.01 ± 2.41 cm and 2.85 ± 0.53 cm respectively. The mean placental area, volume and number of cotyledons were also recorded as 287.40 ± 74.28 cm^2, 623.20 ± 109.80 cm^3 and 16.99 ± 1.47 respectively. These values demonstrate that, morphological characteristics of the

studied placentae were normal. The present study finding is comparable to the results of placental morphology and foetal outcome in preeclampsia and normotensive pregnancy study which recorded mean placental weight of 502.00 ± 58.42 g, diameter of 18.70 ± 1.55 cm; mean thickness of 2.30 ± 0.43 cm and number of cotyledons to be 18.90 ± 1.98 for the control group as these values were higher than observed for the study group (Shevade1 *et al.,* 2015). In another study, the mean placental weight, area and volume were also recorded as 401.80 ± 54.62 g, 212.48 ± 54.51 cm^2 and 439.48 ± 135.14 cm^3 respectively for the normotensives and these were also significantly higher than in the study group (Londhe and Mane, 2011). The observed results of this current study and others confirm that, in normal pregnancies, the morphometric parameters of placenta are higher than in complicated pregnancies. However, whereas morphometric indices of placenta were higher in normal uncomplicated pregnancies than in pregnancies complicated by hypertensive disorders; the same cannot be said of placentae from pregnancies complicated by *diabetes mellitus*. In comparing morphology and morphometry of placenta from normal, hypertensive and diabetic pregnancies among rural population in Eastern India, the following mean results were recorded; placental weight was 510.10 g – normal, 493.18 g – hypertensive and 577.90 g – diabetics; diameter was 15.44 cm – normal, 15.08 cm – hypertensive and 16.74 cm – diabetic; thickness was; 1.68 cm – normal, 1.54 cm – hypertensive and 2.32 cm – diabetic; area was 183.35 cm^2- normal, 179.54 cm^2 – hypertensive and 219.30 cm^2 – diabetic; volume was 431.84 cm^3 – normal, 406.80 cm^3 – hypertensive and 494.10 cm^3 – diabetic (Karmakar *et al.,* 2018).

The mean for umbilical cord measurements reported by the present study were; cord length, 38.10 ± 7.86 cm; diameter, 1.04 ± 0.17 cm; area, 66.10 ± 24.49 cm^2 and volume was 34.02 ± 11.16 cm^3. The mean cord weight was 65.01 ± 21.35 g. These observed measurements are closer

to earlier studies conducted in Kumasi (Bimpong, 2012; Tetteh, 2015). The cord length and diameter in the present study are lower than that recorded in other studies, but these mean values are considered to fall within the normal ranges as reported by several researchers (Balkawade and Shinde, 2012; Olumuyiwa and Ogunlaja, 2015).

In the current study, mean maternal booking biometric parameters included 119.29 ± 28.31 mmHg systolic blood pressure, 73.84 ± 13.65 mmHg diastolic blood pressure, 4.03 ± 1.10 mmol/L total cholesterol, 1.48 ± 0.77 mmol/L triglyceride, 1.11 ± 0.47 mmol/L HDL-C and 2.24 ± 0.84 mmol/L LDL-C. These findings of the present study clearly indicate that, the study participants were healthy as mean values were within the normal ranges of the respective parameters. Both American Heart Association and American College of Cardiology define normal blood pressure as systolic pressure < 120 mmHg and diastolic pressure < 80 (American College of Cardiology, 2017; American Heart Association, 2019). The Japanese Society for Hypertension defines normal blood pressure as systolic pressure < 125 mmHg and diastolic pressure < 80 mmHg (Japanese Society of Hypertension, 2009). The European Society of Cardiology, however, describes normal blood pressure as 120 – 129 mmHg systolic pressure and 80 – 84 mmHg diastolic pressure (William *et al.,* 2018). A study on worldwide trends in blood pressures found the global age – standardized mean systolic and diastolic pressures of 122.3 mmHg and 76.7 mmHg respectively (Non-Communicable Disease Risk Factor Collaboration, NCD-RisC, 2017). According to these reports, it presupposes that, the maternal booking systolic and diastolic blood pressures recorded in the present study align themselves to the definitions of blood pressure by American Heart Association and American College of Cardiology than with the definitions of European Society of Cardiology, Japanese Society for Hypertension and NCD – RisC.

In comparing the maternal booking vist TC, TG, HDL – C and LDL – C observed in the current study with first trimester concentrations of maternal lipids from other studies, it was realized that, the mean values of the present study, were lower than first trimester mean values recorded in those studies (Jin *et al*., 2016; Boghossian *et al*., 2017; Mishra *et al.*, 2017). This is in line with the observations that, maternal serum concentrations increase significantly with advancement in gestation. The rise in lipid concentration levels as pregnancy progresses is attributed to the increasing foetal energy demand on maternal metabolism. There is therefore, a switch from carbohydrate metabolism in providing energy to lipid metabolism which serves as alternative energy pathway for the developing foetus. Also, there is high demand for cholesterol in the synthesis of plasma membranes of the cells as organogenesis begins (Mishra *et al.*, 2017).

5.5.2 Pearson's Correlation between Placental and Maternal booking Biometric Indices

The relationships between placental indices and maternal booking biometric indices were found to be weakly correlated in the present study. Both maternal systolic and diastolic blood pressures were found to negatively correlate with all the placental indices, except the relationship between diastolic blood pressure and number of placental cotyledons. Similarly, both total cholesterol and HDL showed positive correlation with majority of the placental indices, except total cholesterol which related negatively with number of placental cotyledons. Triglyceride levels correlated positively with placental weight and area while correlating negatively with diameter, thickness, volume and number of cotyledons. The LDL levels negatively correlated with placental area and number of cotyledons but showed positive relation with the weight, diameter, thickness and volume.

It appears that, currently, there is little or no information on correlation between maternal booking biometric indices and placental morphometry. However, maternal booking biometry and pregnancy outcomes have been extensively studied with the focus on its relationship with race/ethnicity (Schreuder *et al.,* 2011; Frank *et al.,* 2014), preterm birth (Catov *et al.,* 2010), cardiovascular risks (Harville *et al.,* 2018), gestational BMI and *diabetes mellitus* (Rebelo *et al*., 2015; Chen *et al*., 2016) and birth indices (Mitra *et al*., 2012). One such study which used maternal measurements at first antenatal visit found positive correlation between placental volume and maternal weight, BMI and haemoglobin levels but not with blood pressure (Thame *et al.,* 2000). Another study also reported that, risk of cardiovascular incidence is likely to have adverse consequences on birth outcomes as a result of dysfunctional placenta. A significant relation of booking lipid levels and a non-significant relation of blood pressure with birth weight have been reported (Harville *et al.,* 2018).

The weak non-significant correlations of the present study could mean that, the booking biometric recordings at first antenatal visit set the preliminary stage for other developmental processes as gestation progresses. It is evident that, maternal blood pressure and lipid levels increase with advancing gestation (Grindheim *et al.,* 2012; Leiva *et al.,* 2013) while the placenta begins to become fully functional after week 26 of gestation (Larsen, 2001).

5.5.3 Maternal booking Biometric and Placental Indices Modelling

Following the weak Pearson's correlations observed between maternal booking biometric indices and placental morphometric parameters in this study, the effects of interaction between maternal booking biometric and placental morphometric indices were tested by developing multivariate

multiple regression models for the prediction of successful outcomes. Six models were fitted with placental response variables (weight, diameter, thickness, area, volume, number of cotyledons) against six maternal explanatory variables (systolic and diastolic blood pressures – SBP and DBP, total cholesterol – TC, triglyceride – TG, high density – HDL-C and low density lipoproteins – LDL-C). Explanatory variable with $p < 0.05$ in at least one of the six models was included in a final model. The booking TC, TG, HDL-C and LDL-C all had significant joint effect on placental volume ($p < 0.05$). This implies that, maternal booking lipids could predict placental volume outcome. The combined estimation of the joint effects between maternal booking biometric indices and other placental response variables however, were not significant.

In order to evaluate the performance of the multivariate multiple regression models in the prediction of outcome of placental indices, a Type II MANOVA Test – Pillai's Test statistic was performed. Even though maternal booking lipids had significant joint effect on the placental volume, the Pillai's Test statistic showed that, none of the individual booking lipid parameters could independently predict the placental outcome. The findings of the present study probably add up to the body of evidence on the importance of placental transfer of these maternal fuels. Though the mechanism underlying the prediction of placental volume by these maternal booking lipids is not clear, it could be appreciated in view of the availability and quantity of cholesterol transporters localized in the placenta. The placenta is key to the transfer of cholesterol from the mother to foetus and is known that, in the first week of intrauterine life, it solely depends on maternal cholesterol as the main source of structural and functional development (Zhang *et al.,* 2017). Placental trophoblast has been found to express significant level of low density lipoprotein (LDLR) receptors, very low density lipoprotein (VLDLR) receptors, scavenger receptor class B type I (SR B1) and Apo-protein B-100 (ApoB-100) all of which facilitate

the transportation of cholesterol to the foetus (Zeng *et al*., 2017). Odibo *et al.* (2011) in a study postulated that, early first trimester abnormal serum parameters directly relate to abnormal placental morphometric variables leading to poor perinatal outcomes. It was realized that, an abnormal early first trimester trophoblast invasion led to variations in the placental morphology. Therefore, markers of early first trimester placental function are crucial in initiating maternal – foetal exchange in pregnancy.

Hence, the volume of placenta which is an indication of the amount of substances it contains including large amount of trophoblast cells could contribute to the serum lipid transport efficiency. Following scarcity of literature in relating placental volume to maternal booking lipids, it is tempting to speculate that, the prediction of placental volume by these maternal booking lipids clearly shows foetal dependency on maternal cholesterol supply during first trimester of gestation.

5.5.4 Pearson's Correlation between Umbilical Cord and Maternal booking Biometric Indices

This study performed Pearson's correlations to determine relationships between maternal booking biometric and umbilical cord indices. Most of the relationships were weak though, some moderate to strong correlations were also observed. It was found that, umbilical cord length related negatively with LDL-C. It also showed weak positive correlation with other maternal biometric indices, and had strong relationship with diastolic blood pressure. This positive relation between cord length and blood pressure could speculatively be attributed to the idea that, an increased blood pressure enhances progressive proliferation of vascular mechanical properties of the umbilical cord following the contractile responses inherent of smooth muscles. Indeed,

significant impact of the state of maternal vascular system and placenta on the successive progression of intrauterine environment of the developing foetus has been reported by Barnwal *et al.* (2012). The inverse association observed between umbilical cord length and LDL-C was also in support of the fact that, high levels of LDL-C in early pregnancy is a risk factor for adverse pregnancy outcomes such as preterm delivery (Aghaie *et al.,* 2018). Consequently, an increase in cord length results in decrease in LDL-C levels.

Umbilical cord weight showed strong positive relation with diastolic blood pressure. Also its relationship with systolic blood pressure and HDL-C were positive but negative for total cholesterol, triglyceride and LDL-C. The umbilical cord weight's positive association with maternal blood pressures and HDL-C indirectly could be an indication of good health of the foetus. This study defines umbilical cord weight to include cord length, areas of cord and Wharton's jelly; which associate positively with maternal blood pressure (Inan *et al.,* 2002; Acharya *et al.,* 2016). Foetal starvation has been associated with reduced area of Wharton's jelly following poor maternal nutrient supply (Barnwal *et al.,* 2012). Umbilical cord weight relation with HDL-C is also in line with the observation that, normal level of HDL-C plays protective role in the event of adverse pregnancy complications (Kramer *et al.,* 2009).

There were weak negative correlations between cord diameter and systolic blood pressure and triglyceride but positive for diastolic blood pressure, total cholesterol, HDL-C and LDL-C. Umbilical cord area negatively correlated with only systolic blood pressure. However, relations with other biometric indices were positive. Negative relations were found between umbilical cord diameter and area with systolic blood pressure, but were positive with diastolic pressure.This not surprising as cord area is derived from diameter. Similar associations have

been reported, where early pregnancy systolic blood pressure negatively related with gestation age, while the association was positive with diastolic blood pressure. Also, whereas systolic blood pressure at 8 weeks was not associated with birth weight, diastolic blood pressure was associated with heavier birth weight (Macdonald-Wallis *et al.,* 2014).

The correlations observed between cord volume, centric and marginal insertions with biometric indices were weak. Eccentric insertion on the other hand, showed positive relations with all maternal booking biometric indices.

This study found that, maternal booking diastolic blood pressure and HDL-C had strong positive relationships with umbilical cord length and weight, and cord area and eccentric insertion. Accordingly, an increase in maternal booking diastolic blood pressure results in corresponding increase in umbilical cord weight and length. Again, increase in maternal booking HDL-C leads to an increase in umbilical cord area and allows for eccentric umbilical cord insertion.

5.5.5 Maternal booking Biometric and Umbilical cord Indices Modelling

The weak Pearson's correlations observed between maternal booking biometric and umbilical cord indices were followed up with multivariate regression model. The intergroup mean differences of the data were established using multivariate analysis variance (MANOVA) techniques. The basic multivariate regression model contains standardized regression coefficient in predicting the corresponding outcome of the response variable and is generally expressed as:

$\widehat{\boldsymbol{\gamma}} = \widehat{\boldsymbol{\beta}}_{\mathbf{0}} + \widehat{\boldsymbol{\beta}}_{\mathbf{1}}\mathbf{x}_{\mathbf{1}} + \widehat{\boldsymbol{\beta}}_{\mathbf{2}}\mathbf{x}_{\mathbf{2}} + \widehat{\boldsymbol{\beta}}_{\mathbf{3}}\mathbf{x}_{\mathbf{3}} + \ldots\ldots\ldots + \widehat{\boldsymbol{\beta}}_{\mathbf{k}}\mathbf{x}_{\mathbf{k}}$, Where ;

$\hat{y}$ is the predicted response variable.

$\hat{\beta}_1$'s are the estimated regression coefficients

$\hat{\beta}_0$ is the intercept when all of the explanatory variables are equal to zero and

x_i ($_i$ = $_1$, ……$_k$) is the estimated explanatory variable

Five models were fitted with umbilical cord response variables (Length, weight, diameter, volume and area) against six maternal explanatory variables (systolic and diastolic blood pressures, total cholesterol, triglyceride, high density and low density lipoproteins). Explanatory variables which showed statistical significant at $p < 0.05$ in the regression models were refitted into a final model.

The initial multivariate regression models indicated that, there were significant joint effects of booking diastolic blood pressure with umbilical cord length, total cholesterol with cord diameter, triglyceride with cord area, HDL-C with cord diameter and area; LDL-C with cord area (Table 21). These maternal booking explanatory variables were refitted into a final model using Type II MANOVA Test: Pillai's Test statistic produced results which showed that, booking systolic and diastolic blood pressures and triglyceride could not independently influence the outcome of umbilical cord indices. However, maternal booking total cholesterol, HDL-C and LDL-C significantly could influence umbilical cord indices (Table 22). In the final post hoc analysis, it was observed that, a unit increase in the maternal booking explanatory variables implied the following: total cholesterol could increase umbilical cord length by 2.33 units, HDL-C could result in 0.06 unit increase in cord diameter while LDL-C decreases cord length by 3.31 units (Table 23).

The influence of maternal booking total cholesterol on umbilical cord length presupposes that, increase in umbilical cord length is not only influenced by the tension theory (Lyndon *et al.*, 1994) and genetic principles (Benirschke, 2004), but also maternal pregnancy total cholesterol

levels. Available evidence suggests that, maternal cholesterol becomes the foetus's main source of cholesterol supply in early parts of pregnancy for most structural and functional developments (Kulkarni *et al.,* 2013; Zhang *et al.,* 2017). Cholesterol is essential requirement for cell proliferation, structural development, cell differentiation, cellular communication and oxysterol necessary for metabolic activity (Herrera and Ortega-Senovilla, 2010). Wharton's jelly possesses large quantities of cholesterol esters. Cholesterol has been shown to exhibit concentration – effect on membranes and as such regulates membrane permeability through conformational sequencing of the lipid chains (Romanowicz and Bankowski, 2010). These could contribute to structural changes of cord length. This is also, supported by the significant correlations found between maternal and umbilical cord blood lipids and neonatal outcome (Ghiasi *et al.,* 2014).

Significant relationship between HDL-C and umbilical cord diameters reported by the current study is very essential. Wharton's jelly characteristics determine the umbilical cord area and hence its diameter. It is a known fact that, mechanical and morphological nature of the umbilical cord is influenced by the Wharton's jelly content (Barnwal *et al.,* 2012). Physiological role played by maternal booking HDL-C in influencing the cord diameter is unknown, however, it has been reported that, HDL-C is involved in reverse transport of cholesterol, where it picks up excess cholesterol from surrounding cells and tissues and exports them to the liver for breakdown into bile substance (Chen *et al.,* 2017). For this reason, HDL-C is able to reduce cholesterol levels in the Wharton's jelly.

Wharton's jelly being amorphous with hydrated extracellular matrix contains fewer cells per gramme of tissue relative to umbilical cord arterial wall. It also has low cholesterol and large amount of free fatty acids and cholesterol esters (Romanowicz and Bankowski, 2010).

Speculatively, the high amount of HDH-C per unit area could be the reason for low cholesterol in the umbilical cord because increased cholesterol level in relation to low cell numbers renders the umbilical cord rigid and less fluid and this might affect cord functions.

Again, the interconnected cavities within the Wharton's jelly extracellular matrix function in water storage and other substances to enhance exchange of nutrients, electrolytes and gases between the umbilical cord vessels and the amniotic fluid. Consequently it has been reported that, quantitative increase in amount of Wharton's jelly in normal pregnancies corresponds with variations in gross morphology of the umbilical cord in the second and third trimesters during which maternal lipids also increase (Rostamzadeh *et al.*, 2015).

Another finding of the present study was the observation that, a unit increase in maternal booking LDL-C corresponded with a 3.31 units decrease in umbilical cord length. In as much as the exact explanation to this observation could not be offered, it is known that, factors such as tissue sensitivity to changes in metabolism, responsiveness to mechanical irritation and sensitivity to certain hormones could exert influence on organ development and consequently, causing anatomical, physiological or metabolic disturbances (Blanco *et al.*, 2011). Again, small, dense LDL particles are subfractions of LDL -C known to be more likely to generate oxidized LDL species. When tissues are exposed to oxidized LDL, it initiates a chain of endothelial responses such as inhibiting release of vasorelaxation factor (nitric oxide) which has inflammatory and antithrombotic characteristics, controls endothelial permeability and angiogenesis modulation (Mudabasappagol and Kammar, 2015). Another explanation offered for the adverse effect of increased maternal booking LDL-C levels on foetal organ systems development was multifactorial mediations of the various subclasses of LDL-C following

modified epigenetic transmission mechanisms which may be passed on to the gametes or the intrauterine environment through nutrient supply (Mendelson *et al.,* 2016). The interplay of these could promote an adverse metabolic milieu for the determination of umbilical cord indices outcome.

5.6 CONCLUSION

The mean values of placental indices observed in the current study were similar to the findings of studies of placentae from normal uncomplicated pregnancies. Also, the Pearson's correlation structure developed for maternal booking biometric and placental indices showed weak relationships. In developing multivariate models, it was found that, all maternal booking lipids (TC, TG, HDL-C, and LDL-C) could jointly predict the outcome of placental volume. However, when Pillai's text statistic was performed, none of the individual lipids could influence the outcome of the placental volume independently.

The mean values of umbilical cord indices observed in the present study were similar to the findings of previous studies conducted in the Kumasi Metropolis on normal uncomplicated pregnancies.

The Pearson's correlation structure developed for maternal booking biometric and umbilical cord indices showed weak relationships. However, strong correlations were observed between umbilical cord length and weight with maternal booking diastolic blood pressure. Umbilical cord area and eccentric cord insertion showed strong relationship with HDL-C.

In the development of multivariate models, it was found that, maternal booking diastolic blood pressure could predict umbilical cord length. Also, 'TC, HDL-C, LDL-C**l** and –TG and HDL-C'' levels could significantly predict the outcome of umbilical cord diameter and area respectively.

Maternal booking TC, HDL-C and LDL-C could influence the outcome of umbilical cord indices. Individually, a unit increase in level of maternal booking TC could results in 2.33 units increase in cord length, while HDL-C could lead to 0.06 units increase in cord diameter and LDL-C also results in 3.31 units decrease in cord length.

CHAPTER SIX

GENERAL DISUSSION

6.1 General Discussion

In this thesis, maternal sociodemographic, biometric, placental, umbilical cord and neonatal indices were described. Maternal biometric indices were modeled against neonatal, placental and umbilical cord parameters. These models were developed with the aim of developing mathematical relations to predict possible outcomes of placental, umbilical cord and neonatal indices using maternal booking visit biometric indices. This would help in early detection of pregnancies at risk of adverse outcomes for timely and optimum care.

Prior to the development of the mathematical models, two preliminary studies were conducted in chapter two and three where maternal sociodemographic parameters were related with the biometric indices and the associations between umbilical cord and placental indices were determined.

Maternal sociodemographic characteristics were compared with the booking visit biometric indices in chapter two of this thesis. The booking visit sociodemographic characteristics comprised anthropometric parameters (including weight, height, body mass index and waist circumference) and demographic characteristics such as age, parity, gestational age, religion, occupation, education, marital status and ethnicity. The booking visit biometric indices were the total cholesterol, triglyceride, low density lipoprotein, high density lipoprotein, and systolic and diastolic blood pressures. The relationship of sociodemographic with biometric indices was able to establish association between level of maternal education and total cholesterol level. Also, maternal ethnicity associated with low density lipoprotein level. Maternal weight, height, BMI

and pregnancy weight gain are known to affect birth weight outcomes because assessment of maternal nutritional status are based on these parameters (Jananthan *et al.,* 2009). For this reason, the transfer of nutrients and other essential materials from the mother to the foetus requires efficient placenta and blood pressure. It is evident that, significant positive associations exist between maternal anthropometric parameters and birth weight and placental volume (Thame *et al.,* 2000). The importance of maternal booking visit lipids cannot be over emphasized, as cholesterol transport from mother to foetus across the placental barrier in the first trimester principally contributes to foetal cholesterol needs for the synthesis of cell membranes, metabolic regulators and precursors of steroid hormones (Zhang *et al.,* 2017). It has been suggested that understanding ethnic variations in total cholesterol and triglyceride together with sociodemographic factors is necessary to strategically offer precise interventions so as to prevent pregnancy complications (Schreuder *et al.*, 2011).

In the chapter three, associations between placental and umbilical cord indices using the type of umbilical cord insertion into the placenta were determined and placental indices of neonates with normal and short cord length were compared. Significant relationships were observed for umbilical cord volume, where it correlated negatively with placental thickness for centrally inserted umbilical cords and positive correlation with placental weight in eccentrically inserted cords. Also, differences in placental indices between neonates with normal and short umbilical cord length neonates were statistically significant. Knowledge in quantitative characteristics of placental and umbilical cord indices may offer useful understanding into the causes of neonatal and maternal complications (Bimpong, 2012). Association between short and long cord lengths with increasing number of caesarian section and neonatal intensive care unit admission have been reported (Algreis *et al.,* 2016; Masarat *et al.,* 2017). It has been reported that, probable

causes of differences in placental and umbilical cord morphometric indices apart from underlying maternal medical conditions are maternal socioeconomic status, quality antenatal services, nutrition and ethnicity (Nair and Raju, 2017). Both chapters two and three therefore portray the significance of developing the mathematical models in chapters four and five.

The first model development in this thesis is on relationship between maternal booking visit biometric indices and neonatal anthropometric parameters in chapter four. Building the models started with Pearson correlation structure to establish relations among the indices. These correlations were found to be weak between neonatal anthropometric parameters and maternal biometric indices. This was followed up with multivariate multiple regression. Although, multivariate multiple regressions were built for individual neonatal anthropometric parameters against the six maternal biometric indices, it was only maternal booking visit systolic blood pressure which could predict neonatal body length at birth.

This means, a unit increase in maternal booking systolic blood pressure could lead to 0.031 unit increase in neonatal body length. Therefore knowing the value of booking systolic blood pressure, one can estimate the expected body length at birth right from the first semester using this model. During pregnancy, maternal blood pressure becomes important determinant of *utero – placental* functioning, which possibly could serve as the underlining mechanism for the inverse relationship between maternal blood pressure and birth size (Lim *et al.*, 2014).

The second batch of models developed in chapter five were on maternal booking visit biometric indices with placental and umbilical cord parameters. Typically, the models used are multivariate regression models that include pools of maternal biometric indices (systolic and diastolic blood pressures, total cholesterol, triglyceride, low density lipoprotein, high density lipoprotein). These

biometric indices were related to the placental parameters (weight, diameter, thickness, area, volume and number of cotyledons) and umbilical cord parameters (length, diameter, area, volume and weight). The results indicated that, among the various placental parameters, placental volume could be predicted by four maternal booking visit lipids (TC, TG, LDL-C and HDL-C). These had statistically significant joint effect on placental volume, though, individual multivariate regressions were developed for the placental parameters. Observations made on the umbilical cord modeling were that;

1. Maternal booking diastolic blood pressure could predict outcome of umbilical cord length in the individual multivariate regression;
2. Maternal booking TC, LDL-C and HDL-C could predict umbilical cord diameter outcome in the multivariate regression; and
3. Both booking TG and LDL-C could predict outcome of umbilical cord area in the multivariate regression.

These models when refitted to estimate the extent to which each of these biometric indices could affect the individual umbilical cord parameters, the results were that, a unit increase in maternal booking TC could lead to 2.33 units increase in umbilical cord length while a unit increase in booking LDL-C could decrease cord length by 3.31 units. A unit increase in booking HDL-C could also result in 0.06 unit increase in cord diameter.

Following the various roles play by maternal demographic, anthropometric and biometric indices in the development of foetus and maternal health, as identified by the current studies in this thesis, these models are inspired by practical considerations and can be used to investigate pregnancy outcomes in various ways. For instance, unequal distribution of maternal TG either

before or during pregnancy is associated with maternal risk of developing preeclampsia, gestational *diabetes mellitus* and neonatal pathologies such as; preterm delivery, intrauterine growth restriction or macrosomia (Cortés-Vásquez *et al*., 2018). The studies conducted in chapters two, three, four and five in this thesis are probably in line with a suggestion that, a study which incorporates maternal demographic parameters, biometric indices and placental growth factors is likely to observe large percentage of pregnancies which may be at increasing risk of developing an early onset of preeclampsia (Poon and Nicolaides, 2014).

6.2 Summary of Key Findings

With regard to the relationship between maternal sociodemographic characteristics and booking biometric indices, a significant difference in the mean TC level was observed for different stages of maternal education while the difference in mean LDL-C level among three predominant ethnic groups was also significant.

It was observed that, significant differences existed in mean TC levels among the mothers. Mean total cholesterol level was high for mothers with Primary, Junior and Senior High education, but was low for the no formal education and tertiary categories. This finding is consistent with the observation that, early pregnancy TC level associates positively with lower socioeconomic status (Oluwole *et al.*, 2014). Women with no formal education and those with tertiary education are at the extremes of the socioeconomic ladder for countries with unsatisfactory social and economic markers of which Ghana is not an exception. Therefore the finding pregnant women with no formal education who exhibited lower TC level agrees with that by Vogel *et al*. (2014). In view of this, the pregnant women with no formal education showing low TC level could not be explained in terms of influence of education on feeding practices and choice of household foods

(Mosha and Napendaeli, 2010), but on the basis of economic activities that –no formal education‖ pregnant women engage in. The nature of economic activities in Kumasi although viable, involves long hours of standing, walking, lifting and carrying heavy loads as well as tight business schedules which associate with poor perinatal outcomes including preterm delivery and low birth weight (Naidoo *et al.,* 2011). This indirectly improves physical activity of pregnant women and in turn cuts down certain negative effects of low education on cholesterol biomarkers.

Also, the other aspect of the present finding where tertiary educated pregnant women showed low TC level is in support of finding by Lara and Amigo (2018), which reported that, pregnant women with low education level showed high or worse lipid profile levels compared to their highly educated counterparts, although the authors reported no statistically significant difference. It has been hypothesized that, a highly educated woman is enlightened and practises healthy behaviour, enjoys better employment with good income levels, she is also aware of prevailing social and psychosocial factors leading to better health and management of lipid profile level (Egerter *et al.*, 2011). The differences in findings between the present study and other studies elsewhere could be appreciated in terms of economic advancement which prevails among the settings within which these two studies were conducted.

Also, there was statistically significant difference in the mean LDL-C level with the Fantes having higher LDL – C than Ashantis and the Northerners. Ethnic variations in lipid profile levels have been well studied, where findings from these studies ascribed genetics, changes in *oestrogen* content, demographic, environmental and behavioural factors such as smoking, alcoholism, physical activity and dietary patterns to contribute substantially to serum lipid levels (Bhalodkar *et al.,* 2005; Godsland *et al.,* 2007; Agongo *et al.,* 2018). The present observation

could be explained on the basis of environmental and behavioural factors together with genetic concept although the study is conducted among Ghanaian population. Genetic variation accounting for the present finding could not be ruled out because Agongo *et al.* (2018) reported of ethno-linguistic sub-group differences in lipid levels even within the same ethnic group. On the environmental and behavioural factors, it is obvious that, the Fantes and Ashantis are more characterized by westernized lifestyles as most of their communities are urbanized while Northerners with majority of their communities classified as rural are known to be physically active and rely mostly on vegetarian diet (Kuutiero *et al.,* 2011). Earlier studies which compared lipid profiles among urban and rural population in Ghana recorded significant higher TC and LDL-C levels in the urban populace than their rural counterparts and assigned western lifestyle including dietary patterns, sedentary jobs and reduced physical activity as the cause of rise in these lipid levels (Kodaman *et al.,* 2016; Agongo *et al.,* 2018). Serum lipid levels have been found to strongly and positively associate with body fat distribution particularly visceral adipose tissue. African ancestry had shown lower visceral adipose tissue compared to their American and European counterparts which might explain low cholesterol and triglyceride levels among Ghanaian population (Bentley and Rotimi, 2017). It has been clearly concluded that, Ghanaian women generally have low levels of cholesterol and triglyceride compared to Dutch, Moroccan or African – Caribbean women (Schreuder *et al.,* 2011). Bentley and Rotimi (2017) observed that, the West African individual is leaner and physically active relative to the African American colleague. However, with high rate of westernization and urbanization, these inherent characteristics unique to the African, especially Ghanaians are gradually being modified or getting extinct.

Another study prior to modeling was undertaken to compare placental indices among neonates with short and normal umbilical cord lengths. The study observed significant differences in placental indices between neonates with normal and short cord length as follows: placental weight 518.60 ± 6.32 g and 486.50 ± 10.22 g, p = 0.0090; diameter 19.67 ± 0.13 cm and 18.75 ± 0.26 cm, p = 0.0009; and area 306.80 ± 4.20 cm^2 and 279.9 ± 8.17 cm^2, p = 0.0018 and number of cotyledons of 18.21 ± 0.16 and 15.47 ± 0.38, p = 0.0001 respectively. However, no significant differences were observed for placental thickness and volume. Bimpong (2012) found that placental weight for normal cord length neonates was heavy compared to that of short cord length counterparts and speculated that, both umbilical cord and placenta may be controlled by similar regulatory mechanisms. In addition, findings from other studies reported significantly positive relationship between normal umbilical cord length and placental weight (Olumuyiwa and Ogunlaja, 2015; Algreis *et al.,* 2016). Placental thickness not showing significant difference between normal and short cord length neonates has also been reported in other studies where significant relations were established between placental thickness and gestational age (Ohagwu *et al.,* 2009; Kaushal1 *et al.,* 2015; Elangovan and Raviraj, 2016). It seems no particular study has paid attention to the relationship between placental and umbilical cord indices, yet it is the conduit along which the functional interaction between the foetus and placenta is established. Therefore, the findings of the present study could serve as a prognostic marker in providing information on placental morphometric characteristics once cord length is measured prenatally with ultrasound and after postnatal measurement.

Another aspect of this study was to establish the relationship between placental and umbilical cord indices based on the type of cord insertion into the placenta. In the present study, a

significant negative relationship existed between placental thickness and umbilical cord volume when cord inserts centrally into the placenta (R^2 = -0.188, $p < 0.05$). On the other hand, a significant positive relation was observed between placental weight and umbilical cord volume for eccentric cord insertions (R^2 = 0.150, p = 0.0394). This observation also adds to the varied findings of studies examining relationship between placental and umbilical cord indices with respect to cord insertion. Tsegah and Asante (2018) found positive relationship between placental index and umbilical cord length with eccentric cord insertion while significant association between umbilical cord vessel diameters with placental weight has been reported with central insertion (Petekkaya1 *et al.,* 2011). These results point to the fact that, where the umbilical cord inserts into the placenta may not have any major influence on morphological development of the placenta.

In developing predictive models for the outcome of neonatal characteristics using maternal booking biometric indices, four multiple regression models were fitted. After which post hoc analysis was performed by refitting the models to establish mathematical relationship that distinguishes one maternal explanatory variable from the other on the neonatal response variables. It was found that, maternal systolic blood pressure could independently predict body length at birth according to the model equation:

$\mathbf{Y_{length} = 35.39 + 0.03M_{systolic,}}$ (p = 0.0340);

Where Y_{length} is the neonatal body length and

$M_{systolic}$ is the maternal systolic blood pressure.

This implies that a unit increase in maternal booking systolic blood pressure results in 0.03 unit increase in body length at birth. The present study finding is the first of its kind as no other study has related maternal booking biometric indices with all neonatal outcome indices with the exception of maternal booking BMI and weight gained with birth weight (Du *et al.,* 2016). On the other hand, maternal weight and occupation have been found to significantly associate with neonatal body length (Kierans *et al.,* 2007; Dwivedi and Verma, 2015). Body length is an expression of differential growth of the head, trunk and long bones in the legs which could serve as an important prognostic and aetiologic index in examining intrauterine quality of life (Kierans *et al.,* 2007; Qaiser and Omair, 2016). Therefore, this current study finding is worthy of consideration when developing guidelines for maternal and perinatal health.

In respect of placental indices modelling with maternal booking biometric parameters, the results showed that, all booking lipids (TC, TG, HDL-C, and LDL-C) could jointly predict placental volume outcome in a multivariate regression model:

$\mathbf{P_V = 647.18 + 96.27M_{TC} - 44.76M_{TG} - 88.66M_{HDL} - 91.39M_{LDL}}$, ($p < 0.05$); where P_V is the predicted placental volume,

M_{TC} is maternal total cholesterol;

M_{TG} is maternal triglyceride,

M_{HDL} is the maternal high density lipoproteins and

M_{LDL} is maternal low density lipoprotein

However, in a post hoc analysis, none of these lipids could independently influence the outcome of placental volume.

The present study could not clearly explain the mechanisms underlying predictive power of the maternal booking lipids on the outcome of placental volume. Notwithstanding, placenta as a key

organ in transferring cholesterols from mother to the developing foetus requires capacity to accommodate the availability and quantities of cholesterol transporters. It has been reported that, significant levels of low density lipoprotein receptors (LDLR), very low density lipoprotein receptors (VLDLR), scavenger receptor class B type I (SR B1) and Apo-protein B-100 (ApoB-100) which are involved in transportation of cholesterol to the foetus are expressed by the placental trophoblast (Zeng *et al.*, 2017). Also, direct association between abnormal placental morphometry and dysfunctional early first trimester maternal serum lipids has been observed (Odibo *et al.*, 2006). Following paucity of information on relationship between placental volume and maternal booking lipids, it could be speculated that, placental volume may influence efficiency of maternal serum cholesterol transport to the foetus and hence, foetal dependency on maternal cholesterol supply in early first trimester.

Modelling the umbilical cord parameters with maternal booking biometric indices showed that, umbilical cord length could be predicted according to the following multivariate regression models:

$\mathbf{Y_{Length} = 29.49 + 0.10M_{DBP}\ (p < 0.05);}$

where Y_{Length} is umbilical cord length,

M_{DSP} is maternal booking diastolic blood pressure.

$\mathbf{Y_{length} = 35.81 + 2.33M_{Cholesterol} - 3.31M_{LDL.}}$ ($p < 0.05$).

Where; Y_{Length} is the predicted umbilical cord length.

$\mathbf{M_{Cholesterol}}$ is maternal booking TC

$\mathbf{M_{LDL}}$ is maternal booking LDL-C

These findings of the present study where maternal booking TC, LDL-C and diastolic blood pressure could influence umbilical cord length and presuppose that, increase in umbilical cord length is not only influenced by the tension theory (Lyndon *et al.,* 1994) and genetic principles (Benirschke, 2004), but also maternal pregnancy total cholesterol levels and diastolic blood pressure. Total cholesterol exhibits concentration – effect on membranes and therefore regulates membrane permeability through conformational sequencing of the lipid chains (Romanowicz and Bankowski, 2010). The Wharton's jelly contains large amount of cholesterol esters which could contribute to structural changes in umbilical cord length. This is also supported by the significant correlations found between maternal and umbilical cord blood lipids and neonatal outcome (Ghiasi *et al.,* 2014).

The negative influence of maternal booking LDL-C on cord length could be attributed to tissue sensitivity of the cord endothelial cells to LDL-C. The small dense LDL subfractions of LDL-C generate oxidized LDL species which when it comes into direct contact with tissue, initiates chain of endothelial responses. This has the ability to down regulate endothelial permeability and angiogenesis modulation (Mudabasappagol and Kammar, 2015). Tissue sensitivity to the oxidized species of LDL may modify organ development through anatomical, physiological or metabolic disturbances (Blanco *et al.*, 2011).

The multivariate regression for cord diameter with maternal booking TC, HDL-C and LDL-C is expressed in the relation below:

$$\mathbf{Y_{Diameter} = 1.01 - 0.14M_{TC} + 0.16M_{HDL} + 0.13M_{LDL}\ (p < 0.05)};$$

where $Y_{Diameter}$ is umbilical cord diameter,

M_{TC} is maternal booking total cholesterol,

M_{HDL} is maternal booking high density lipoprotein and

M_{LDL} is maternal booking low density lipoprotein

Further post hoc analysis using descriptive discriminant analysis (DDA) also showed that, maternal booking HDL-C could independently predict outcome of umbilical and diameter according to the following refitted model:

$\mathbf{Y_{Diameter} = 1.02 + 0.06M_{HDL}}$ ($p < 0.05$).

Where $Y_{Diameter}$ is the predicted umbilical cord area,

$\mathbf{M_{HDL}}$ is maternal booking HDL-C

This means that, a unit increase in maternal booking HDL-C could result in 0.06 unit increment in umbilical cord diameter. It has been observed that, HDL-C is involved in reverse transport of cholesterol, where it cleans up excess cholesterol from surrounding cells and tissues and transport them to the liver for breakdown into bile substance (Chen *et al.*, 2017). For this reason, HDL-C is able to reduce cholesterol levels in the Wharton's jelly. Another evidence also points to the fact that, quantitative increase in amount of Wharton's jelly in normal pregnancies corresponds with alterations in gross morphology of the umbilical cord in the second and third trimesters during which maternal lipids also increase in level (Rostamzadeh *et al.*, 2015).

Also, the study established multivariate regression relationship between umbilical cord area with maternal booking TG and LDL-C as represented in the equation below:

$\mathbf{Y_{Area} = 49.06 + 9.99M_{TG} + 25.34M_{HDL}\ (p < 0.05)}$;

Where Y_{Area} is umbilical cord area,

M_{TC} is maternal booking total cholesterol and

M_{LDL} is maternal booking low density lipoprotein.

However, post hoc analysis of maternal booking biometric indices did not produce significant influence on umbilical cord area. Umbilical cord area is derived from the cord diameter; hence, physiological and metabolic influence on the cord diameter also influences the cord area.

6.3 CONCLUSION

The levels of maternal booking total cholesterol among pregnant women could differ with their educational backgrounds. Also, ethnicity could affect the levels of maternal booking LDL – C. Neonates with normal umbilical cord lengths had better outcome of placental indices than the short cord length neonates. Again, positive correlation exists between placental weight and umbilical cord volume when umbilical cord insertion is eccentric while cord volume relates negatively with placental thickness when cord insertion is central.

From the neonatal modelling, a unit increase in maternal booking systolic blood pressure could lead to 0.031unit increase in length at birth.

The placental modeling observed that, all the maternal booking lipids could predict placental volume in a multivariate regression, but could not independently influence outcome of placental volume.

In the umbilical cord models, a unit increase in maternal booking TC could lead to 2.33 units increase in cord length and a unit increase in LDL-C results in 3.31 units decrease in cord length. Also, a unit increase in maternal booking HDL-C ends up increasing cord diameter by 0.06 unit.

6.4 STRENGTHS AND LIMITATIONS OF THE STUDY

The strengths of this current study include the fact that, this thesis has added new information to the body of literature that provides quantitative description of influence of maternal booking biometric parameters on perinatal outcome. It also advances knowledge on developing accurate, simple to use and low cost but effective approaches in early screening for pregnancies at risk of adverse perinatal consequences. Also, the use of multivariate analysis in this study population has led to the identification of independent predictive value of each placental, umbilical cord and neonatal index. Again, the mathematical models with their high predictive abilities can be applied even in the deprived health facilities in Ghana once a calculator is available. This simple and noninvasive scientific approach would help in intervening appropriately, and also reduce unnecessary and potentially harmful interventions in pregnancies which do not even need such treatments.

Among the limitations of this study are:

(1). The study was not able to take into account all known potential risk factors in the modeling, since it was carried out among healthy participants from a single health facility. Therefore, the findings have no external validation.

(2). The development of the mathematical models was also challenged by insufficient experimental data crucial for validation of the models.

(3). The study did not adjust for the measured maternal serum concentrations in order to correct for some of the maternal and pregnancy characteristics such as smoking, alcohol intake, substance abuse and night clubs, machine and reagents used and other potential confounders which certainly could affect the outcome of the results.

(4). Maternal booking non-fasting lipids were measured once and this could overestimate the results for the cholesterols and triglyceride because values of these lipids are known to be influenced by normal food intake.

6.5 RECOMMENDATIONS FOR FUTURE STUDIES

A future prospective population –based study of large sample size of pregnant women is needed to validate the predictive power of the modeling approach which may integrate maternal booking socioeconomic and biometric characteristics together with obstetric history in order to identify pregnancies at risk in the first trimester.

Also, conducting further studies with larger sample size across the sixteen regions in Ghana among pregnant women with diverse ethnic and socioeconomic backgrounds at various stages of pregnancy is required to establish reference values for neonatal, umbilical cord and placental indices rather than relying on foreign reference values which may not give a true reflection of the situation in Ghana.

A population based study of pregnant women that uses sensitive and high accuracy modern laboratory equipment and standards is needed to establish reference values for maternal pregnancy lipids which could be considered as normal at different stages of gestation.

REFERENCES

Abaidoo, C. S., Boateng, K. A. and Warren, M. A. (2008). Morphological variations of the "Baby's supply line*". Journal of Science and Technology*, **28**: 1- 9.

Abramowicz, J. and Sheiner, E. (2008). Ultrasound of the placenta: a systematic approach. Part I: Imaging. *Placenta*, **29**: 225–240.

Acharya, G., Sonesson, S.-E., Flo, K., Rasanen, J. and Odibo, A. (2016). Hemodynamic aspects of normal human feto-placental (umbilical) circulation. *Acta Obstetricia et Gynecologica Scandinavica*, **95**: 672–682.

Addo, V. (2010). Body Mass Index, Weight Gain During Pregnancy And Obstetric Outcomes. *Ghana Medical Journal*, **44**: 64-69.

Adebami, O. J., Owa, J. A., Oyedeji, G. A., Oyelami, O. A. and Omoniyi-Esan, G. O. (2007). Associations between placental and cord blood malaria infection and fetal malnutrition in an area of malaria holoendemicity. *American Journal of Tropical Medicine and Hyg*iene, **77:** 209-213.

Aderinsola, O. J. and Joseph, A. O. (2007). Looking for the best indicator fetal malnutrition, an overview. *Nigeria Journal of Paediatric*, **4**(1): 111-117.

Adesina, K. T., Ogunlaja, O. O., Aboyeji, A. P., Akande, H. J., Adeniran, A. S., Olarinoye, A. and Fawola, A. A. (2016). Relationship between gross placental characteristics and perinatal outcome of low-risk singleton deliveries. *Nigerian Postgraduate Medical Journal*, **23**: 191 - 195.

Afodun, A., Ajao, M. and Enaibe, B. (2015). Placental Anthropometric Features: Maternal and Neonate Characteristics in North Central Nigeria. *Advances in Anatomy*, pp. 1-6.

Afroze, K. H., Prabha, S., Chandrakala, V. and Deepakpak, M. (2017). Sonographic Estimation of Umbilical Cord Cross-section Area and its Reference Value in Normal Pregnancy. *Journal of Clinical and Diagnostic Research*, **11**: AC04-AC06.

Agarwal, G., Saini, P., Pankaj, J., Pandey, L. and Jain, A. (2015). Morphological study of placenta in normal and hypertensive pregnancies. *International Archives of Integrated Medicine*, **2**: 121-128.

Aghaie, Z., Hajian, S. and Abdi, F. (2018). The relationship between lipid profiles in pregnancy and preterm delivery: a systematic review. *Biomedical Research and Therapy*, **5**: 2590-2609.

Agongo, G., Nonterah, A. E., Debpuur, C., Amenga-Etego, L., Ali, S., Oduro, A., Crowther, N. J. and Ramsay, M. (2018). The burden of dyslipidaemia and factors associated with lipid levels among adults in rural northern Ghana: An AWI-Gen sub-study. *PLoS ONE*, **13**: e0206326.

Ajiboye, O. and Adibayo, K. (2012). Socio-Cultural Factors Affecting Pregnancy Outcome Among The Ogu Speaking People Of Badagry Area Of Lagos State, Nigeria. *International Journal of Humanities and Social Science,* **2**: 133-144.

Akshara, V., Ramakrishnan, P., Chitra, S., Kumar, S., Senthil, K. S. and Seema, V. (2018). Morphology and the morphometric parameters ts of hypertensive and normotensive placenta. *Biomedical Research***, 29**: 3522-3525.

Aletayeb, S., Dehdashtian, M., Aminzadehm, M., Moghaddam, A.-R. E., Mortazavi, M., Malamiri, R., Habibzadeh, M. and Javaherizadeh, H. (2013). Correlation between umbilical cord blood lipid profile and neonatal birth weight. *Pediatria Polska*, **88**: 521 – 525.

Algreisi, F., Brown, R., Shrim, A., Albasri, S., Shamarani, H. and AlZoubiadi, A. (2016). Effect of long and short umbilical cord on perinatal outcome. *International Journal of Reproduction, Contraception, Obstetrics and Gynaecology*, **5**: 4228-4231.

American College of Cardiology (2017). 2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. *Journal of American College of Cardiology*, pp.1 – 28.

American Heart Association (2019). Measurement of Blood Pressure in Humans: A Scientific Statement From the American Heart Association. *Hypertension*, **73**: e35–e66.

Amiel-Tison, C. (1994). The newborn infant: one brain for life. Editions Inserm.

Amoakoh-Coleman, M., Ogum-Alangea, D., Modey-Amoah, E., Ntumy, M., Adanu, R. and Oppong, S. (2017). Blood pressure patterns and body mass index status in pregnancy: An assessment among women reporting for antenatal care at the Korle-Bu Teaching hospital, Ghana. *PLoS ONE*, **12**: e0188671.

Amosu, A. and Degun, A. (2014). Impact of maternal nutrition on birth weight of babies. *Biomedical Research*, **25**: 75-78.

Amosu, A. M., Degun, A. M. and Ter Goon, D. (2014). Maternal socio-demographic characteristics as correlates of newborn birth weight in urban Abeokuta, Nigeria. *Biomedical Research*, **25**: 612-616.

Anjum, A., Suseelamma, D., Saritha, S., Ramani, T. V. and Nagajyothi D. (2015). Study of morphological variations of 50 placentae with umbilical cords and its developmental relevance. *International Journal of Anatomy and Research*, **3**: 1259-1266.

Antoniou, E., Derom, J., Thiery, E., Fowler, T., Southwood, T. R. and Zeegers1, P. (2011). The Influence of Genetic and Environmental Factors on the Aetiology of the Human Umbilical Cord: The East Flanders Prospective Twin Survey. *The Society for the study of Reproduction,*

Appiah, P. (2009). Relationship between the morphology of placenta, Umbilical cord and Perinatal Outcome. In: Anatomy. Kumasi: Kwame Nkrumah University of Science and Technology.

Arthur, F. K., Adu-Frimpong, M., Osei-Yeboah, J., Mensah, F. O. and Owusu, L. (2012). Prediction of metabolic syndrome among postmenopausal Ghanaian women using obesity and atherogenic markers. *Lipids in Health and Disease*, **11**(1): 101.

Aryee, P., Helegbe, G., Baah, J., Sarfo-Asante, R. and Quist-Therson, R. (2013). Prevalence and Risk Factors for Overweight and Obesity among Nurses in the Tamale Metropolis of Ghana. *Journal of Medical and Biomedical Sciences*, **2**: 13-23.

Asah-Opoku, K., Ameme, D. K., Yawson, A., Guure, C. B., Aduama, D. E. M., Mumuni, K. and Maya, E. T. (2019). Adherence to the recommended timing of focused antenatal care in the Accra Metropolitan Area, Ghana. *The Pan African Medical Journal*, **33**: 1–15.

Asamoah, B. and Agardh, A. (2017). Inequality trends in maternal health services for young Ghanaian women with childbirth history between 2003 and 2014. *British Medical Journal Open*, **7:** e011663.

Asgharnia, M., Esmailpour, N., Poorghorban, M. and Atrkar-Roshan, Z. (2008). Placental weight and its association with maternal and neonatal characteristics. *Acta Medica Iranica*, **46**: 467-472.

Auger, N., Daniel, M., Platt, R., Luo, Z.-C., Wu, Y. and Choinière, R. (2008). The joint influence of marital status, interpregnancy interval, and neighborhood on small-for-gestational age birth: a retrospective cohort study. *BioMed Central: Pregnancy and Childbirth*, **8**:1-9.

Ayuba, I. and Ibukun, O. (2012). Socio-demographic determinants of teenage pregnancy in the Niger Delta of Nigeria. *Journal of Obstetrics and Gynaecology*, **2**: 239-243.

Aziato, L., Odai, P. and Omenyo, C. (2016). Religious beliefs and practices in pregnancy and labour: an inductive qualitative study among post-partum women in Ghana. *BioMed Central: Pregnancy and Childbirth*, **16**: 1-10.

Baergen, R., Malicki, D., Behling, C. and Benirschke, K. (2001). Morbidity, mortality and placental pathology in excessively long umbilical cords: retrospective study. *Paediatric Developmental Pathology*, **4**: 144-153.

Baeyens, A. (2012). Kumasi, Ghana: Critical Study of an African Urban Structure. In. Holland: Universeit Gent. pp.1-91.

Baghel, P., Bahel, V., Paramhans, R., Sachdev, P. and Onkar, S. (2015). Correlation of Placental thickness with Gestational Age and Foetal Outcome. *Indian Journal of Neonatal Medicine and Research*, **3**: 19-24.

Bakker, R., Steegers, E., Hofman, A. and Jaddoe, V. (2011). Blood Pressure in Different Gestational Trimesters, Fetal Growth, and the Risk of Adverse Birth Outcomes: The Generation R Study. *American Journal of Epidemiology,* **174**: 797-806.

Balayla, J., Azoulay, L. and Abenhaim, H. (2011). Maternal Marital Status and the Risk of Stillbirth and Infant Death: A Population-Based Cohort Study on 40 Million Births in the United States. *Women's Health Issues*, **21**: 361–365.

Balihallimath, R., Shirol, V., Tyagi, N., Gan, A. and Desai, S. (2015). Maternal determinants of placental morphometry and birth weight. *International Journal of Medical Science and Public Health*, **4**: 508-515.

Balkawade, N. and Shinde, M. (2012). Study of Length of Umbilical Cord and Fetal Outcome: A Study of 1,000 Deliveries. *The Journal of Obstetrics and Gynaecology of India,* **62**: 520–525.

Balla, E. A. A., Ahmed, M. S., Ayad, C. E. and Ahmed, A. S. (2014). Prediction of fetal growth by measuring the placental thickness using ultrasonography. *Journal of Gynaecology and Obstetrics*, ***2***(2), 26-31.

Bancroft, J. D. and Gamble, M. (2008). Theory and practice of histological techniques, 6th ed. Edinburgh: Churchill Livingstone.

Baptiste-Roberts1, K., Salafia, C., Nicholson, W., Duggan, A., Wang, N. and Brancati1, F. (2009). Gross placental measures and childhood growth. *Journal of Maternal – Foetal and Neonatal Medicine,* **22**: 13-23.

Barham, D. and Trinder, P. (1972). An improved colour reagent for the determination of blood glucose by the oxidase system. *Analyst,* **97**(1151): 142-145.

Barker, D. J., Thornburg, K. L., Osmond, C., Kajantie, E. and Eriksson, J. G. (2010b). The surface area of the placenta and hypertension in the offspring in later life. *International Journal of Developmental Biology*, **54**: 525-530.

Barker, D., Gelow, J., Thornburg1, K., Osmond, C., Kajantie, E. and Eriksson, J. (2010a). The early origins of chronic heart failure: impaired placental growth and initiation of nsulin resistance in childhood. *European Journal of Heart Failure,* **12**: 819–825.

Barker, D., Osmond1, C., Grant, S., Thornburg, K., Cooper, C., Ring, S. and Smith, G. (2013). Maternal cotyledons at birth predict blood pressure in childhood. *Placenta*, **34**: 672–675.

Barnwal, M., Rathi, S., Chhabra, S. and Nanda, S. (2012). Histomorphometry of Umbilical Cord and its Vessels in Pre-Eclampsia as Compared to Normal Pregnancies. *National Journal of Obstetric and Gynaecology*, **7**: 28-32.

Baskaradoss, J., Geevarghese, A. and Al Dosari, A. A. (2012). Causes of Adverse Pregnancy Outcomes and the Role of Maternal Periodontal Status – A Review of the Literature. *The Open Dentistry Journal*, **6**: 79-84.

Bayhan, G., Koçyigit, Y., Atamer, A., Atamer, Y. and Akkus, Z. (2005). Potential atherogenic roles of lipids, lipoprotein(a) and lipid peroxidation in preeclampsia. *Gynaecology and Endocrinology*, **21**: 1-6.

Benirschke, K. (2004). The Umbilical Cord. *NeoReviews*, **5**: 134-141.

Benirschke, K. and Kaufmann, P. (1995). Anatomy and Pathology of the umbilical cord and major foetal vessels. Pathology of human placenta 28th edition. New York: Springer, pp.335-397.

Benirschke, K. and Kaufmann, P. (2000). Pathology of the Human Placenta, 4th edition, New York: Springer.

Benirschke, K., Burton, G. J. and Baergen, R. N. (2012). Pathology of Human Placenta. New York: Springer.

Benirschke, K., Kaufmann, P. and Baergen, R. (2006). Pathology of the human placenta. New York: Springer Science and Business Media, 5th edition.

Benkeser, R., Biritwum, R. and Hill, A. (2012). Prevalence of Overweight And Obesity And Perception Of Healthy And Desirable Body Size In Urban, Ghanaian Women. *Ghana Medical Journal*, **46**: 66-75.

Bentley, A. and Rotimi, C. (2017). Interethnic Differences in Serum Lipids and Implications for Cardiometabolic Disease Risk in African Ancestry Populations. *Global Heart*, **12**: 141-150.

Bhalodkar, N., Blum, S., Rana, T., Kitchappa, R., Bhalodkar, A. and Enas, E. (2005). Comparison of highdensity and low-density lipoprotein cholesterol subclasses and sizes in Asian Indian women with Caucasian women from the Framingham Offspring Study. *Clinical Cardiology*, **28**: 247-251.

Bhatia, P. and Chhabra, S. (2018). Physiological and anatomical changes of pregnancy: Implications for anaesthesia. *Indian Journal of Anaesthesia*, **62**: 651-657.

Bhatt, R. V., Modi, N. S. and Acharya, P. T. (1967). Height and reproductive performance. *Journal of Obstetrics and Gynaecology of India*, **17**: 75-79.

Biga, L., Dawson, S., Harwell, A., Hopkins, R., Kaufmann, J., LeMaster, M., Matern, P., Morrison-Graham, K., Quick, D. and Runyeon, J. (2016). Anatomy and Physiology. In: Whittier L, editor. Oregon State University, p 2110.

Bilszta, J., Tang, M., Meyer, D., Milgrom, J., Ericksen, J. and Buist, A. (2008). Single motherhood versus poor partner relationship: outcomes for antenatal mental health. *Australian and New Zealand Journal of Psychiatry*, **42**: 56-65.

Bimpong, S. (2012). Quantitative Evaluation of Umbilical Cord and Placental Indices and Pregnancy Outcome. In: Department of Theoretical and Applied Biology. Ghana: Kwmae Nkrumah University of Science and Technology, Kumasi, p 123.

Bimpong, S., Abaidoo, C. S., Ohene-Djan, A. and Tetteh, J. (2019). Morphometric characterization of umbilical cord vessels and neonatal outcome. *International Journal of Anatomy and Research*, **7**: 6050-6058.

Blanco, M., Vega, H., Guerri-Guttenberg, R., Giuliano, R., Grana, D., Azzato, F. and Milei, J. (2011). Histopathology and histomorphometry of umbilical cord blood vessels. Findings in normal and high risk pregnancies. *Artery Research*, pp. 1-9.

Blomberg, M., Birch, T. R. and Kjølhede, P. (2014). Impact of maternal age on obstetric and neonatal outcome with emphasis on primiparous adolescents and older women: a Swedish Medical Birth Register Study. *British Medicalm Journal*, **4**: e005840.

Boghossian, N., Mendola, P., Liu, A., Robledo, C. and Yeung, E. (2017). Maternal serum markers of lipid metabolism in relation to neonatal anthropometry. *Journal of Perinatology*, **37**: 629–635.

Bolanle, A. (2017). Waist Circumference Disparity: A Comparison of American, European and Asian Cut Offs Among Africans. *Journal of Applied Biotechnology and Bioengineering*, **4**: 1-4.

Borges, K., Hassan, N., Hussain, R. and Akhtar, M. (2013). Effects of variation in umbilical artery resistive index on placental morphology and birth weight in pregnancy induced hypertension. *Journal of Ayub Medical College Abbottabad***, 25**: 23-26.

Bratati, B. and Hazra, S. (2004). Socio-demographic determinants of Pregnancy Wastage. *Journal of Obstetrics and Gynaecology*, **54**(4): 355-360.

Brett, K., Ferraro, Z., Yockell-Lelievre, J., Gruslin, A. and Adamo, K. (2014). Maternal–Foetal Nutrient Transport in Pregnancy Pathologies: The Role of the Placenta. *International Journal of Molecular Sciences*, **15**: 16153-16185.

Brodsky, D., Christou, H. and Brodsky, D. (2004). Current concepts in intrauterine growth restriction. *Journal of Intensive Care Medicine*, **19**: 307-319.

Bruch, J. F., Sibony, O., Benali, K., Challier, J. C., Blot, P. and Nessmann, C. (1997). Computerized microscope morphometry of umbilical vessels from pregnancies with intrauterine growth retardation and abnormal umbilical artery Doppler. *Human Pathology*, **28**: 1139-1145.

Burdette, A., Weeks, J., Hill, T. and Eberstein, I. (2012). Maternal religious attendance and low birth weight. *Social Science and Medicine*, **74**: 1961-1967.

Burton, G., Charnock-Jones, D. and Jauniaux, E. (2009). Regulation of vascular growth and function in the human placenta. *Reproduction*, **138**: 895–902.

Camerota, M. and Bollen, K. (2016). Birth Weight, Birth Length, and Gestational Age as Indicators of Favorable Fetal Growth Conditions in a US Sample. *PLoS ONE*, **11**: 1-15.

Cape Town Metropole Paediatric Interest Group (2009). Anthropometry Guideline in Paediatrics. In. pp 1-26.

Casas, M., Cordier, S., Martínez, D., Barros, H., Bonde, J. P., Burdorf, A. and Fernandez, M. F. (2015). Maternal occupation during pregnancy, birth weight, and length of gestation: combined analysis of 13 European birth cohorts. *Scandinavian Journal of Work, Environment and Health*. 384-396.

Casola, G., Scheible, W. and Leopold, G. R. (1985). Large umbilical cord: a normal finding in some fetuses. *Radiology*, **156**: 181-182.

Catov, J., Ness, R., Wellons, M., Jacobs, D., Roberts, J. and Gunderson, E. (2010). Prepregnancy lipids related to preterm birth risk: the coronary artery risk development in young adults study. *Journal of Clinical Endocrinology and Metabolism*, **95**: 3711–3718.

Chaddhaa, V., Vierob, C. S., Huppertzd, B. and Kingdom, J. (2004). Developmental biology of the placenta and the origins of placental insufficiency. *Seminars in Foetal and Neonatal Medicine*, **9**: 357-369.

Chang, J., Mulgrew, A. and Salafia, C. (2012). Characterizing Placental Surface Shape with a High-Dimensional Shape Descriptor. *Applied Mathematics*, **3**: 954-968.

Chen, W., Weiwei, Z., Yumei, W., Rina, S., Hui, F., Li, L. and Yang, H. (2016). The Predictive Effects of Early Pregnancy Lipid Profiles and Fasting Glucose on the Risk of Gestational *diabetes mellitus* Stratified by Body Mass Index. *Journal of Diabetes Research*, **2016**: 1-8.

Chen, X., Scholl, T., Stein, T., Steer, R. and Williams, K. (2017). Maternal Circulating Lipid Profile during Early Pregnancy: Racial/Ethnic Differences and Association with Spontaneous Preterm Delivery. *Nutrients*, **9**: 1-12.

Choudhury, M. and Friedman, J. (2012). Epigenetics and microRNAs in preeclampsia. *Clinical Experiment in Hypertension*, **34**: 334–341.

Clausen, T., Burski, T. K., Øyen, N., Godang, K., Bollerslev, J. and Henriksen, T. (2005). Maternal anthropometric and metabolic factors in the first half of pregnancy and risk of neonatal macrosomia in term pregnancies. A prospective study. *European Journal of Endocrinology*, **153(**6): 887-894.

Coall, D., Charles, A. and Salafia, C. (2009). Gross placental structure in a low - risk population of singleton, term, first-born infants. *Paediatric Developmental Pathology,* **12**: 200-210.

Collins, J. (1992). The short umbilical cord. *American Journal of Obstetrics and Gynaecology,* **166**: 268-269.

Collins, J. (2014). Umbilical cord accidents and legal implications. *Seminar in Foetal Neonatal Medicine,* **19**: 285 – 289.

Collins, J. H. (2002). Umbilical cord accidents: human studies. In *Seminars in Perinatology* **26**(1): 79-82.

Collins, J. H., Collins, C. L. and Collins, C. C. (2010). Umbilical Cord Accidents. Online*). A vailablefrom: http://www. preginst. com/UCA_2010. pdf (September 03, 2010)..*

Cortés-Vásquez, J., Noreña, I. and Mockus, I. (2018). Hypertriglyceridemia and adverse outcomes during pregnancy. *Revista de la Facultad de Medicina*, **66**: 247-253.

Coward, K. and Wells, D. (2013). Text Book of Clinical Embryology. United States of America: Cambridge University Press.

Cox, R. R. and García-Palmieri, M. (1990). Cholesterol, Triglycerides, and associated Lipoproteins.

Crocker, J. and Burnett, D. (2005). The science of laboratory diagnosis.2nd ed. John Wiley and Sons.

Cunningham, F., Hauth, J., Leveno, K., Gilstrap, L., Bloom, S. and Wenstrom, K. (2005). Williams Obstetrics, 22nd ed. United States of America.: McGraw-Hill Companies, Inc.

Day, P., Ntani, G., Crozier, S., Mahon, P., Nskip, H., Cooper, C., Harvey, N., Godfrey, K., Hanson, M., Lewis, R. and Cleal, J. (2015). Maternal Factors Are Associated with the Expression of Placental Genes Involved in Amino Acid Metabolism and Transport. *PLoS ONE*, **10**: 1-17.

De Carvalho, P., Accioly, E., Chagas, C., Portela, E., Da Silva, C. and Saunders, Y. C. (2009). Birth weight variation according to maternal characteristics and gestational weight gain in Brazilian women. *Nutricion Hospitalaria*, **24**: 207-212.

Denison, F., Norwood, P., Bhattacharya, S., Duffy, A., Mahmood, T., Morris, C., Raja, E., Norman, J., Lee, A. and Scotland, G. (2014). Association between maternal body mass index during pregnancy, short-term morbidity, and increased health service costs: a population-based study. *British Journal of Obstetric and Gynaecology*, **121**: 72–82.

Di Naro, E., Ghezzi, F., Raio, L., Franchi, M., D'Addario, V., Lanzillotti, G. and Schneider, H. (2001). Umbilical vein blood flow in fetuses with normal and lean umbilical cord. *Ultrasound* in *Obstetrics* and *Gynaecology,* **17**: 224-228.

Dobbelsteyn, C. J., Joffres, M. R., MacLean, D. R. and Flowerdew, G. (2001). A comparative evaluation of waist circumference, waist-to-hip ratio and body mass index as indicators of cardiovascular risk factors. The Canadian Heart Health Surveys. *International Journal of Obesity*, **25***:* 652 – 661.

Du, M. K., Ge, L. Y., Zhou, M. L., Ying, J., Qu, F., Dong, M. Y. and Chen, D. Q. (2017). Effects of pre-pregnancy body mass index and gestational weight gain on neonatal birth weight. *Journal of Zhejiang University-SCIENCE B*, **18**(3), 263-271.

Dwivedi, D. and Verma, A. (2015). Maternal and fetal factors affecting birth length of healthy newborn babies: An observational study. *Indian Journal of Child Health*, **2**: 109-112.

Egerter, S., Braveman, P., Sadegh-Nobari, T., Grossman-Kahn, R. and Dekker, M. (2011). Issue brief 5-education and health. In: Robert Wood Johnson Foundation. San Francisco, pp.1 -22.

Elangovan, M. and Raviraj, K. (2016). Analysis of Morphology and Morphometry of Human Placenta and Its Clinical Relevance. *Imperial Journal of Interdisciplinary Research (IJIR),* **2**: 1531-1534.

Elarbah, I., Elbareg, A., Essadi, F., Algharaz1, A. and Adam, I. (2014). Umbilical Cord Length in Singleton Gestations at Misurata Hospital, Libya. *Journal of Science*, **4**: 657-660.

Elghazaly, E., Ali, Q. and Babikir, H. (2016). Umbilical cord abnormalities. *Sudan Medical Monitor*, **11**: 1-6.

Elsenbruch, S., Benson, S., Rücke, M., Rose, M., Dudenhausen, J., Pincus-Knackstedt, M. K., Klapp, B. F. and Arck, P. C. (2007). Social support during pregnancy: effects on maternal depressive symptoms, smoking and pregnancy outcome. *Human Reproduction*, **22**: 869-877.

Elshibly, E. and Schmalisch, G. (2008). The effect of maternal anthropometric characteristics and social factors on gestational age and birth weight in Sudanese newborn infants. *BioMed Central: Public Health*, **8**: 244.

Ephraim, R., Doe, P., Amoah, S. and Antoh, E. (2014). Lipid Profile and High Maternal Body Mass Index is Associated with Preeclampsia: A Case-Control Study of the Cape Coast Metropolis. *Annals of Medical and Health Sciences Research*, **4**: 746-750.

Essex, B. V. J. E. (1977). Use of an action-orientated record for antenatal screening. *Tropical Doctor*, **7**: 138-138.

Farbu, J., Haugen, M., Meltzer, H. and Brantsæter, A. (2014). Impact of singlehood during pregnancy on dietary intake and birth outcomes- a study in the Norwegian Mother and Child Cohort Study. *BioMed Central: Pregnancy and Childbirth,* **14**: 1-9.

Fayyaz, J. (2005). Ponderal Index. *Journal of the Pakistan Medical Association,* **55**: 228-229.

Ferguson, V. and Dodson, R. (2009). Bioengineering aspects of the umbilical cord. *European Journal* of *Obstetrics* and *Gynaecology* and *Reproductive Biology,* **144**(Supplementary) 1: S108-113.

Ferreira, A., Ferreira, C., Brito, C., Pitanga, F., Moraes, C., Naves, L., Nóbrega, O. and França, N. (2011). Predição da síndrome metabólica em crianças por indicadores antropométricos. *Arquivos Brasileiros de Cardiologia*, **96**: 121-125.

Flamm, B. (1999). Tight nuchal cord and shoulder dystocia: A potentially catastrophic combination. *American Journal of Obstetrics and Gynaecology*, **94**: 853.

Flamme, I., Frolich, T. and Risau, W. J. (1997). Molecular mechanisms of vasculogenesis and embryonic angiogenesis. *Cell Physiology*, **173**: 206–210.

Folkman, J. (1995). Angiogenesis in cancer, vascular, rheumatoid and other disease. *Nature Medicine,* **1**: 27-31.

Frank, A., Beinan, Z., Powell, O., Azar, K., Fortmann, S. and Palaniappan, L. (2014). Racial/Ethnic Differences in Dyslipidemia Patterns. *Circulation*, **129**: 570-579.

Frantz, E., Menezes, H., Lange, K., Abegg, M., Correa, C., Zangalli, L., Vieira, J. and Zettler, C. (2012). The effect of maternal hypercholesterolemia on the placenta and fetal arteries in rabbits. *Acta Cirúrgica Brasileira*, **27**: 7-12.

Friedewald, W. T., Levy, R. I.. and Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry*, **18**(6): 499-502.

Fucntes-Afflicks, E., Hessol, N. and Perez-Stable, E. (1998). Maternal Birthplace, Ethnicity and Low Birth Weight in California. *Archives of Paediatrics and Adolescent Medicine*, **152**: 1105-1112.

Fuenzalida, B., Sobrevia, B., Cantin, C., Carvajal, L., Salsoso, R. and Gutiérrez, J. (2018). Maternal supraphysiological hypercholesterolemia associates with endothelial dysfunction of the placental microvasculature. *Scientific Reports*, **8**: 1-10.

Gademan, M. G., Vermeulen, M., Oostvogels, A. J., Roseboom, T. J., Visscher, T. L., van Eijsden, M. and Vrijkotte, T. G. (2014). Maternal prepregancy BMI and lipid profile during early pregnancy are independently associated with offspring's body composition at age 5–6 years: the ABCD study. *PLoS One*, **9**(4): 1-9.

Gaillard, R., Bakker, R., Willemsen, S., Hofman, A., Steegers, E. and Jaddoe, V. (2011). Blood pressure tracking during pregnancy and the risk of gestational hypertensive disorders: The Generation R Study. *European Heart Journal*, **32**: 3088–3097.

Ganchimeg, T., Ota, E., Morisak, I. N., Laopaiboon, M., Lumbiganon, P., Zhang, J., Yamdamsuren, B., Temmerman, M., Say, L., Tuncalp, O., Vogel, J., Souza, J. and Mori, R. (2014). WHO Multicountry Survey on Maternal Newborn Health Research Network. Pregnancy and childbirth outcomes among adolescent mothers: a World Health Organization multicountry study. *British Journal of Obstetrics and Gynaecology*, **121**: 40–48.

Gebrane-Younes, J., Hoang, N. M. and Orcel, L. (1986). Ultrastructure of human umbilical vessels: a possible role in amniotic fluid formation? *Placenta*, **7**: 173-185.

Georgieff, M. and Sasanow, S. (1986). Nutritional assessment of the neonate. *Clinical Perinatology*, **13**: 72-89.

Geraedts, E., van Dommelen, P., Caliebe, J., Visser, R., Ranke, M., van Buuren, S., Wit, J. and Oostdijk, W. (2011). Association between Head Circumference and Body Size. *Hormone Research In Pædiatrics*, **75**:213–219.

Geraghty, A., Alberdi, G., O'Sullivan, E., O'Brien, E., Crosbie, B., Twomey, P. and McAuliffe, F. (2016). Maternal Blood Lipid Profile during Pregnancy and Associations with

Child Adiposity: Findings from the ROLO Study. *PLoS ONE*, **11**: e0161206.

Ghana Statistical Service (2008). Ghana Living Standards Survey: Report of the Fifth Round. In: Ghana Statistical Service.

Ghezzi, F., Raio, L., Di Naro, E., Franchi, M., Balestreri, D. and D'Addario, V. (2001). Nomogram of Wharton's jelly as depicted in the sonographic cross section of the umbilical cord. *Ultrasound in Obstetrics and Gynaecology*, **18**: 121-125.

Ghezzi, F., Raio, L., Gunter, D. D., Cromi, A., Karousou, E. and Durig, P. (2005). Sonographic umbilical vessel morphometry and perinatal outcome of fetuses with a lean umbilical cord. *Journal of Clinical Ultrasound*, **33**: 18-23.

Ghiasi, A., Ziaei, S. and Faghihzadeh, S. (2014). The Relationship between Levels of Lipids and Lipoprotein B-100 in Maternal Serum and Umbilical Cord Serum and Assess Their Effects on Newborn Infants Anthropometric Indices. *Journal of Midwifery and Reproductive Health*, **2**: 227-232.

Gill, P. and Jarjoura, D. (1993). Wharton's jelly in the umbilical cord. A study of its quantitative variations and clinical correlates. *Journal of Reproductive Medicine*, **38**: 611-614.

Gill, S., May-Benson, T., Teasdale, A. and Munsell, E. (2013). Birth and developmental correlates of birth weight in a sample of children with potential sensory processing disorder. *BioMed Central: Paediatrics*, **13**: 1-8.

Godsland, I., Johnston, D. and Chaturvedi, N. (2007). Mechanisms of Disease: lessons from ethnicity in the role of triglyceride metabolism in ischemic heart disease. *Nature Clinical Practice Endocrinology and Metabolism*, **3**: 530-538.

Goynumer, G., Ozdemir, A., Wetherilt, L., Durukan, B. and Yayla, M. (2008). Umbilical cord thickness in the first and early second trimesters and perinatal outcome. *Journal of Perinatal Medicine*, **36**: 523-526.

Grindheim, G., Estensen, M., Langesaeter, E., Rosseland, L. and Toska, K. (2012). Changes in blood pressure during healthy pregnancy: a longitudinal cohort study. *Journal of Hypertension*, **30**: 342-350.

Gudayu, T., Woldeyohannes, S. and Abdo, A. (2014). Timing and factors associated with first antenatal care booking among pregnant mothers in Gondar Town; North West Ethiopia. *BioMed Central: Pregnancy and Childbirth*, **14**: 1-7.

Guner, Y., Chokchi, N., Petrosyan, M., Upperman, J., Ford, H. and Grikschet, T. (2008). Necrotizing enterocolitis – bench to bedside: novel and emerging strategies. *Seminars in Paediatric Surgery*, **17**: 255 – 265.

Gupta, A., Mann, S. and Sethi, S. (2015). Can Waist Circumference Be Used as an Anthropometric Parameter to Assess the Obesity Related Pregnancy Outcome: A Case Control

Study. *Open Journal of Obstetrics and Gynaecology*, **5**: 528-534.

Hajianfar, H., Esmaillzadeh, A., Feizi, A., Shahshahan, Z. and Azadbakht, L. (2018). Major Maternal Dietary Patterns during Early Pregnancy and Their Association with Neonatal Anthropometric Measurement. *Hindawi BioMed Research International*, pp.1-11.

Haq, I., Azad, A., Khan, N. and Afzal, M. (2017). Association of Maternal demographic and Anthropometric Characteristics with Birth Weight of the Newborn. *Annals of Pakistan Institute of Medical Science*, **13**: 231-235.

Harding, J. E. (2001). The nutritional basis of the foetal origins of adult disease. *International Journal of Epidemiology*, **30**: 15-23.

Harville, E., Myers, L., Shu, T., Wallace, M. and Bazzano, L. (2018). Pre-pregnancy cardiovascular risk factors and racial disparities in birth outcomes: the Bogalusa Heart Study. *BioMed Central: Pregnancy and Childbirth*, **18**: 1-10.

Hassan, N., Shalaan, A. and El-Masry, S. (2011). Relationship between maternal characteristics and neonatal birth size in Egypt. *Eastern Mediterranean Health Journal*, **17**: 281- 289.

Hermann, S., Rohrmann, S., Linseisen, J., May, A. M., Kunst, A., Besson, H. and Dorronsoro, M. (2011). The association of education with body mass index and waist

circumference in the EPIC-PANACEA study. *BioMed Central Public Health*, **11**(1): 169.

Hermida, R., Ayala, D., Mojon, A., Fernandez, J., Alonso, I., Silva, I., Ucieda, R. and Iglesias, M. (2000). Blood pressure patterns in normal pregnancy, gestational hypertension and preeclampsia. *Hypertension*, **36**: 149-158.

Herrera, E. (2002). Lipid metabolism in pregnancy and its consequences in the fetus and newborn. *Endocrine*, **19**: 43-45.

Herrera, E. and Ortega-Senovilla, H. (2010). Maternal lipid metabolism during normal pregnancy and its implications to fetal development. *Clinical Lipidology*, **5**: 899-911.

Herrera, E., Amusquivar, E., López, S. I. and Ortega, H. (2006). Maternal lipid metabolism and placental lipid transfer. *Hormonal Research*, **65**: 64-69.

Hersh, J. and Buchino, J. (1988). Umbilical cord torsion/constriction sequence. *In Saul RA, edition Proceedings of the Greenwood Genetics Conference Clinton Jacobson Press*, **7**: 181-182.

Hirano, D., Ishikura, K. and Uemura, O. (2016). Association between low birth weight and childhood-onset chronic kidney disease in Japan: A combined analysis of a nationwide survey for paediatric chronic kidney disease and the National Vital Statistics Report. *Nephrology Dialysis Transplantation*, **31**: 1895–1900.

Huang, L., Sauve, R., Birkett, N., Fergusson, D. and van Walraven, C. (2008). Maternal age and risk of stillbirth: a systematic review. *Canadian Medical Association Journal*, **178**: 165–172.

Huda, S., Sattar, N. and Freeman, D. (2009). Lipoprotein Metabolism and Vascular Complications in Pregnancy. *Clinical Lipidology*, **4**: 91 – 102

Hughes, S. and Lau, J. (2008). A technique for fast and accurate measurement of hand volumes using Archimedes‘ principle. *Australasian Physical and Engineering Sciences in Medicine*, **31**: 56-59.

Huppertz, B. (2008). The anatomy of the normal placenta. *Journal of Clinical Pathology*, **61**: 1296–1302.

Huxley, R., Mendis, S., Zheleznyakov, E., Reddy, S. and Chan, J. (2010). Body mass index, waist circumference and waist:hip ratio as predictors of cardiovascular risk—a review of the literature. *European Journal of Clinical Nutrition*, **64**: 16–22.

Iaccarino, M., Baldi, F., Persico, O. and Palagiano, A. (1986). Ultrasonographic and pathologic study of mucoid degeneration of umbilical cord. *Journal of Clinical Ultrasound*, **14**: 127-129.

Iffy, L. and Varardi, V. (1994). Cerebral palsy following cutting of the nuchal cord before delivery. *Medical Law*, **13**: 323-330

Inan, S., Sanci, M., Can, D., Vatansever, S., Oztekin, O. and Tinar, S. (2002). Comparative morphological differences between umbilical cord from chronic hypertension and preeclampsia

pregnancies. *Acta Medica Okayama*, **56**: 177-186.

Isiugo-Abanihe, U. and Oke, O. (2011). Maternal and environmental factors influencing infant birth weight in Ibadan, Nigeria. *African Population Studies*, **25**: 250-266.

Jafari, H. and Latifnejad, R. (2014). Horseshoe-shaped Placenta and Preterm Labour: A Case Report. *Journal of Midwifery and Reproductive Health*, **2**: 147-149.

Jain, A., Jain, R. and Baweja, S. (2017). Variable placental attachment of umbilical cords and its effects on placental outcomes. *Indian Journal of Clinical Anatomy and Physiology*, **4**(3): 324-328.

James, J., Stone, P. and Chamley, L. (2006). The regulation of trophoblast differentiation by oxygen in the first trimester of pregnancy. *Human Reproduction Update*, **12**: 137-144.

Jananthan, R., Wijesinghe, D. and Sivananthawerl, T. (2009). Maternal Anthropometry as a Predictor of Birth Weight. *Tropical Agricultural Research*, **21**: 89 - 98.

Janssen, I., Heymsfield, S., Allison, D., Kotler, D. and Ross, R. (2002). Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat. *American Journal of Clinical Nutrition*, **75**: 683–638.

Janssen, I., Katzmarzyk, P. and Ross, R. (2004). Waist circumference and not body mass index explains obesityrelated health risk. *American Journal of Clinical Nutrition*, **79**: 379–384.

Janssen, P., Thiessen, P., Klein, M., Whitfield, M., MacNab, Y. and Cullis-Kuhl, S. (2007). Standards for the measurement of birth weight, length and head circumference at term in neonates of European, Chinese and South Asian ancestry. *Open Medicine*, **1**: e74-e88.

Japanese Society of Hypertension Guidelines (2009). Chapter 2**.** Measurement and clinical evaluation of blood pressure. *Hypertension Research*, **32**: 11–23.

Jin, W.-Y., Lin, S.-L., Hou, R.-L., Chen, X.-Y., Han, T., Jin, Y., Tang, L., Zhu, Z.-W. and Zhao, Z.-Y. (2016). Associations between maternal lipid profile and pregnancy complications and perinatal outcomes: a population-based study from China. *BioMed Central: Pregnancy and Childbirth*, **16**: 1-9.

Juneja, K., Khalique, N., Ansari, M., Ahmad, A., Khan, M. and Rehman, S. (2016). Influence of Maternal Anthropometric Characteristics on Birth Weight of Newborn. *National Journal of Community Medicine*, **7**: 485-489.

Kajantie, E., Thornburg, K. L., Eriksson, J. G., Osmond, C. and Barker, D. J. (2010). In preeclampsia, the placenta grows slowly along its minor axis. *International Journal of Developmental Biology*, **54**: 469-473.

Kallol, S., Huang, X., Müller, S., Ontsouka, C. and Albrecht, C. (2018). Novel Insights into Concepts and Directionality of Maternal–Fetal Cholesterol Transfer across the Human Placenta. *International Journal of Molecular Science,* **19**: 1-17.

Kappel, B., Eriksen, G., Hansen, K. B., Hvidman, L., Krag-Olsen, B., Nielsen, J., Videbech, P. and Wohlert, M. (1987). Short stature in Scandinavian women. An obstetrical risk factor. *Acta Obstetricia et Gynecologica Scandinavica*, **66**: 153-158.

Kardjati, S. R. I., Kusin, J. A. and De With, C. (1988). Energy supplementation in the last trimester of pregnancy in East Java: I. Effect on birthweight. *BJOG: An International Journal of Obstetrics and Gynaecology*, **95**(8): 783-794.

Karmakar, M., Kumar, S., Chattopadhyay, S., Kar, S., Vaid, L. and Sen, S. (2018). A study on the morphology and the morphometry of the human placenta and its clinical significance in rural population in Eastern India. *Asian Pacific Journal of Health Science*, **5**: 202-209.

Karthikeyan, T., Subramanian, R., Johnson, W. and Prabhu, K. (2012). Placental thickness and its correlation to gestational age and foetal growth parameters- a cross sectional ultrasonographic study. *Clinical Diagnostic Research*, **6**: 1732-1735.

Kaushal1, L., Patil, A. and Kocherlak, K. (2015). Evaluation of placental thickness as a sonological indicator for estimation of gestational age of foetus in normal singleton pregnancy. *International Journal of Research in Medical Sciences*, **3**: 1213-1218.

Keith, L. M., Persaud, T. V. N. and Torchia, M. G. (2011). The Placenta. In: Moore K, editor. The Developing Huiman: Clinically Oriented Embryology, 9th ed. USA: Saunders, pp.110-122.

Khalil, A., Rezende, J., Akolekar, R., Syngelaki, A. and Nicolaides, K. (2013). Maternal racial origin and adverse pregnancy outcome: a cohort study. *Ultrasound in Obstetric and Gynaecology*, **41**: 278–285.

Kierans, W., Kendall, P., Foster, L., Liston, R. and Tuk, T. (2007). New birth body length and head circumference charts for the British Columbia population. *British Columbia Medical Journal*, **49**: 72-79.

Kim, E., Park, H., Hong, Y.-C., Ha, M., Kim, Y., Lee, B.-E. and Ha, E.-H. (2015). Effect of maternal job strain during pregnancy on infant neurodevelopment by gender at 6 and 12 months: Mothers and Children's Environmental Health (MOCEH) study. *Annals of Occupational and Environmental Medicine*, **27**: 1-10.

Kim, J., Romero, R., Tarca, A., LaJeunesse, C., Han, Y., Kim, M., Suh, Y., Draghici, S., Mittal, P., Gotsch, F., Kusanovic, J., Hassan, S. and Kim, C. (2008). Gene expression profiling demonstrates a novel role for foetal fibrocytes and the umbilical vessels in human fetoplacental development. *Journal of Cellular and Molecular Medicine*, **12**: 1317-1330.

Kirchengast, S., Mayer, M. and Voigt, M. (2007). Pregnancy outcome is associated with maternal marital status in AustriadEven at the beginning of the 21st century. *Anthropologischer Anzeiger*, **65**: 415-426.

Koech, A., Ndungu, B. and Gichangi, P. (2008). Structural changes in umbilical vessels in pregnancy induced hypertension. *Placenta*, **29**(2): 210-214.

Kodaman, N., Aldrich, M., Sobota, R., Asselbergs, F., Poku, K., Brown, N., Moore, J. and Williams, S. (2016). Cardiovascular Disease Risk Factors in Ghana during the Rural-to-Urban Transition: A Cross- Sectional Study. *PLoS One*, **11**(10): e0162753.

Kotingo, E., Allagoa, D., Apiyanteide, F. and Addah, A. (2015). Maternal Height and Obstetric Outcome in a Tertiary Hospital of Southern Nigeria: a Prospective Anthropometric Study. *European Journal of Advanced Research in Biological and Life Sciences*, **3**: 46-55.

Kowsalya, V., Vijayakumar, R., Valli, G., Bharath, K., Srikumar, R., Kishor, K. C., Gayathri, F. I. and Vanajashi, N. (2013). Morphometry examination of placenta in birth weight of full-term newborns in Puducherry, India. *Pakistan Journal of Biological Sciences*, **16**: 895-897.

Krame, R. M., Kahn, S., Dahhou, M., Otvos, J., Genest, J. and Platt, R. (2013). Maternal lipids and small-for-gestational age birth at term. *Journal of Paediatrics*, **163**: 983–988.

Kramer, M., Kahn, S., Rozen, R., Evans, R., Platt, R. and Chen, M. (2009). Vasculopathic and thrombophilic risk factors for spontaneous preterm birth. *International Journal of Epidemiology*, **38**: 715–723.

Kuhle, S., Maguire, B., Ata, N., MacInnis, N. and Dodds, L. (2017). Birth weight for gestational age, anthropometric measures, and cardiovascular disease markers in children. *Journal of Paediatrics*, **182**: 99–106.

Kulandaivelu, A., Srinivasamurthy, B., Murugan, A. and Mutharasu, A. (2014). Morphology and Morphometric Study of Human Placenta in Rural Southern India. *British Journal of Medicine and Medical Research,* **4**: 2995-3008.

Kulkarni, M. L., Matadh, P. S., Ashok, C., Pradeep, N., Avinash, T. and Kulkarni, A. M. (2007). Absence of Wharton's jelly around the umbilical arteries. *Indian Journal of Paediatrics,* **74**: 787-789.

Kulkarni, S. R., Kumaran, K., Rao, S. R., Chougule, S. D., Deokar, T. M., Bhalerao, A. J., Solat, V. A., Bhat, D. S. and Fall, C. H. (2013). Maternal lipids are as important as glucose for fetal growth: findings from the pune maternal nutrition study. *Diabetes Care*, **36**: 2706–2713.

Kulshreshtha, S. and Saxena, S. (2018). Study of Length and Diameter of Umbilical Cord and Its Embryological Significance. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS),* **17**: 49-50.

Kumar, S., Tharihalli, C., Chandrashekhar, K. and Gaddi, S. (2017). Study of length of umbilical cord and fetal outcome: a study of 1000 deliveries. *International Journal of Reproduction, Contraception, Obstetrics and Gynaecology*, **6**: 3770-3775.

Kumari, S., Rani, A., Diwan, R. K., Srivastava, A. K., Mehta, V. and Suri, R. K. (2016). Morphological and morphometric evaluation of placenta in hypothyroid mothers. *Astrocyte*, **3**(1): 19.

Kuutiero, L., Ahiable, G., Alagskomah, R., Sadat, M.-A., Fosu, A. B., Baidoo, I. E., Korboe, D., Dogbe, T., Hattori, H., Hinton, R. and Norton, A. **(2011).** Participatory Poverty and Vulnerability Assessment: Understanding the Regional dynamics of Poverty with particular focus on Ghana's northern, Upper Eastand Upper West Regions In. p.130.

Kwawukume, E., Ghosh, T. and Wilson, J. (1993). Maternal height as a predictor of vaginal delivery. *International Journal of Gynaecology and Obstetrics*, **41**: 27-30.

Labayen, I., Ruiz, J., Moreno, L., Ortega, F., Beghin, L. and DeHenauw, L. (2011). The Effect of Ponderal Index at Birth on the Relationships Between Common LEP and LEPR Polymorphisms and Adiposity in Adolescents. *Obesity*, **19**: 2038-2045.

Lam, B., Koh, G., Chen, C., Wong, M. and Fallows, S. (2015). Comparison of Body Mass Index (BMI), Body Adiposity Index (BAI), Waist Circumference (WC), Waist-To-Hip Ratio (WHR) and Waist-To-Height Ratio (WHtR) as Predictors of Cardiovascular Disease Risk Factors in an Adult Population in Singapore. *PLoS ONE*, **10**: e0122985.

Lande, B., Andersen, L., Henriksen, T., Bærug, A., Johansson, L., Trygg, K., Bjørneboe, G.-E. and Veierød, M. (2005). Relations between high ponderal index at birth, feeding practices and body mass index in infancy. *European Journal of Clinical Nutrition*, **59**: 1241–1249.

Lara, M. and Amigo, H. (2018). Association between education and blood lipid levels as income increases over a decade: a cohort study. *BioMed Central: Public Health*, p.18.

Larsen, W. (2001). Human Embryology, 3rd ed. New York: Churchill Livingstone.

Law, C., Barker, D. and Bull, A. C. O. (1991). Maternal and fetal influences on blood pressure. *Archives of Disease in Childhood*, **66**: 1291-1295.

Lear, S., James, P., Ko, G. and Kumanyika, S. (2010). Appropriateness of waist circumference and waist-to-hip ratio cutoffs for different ethnic groups. *European Journal of Clinical Nutrition*, **64**: 42–61.

LeFlore, J. and Engle, W. (2002). Clinical Factors Influencing Blood Pressure in the Neonate. *NeoReviews*, **3**: e145-e150.

Leitzmann, M. F., Moore, S. C., Koster, A., Harris, T. B., Park, Y., Hollenbeck, A. and Schatzkin, A. (2011). Waist Circumference as Compared with Body-Mass Index in Predicting Mortality from Specific Causes. *PLoS ONE*, **6**: e18582.

Leiva, A., Diez de Medina, C., Salsoso, R., Sáez, T., San Martín, S., Abarzúa, F., Farías, M., Guzmán-Gutiérrez, E., Pardo, F. and Sobrevia, L. (2013). Maternal Hypercholesterolemia in Pregnancy Associates With Umbilical Vein Endothelial Dysfunction Role of Endothelial Nitric Oxide Synthase and Arginase II. *Arteriosclerosis, Thrombosis and Vascular Biology*, **33**: 2444- 2453.

Lim, W.-Y., Lee, Y.-S., Tan, C.-S., Kwek, K., Chong, Y.-S., Gluckman, P., Godfrey, K., Saw, S.-M. and Pan, A. (2014). The association between maternal blood pressures and offspring size at birth in Southeast Asian women. *BMC Pregnancy and Childbirth*, **14**: 1-10.

Liu, B., Geng, H., Yang, J., Zhang, Y., Deng, L., Chen, W. and Wang, Z. (2016). Early pregnancy fasting plasma glucose and lipid concentrations in pregnancy and association to offspring size: a retrospective cohort study. *BioMed Central: Pregnancy and Childbirth*, **16**: 1-7.

Liu, Y., Tong, G., Tong, W., Lu, L. and Qin, X. (2011). Can body mass index, waist circumference, waist-hip ratio and waist-height ratio predict the presence of multiple metabolic risk factors in Chinese subjects? *BioMed Central: Public Health*, **11**: 1-10.

Lohman, T. G., Roche, A. F. and Martorell, R. (1988). Champaign: Human kinetics books. *Anthropometric standardization reference manual*, **177**: 3-8.

Londhe, P. and Mane, A. (2011). Morphometric study of placenta and its correlation in normal and hypertensive pregnancies. *International Journal of Pharma and Bio Sciences*, **2**: 429 -437.

Long, H., Yi, J. M., Hu, P. L., Li, Z. B., Qiu, W. Y., Wang, F. and Zhu, S. (2012). Benefits of iron supplementation for low birth weight infants: a systematic review. *BioMed Central Paediatrics,* **12**(1): 99.

López, P. and Bréart, G. (2013). Sociodemographic characteristics of mother's population and risk of preterm birth in Chile. *Reproductive Health*, **10**: 26.

Lorch, S. and Enlow, E. (2016). The role of social determinants in explaining racial/ethnic disparities in perinatal outcomes. *Review*, **79**: 141-147.

Lyndon, M., Hill, M., Dawn, M., Di Nofrio, R. and Guziek, D. (1994). Sonographic determination of first trimester umbilical cord length. *Journal of Clinical Ultrasound,* **22**: 435- 438.

Macdonald-Wallis, C., Lawlor, D., Fraser, A., May, M., Nelson, S. and Tilling K. (2012). Blood Pressure Change In Normotensive, Gestational Hypertensive, Preeclamptic And Essential Hypertensive Pregnancies. *Hypertension*, **59**: 1241–1248.

Macdonald-Wallis, C., Tilling, K., Fraser, A., Nelson, S. and Lawlor, D. (2011). Established pre-eclampsia risk factors are related to patterns of blood pressure change in normal term pregnancy: Findings from the Avon Longitudinal Study of Parents and Children (ALSPAC). *Journal of Hypertension,* **29**: 1703–1711.

Macdonald-Wallis, C., Tilling, K., Fraser, A., Nelson, S. and Lawlor, D. (2014). Associations of blood pressure change in pregnancy with fetal growth and gestational age at delivery: findings from a prospective cohort. *Hypertension*, **64**: 36–44.

Makoka, D. (2013). The Impact of Maternal Education on Child Nutrition: Evidence from Malawi, Tanzania, and Zimbabwe. In: Development. USAfI, editor. Calverton, Maryland, USA: ICF International, pp. 1-26.

Malin, G., Morris, E., Riley, R., Teune, M. and Khan, K. (2013). When is birthweight at term abnormally low? A systematic review and meta-analysis of the association and predictive ability of current birthweight standards for neonatal outcomes. *BJOG: An International Journal of Obstetrics and Gynaecology*, **121**: 515-526.

Manikanta, R. V., Geetha, S. and Nim, V. (2012). Variations in Placental Attachment of Umbilical Cord. *Journal of Anatomical society of India,* **61**: 1-4.

Mankuta, D., Elami-Suzin, M., Elhayani, A. and Vinker, S. (2010). Lipid profile in consecutive pregnancies. *Lipids in Health and Disease, BioMed Central*, **9:** 1-4.

Martin, J., Hamilton, B., Ventura, S., Osterman, M., Kirmeyer, S., Mathews, T. and Wilson, E. (2011). Births: final data for 2009. *National Vital Statistics Report,* **60**: 1-70.

Masarat, R., Gul, S., Khurshid, R. and Ahmad, A. (2017). Prospective Study For Evaluation Of The Impact Of Umbilical Cord Length With Fetal Outcome. *International Journal of Current Advanced Research*, **6**: 4458-4462.

Mati, J. K., Aggarwal, V. P., Sanghvi, H. C. G., Lucas, S. and Corkhill, R. (1983). The Nairobi birth survey III. Labour and delivery. *Journal of Obstetrics and Gynaecology of Eastern and Central Africa*, **2**: 47-56.

Mayhew, T. M., Charnock-Jones, D. S. and Kaufmann, P. (2004). Aspects of human fetoplacental vasculogenesis and angiogenesis. III. Changes in complicated pregnancies. *Placenta*, **25**(2-3): 127-139.

Mayhew, T. M. (2005). The Human Placenta and the Search for Structural Correlates of Fetal Well-Being. *Comparative Placentology*, **21**: 36.

Meldere, I., Urtans, V., Kruze, D., Petersons, A. and Abola, Z. (2017). Neonatal Anthropometry: Measurement of the Abdominal Circumference in Newborns. *Acta Chirurgica Latviensis*, **13**: 47-50.

Meldere, I., Urtans, V., Petersons, A. and Abola, Z. (2015). Measurement of abdominal circumference in preterm infants. *BioMed Central: Research Notes*, **726**: pp.1-4.

Mendelson, M., Lyas, A., O'Donnell, C., D'Agostino, S. R. and Levy, D. (2016). Association of Maternal Prepregnancy Dyslipidemia With Adult Offspring Dyslipidemia in Excess of Anthropometric, Lifestyle, and Genetic Factors in the Framingham Heart Study. *Journal of American Medical Association Cardiology*, **1**(1): 26-35.

Mihu, C. M., Suşman, S., Ciucă, D. R., Mihu, D. and Costin, N. (2009). Aspects of placental morphogenesis and angiogenesis. *Romanian Journal of Morphology and Embryol*ogy **50(**4): 549-57.

Mishra, R., Vijayalaxmi, P. and Nirmala Kumari, J. (1987). Correlation of the length of umbilical cord of the fetus with outcome of labour. *Journal of Obstetrics amd Gynaecology of India*, **37:** 781.

Mishra, M., Sharma, R., Sharma, D., Mishra, A. and Sharma, D. (2017). Study of variations in lipid profile in different trimesters of pregnancy. *International Journal of Medical Science and Public Health*, **6**: 456-459.

Misra, V., Trudeau, S. and Perni, U. (2011). Maternal Serum Lipids During Pregnancy and Infant Birth Weight: The Influence of Prepregnancy BMI. *Obesity*, **19**: 1476–1481.

Mitra, S., Misra, S., Nayak, P. and Sahoo, J. (2012). Effect of maternal anthropometry and metabolic parameters on fetal growth. *Indian Journal of Endocrinology and Metabolism*, **16**: 754-758.

Mitra, S., Venkataseshan, V., Von Hagen, S., Barton, P., Delshad, G. and Gill, J. (1997). Morphometric study of the placental vessels and its correlation with umbilical artery Doppler flow. *Obstetrics and Gynaecology*, **89**: 238–241.

Miwa, I., Sase, M., Torii, M., Sanai, H., Nakamura, Y. and Ueda, K. (2014). A thick placenta: a predictor of adverse pregnancy outcomes. *SpringerPlus*, **3**: 353-256.

Mohsen, M. A. and Wafay, H. A. (2007). Influence of maternal anthropometric measurements and serum biochemical nutritional indicators on fetal growth. *Journal of Medical Science,* **7:** 1330-1334.

Molarius, A., Seidell, J. C., Sans, S., Tuomilehto, J. and Kuulasmaa, K. (2000). Educational level, relative body weight, and changes in their association over 10 years: an international perspective from the WHO MONICA Project. *American Journal of Public Health*, **90**(8): 1260.

Mora-García, G., Gómez-Camargo, D., Mazenett, E., Alario, A., Fortich, A. and Gómez-Alegría, C. (2014). Anthropometric parameters‘ cut-off points and predictive value for metabolic syndrome in women from Cartagena, Colombia. *Salud Publica Mex*, **56**: 146-153.

Moraitis, A., Wood, A., Fleming, M. and Smith, G. (2014). BirthWeight Percentile and the Risk of Term Perinatal Death. *Obstetrics and Gynaecology*, **124**: 274-283.

Moran, M. and McAuliffe, F. (2011). Imaging and assessment of placental function. *Journal of Clinical Ultrasound*, **36**: 390-398.

Mosha, T. and Napendaeli, P. (2010). Factors Influencing Pregnancy Outcomes in Morogoro Municipality, Tanzania. *Tanzania Journal of Health Research*, **12**(4): 243 – 251.

Moshiri, M., Zaidi, S., Robinson, T., Bhargava, P., Siebert, J., Dubinsky, T. and Katz, D. (2014). Comprehensive Imaging Review of Abnormalities of the Umbilical Cord. *RadioGraphics*, **34**: 179–196.

Mousumi, G. (2014). Association of Maternal Age and Low Socio-Economic Status of Women on Birth Outcome. *International Research Journal of Social Sciences*, **3**: 21-27.

Mudabasappagol, C. and Kammar, K. (2015). Correlation of anthropometric measurements with LDL levels in young adult females. *Indian Journal of Basic and Applied Medical Research*, **4**: 684-692.

Muslimatun, S., Schmidt, M., West, C., Schultink, W., Gross, R. and Hautvast, J. (2002). Determinants of weight and length of Indonesian neonates. *European Journal of Clinical Nutrition*, **56**: 947–951.

Nagamani, G., Kanaka, S. K. and Geeta, V. R. (2015). Placental Size and Perinatal Outcomes. *Journal of Evidence-based Medicine and Healthcare*, **2**: 1642-1645.

Nagwani, M., Sharma, P., Singh, U., Anita, R. A. and Mehrotra, S. (2015). Ultrasonographic measurement of placental thickness and its correlation with gestational age – a cross-sectional ultrasonographic study. *International Journal of Advanced Research,* **2**: 354-360.

Nahar, S., Mascie-Taylor, C. and Begum, H. (2005). Maternal anthropometry as a predictor of birth weight. *Public Health Nutrition,* **10**: 965–970.

Naidoo, S., London, L., Burdorf, A., Naidoo, R. and Kromhout, H. (2011). Spontaneous miscarriages and infant deaths among female farmers in rural South Africa. *Scand inavian Journal of Work Environmental Health,* **37**: 227-236.

Nair, B. and Raju, U. (2017). Study of Correlation of Neonatal Outcomes with Gross Abnormalities of Placenta and Umbilical Cord**.** *Journal of Nepal Paediatric Society,* **37:** 254-260

Nandini, B., Deepali, J., BalGopal, B., Shaheen, A. and Jyothi, D. (2015). Relationship Between Umbilical Cord Length and Maternal and Fetal Outcome. *Indian Journal of Research,* **4**: 114 - 117.

Ngene, N. and Moodley, J. (2019). Blood pressure measurement in pregnancy and in hypertensive disorders of pregnancy: devices, techniques and challenges. *Cardiovascular Journal of Africa,* **30**: 1-10.

Nili, F., Makipour, M. and Mobini, J. (2003). The value of ponderal index as a prognostic factor in predicting complications in term neonates. *Medical Journal of the Islamic Republic of lran*, **17**: 197-201.

Nisa, F., Jafri, S., Kousar, S. and Rakhashanda, J. (2011). Correlation of Gestational Lipid Profile with Neonatal Birth Weight. *Biomedica,* **27**: 68 – 71.

Non-Communicable Disease Risk Factor Collaboration (NCD-RisC) (2017). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. *Lancet,* **389**: 37–55.

Nourbakhsh, S., Ashrafzadeh, S., Hafizi, A. and Naseh, A. (2016). Associations between maternal anthropometric characteristics and infant birth weight in Iranian population. *SAGE Open Medicine,* **4**:1-8.

NuggedAlla, M. A. A. (2013). A Preliminary Study on the Morphological Variations in the Umbilical Cord of Sundanese. *Time Journal of Medical Sciences Report and Research*, **1**: 10-15.

Nwokoye, I., Uleanya, N., Ibeziako, N., Ikefuna, A., Eze, J. and Ibe, J. (2015). Blood pressure values in healthy term newborns at a tertiary health facility in Enugu, Nigeria. *Nigerian Journal of Clinical Practice,* **18**: 584-588.

Obel, C., Hedegaard, M., Henriksen, T., Secher, N. and Olsen, J. (2003). Stressful life events in pregnancy and head circumference at birth. *Developmental Medicine and Child Neurology*, **45**: 802–806.

Odibo, A. O., Nelson, D., Stamilio, D. M., Sehdev, H. M. and Macones, G. A. (2006). Advanced maternal age is an independent risk factor for intrauterine growth restriction. *American Journal of Perinatology*, **23**(5): 325-328.

Odibo, A. O., Zhong, Y., Goetzinger, K. R., Odibo, L., Bick, J. L., Bower, C. R. and Nelson, D. M. (2011). First-trimester placental protein 13, PAPP-A, uterine artery Doppler and maternal characteristics in the prediction of pre-eclampsia. *Placenta*, **32**(8): 598-602.

Ogunlaja, I. P. and Ogunlaja, O. (2015). Correlation Between Umbilical Cord Length, Birth Weight And Length Of Singleton Deliveries At Term In A Nigerian Population. *Rwanda Medical Journal*, **72**: 17-19.

Ohagwu, C. C., Abu, P. O., Ezeokeke, U. O. and Ugwu, A. C. (2009). Relationship between placental thickness and growth parameters in normal Nigerian foetuses. *African Journal of Biotechnology*, **8**: 133-138.

Olaya, M. and Bernal, J. (2014). Umbilical cord abnormalities in fetal and neonatal pathology in Bogota. *Archives of Perinatal Medicine*, **20**: 22-27.

Olumuyiwa, O. and Ogunlaja, I. (2015). Correlation between Umbilical Cord Length, Birth Weight and Length of Singleton Deliveries at Term in a Nigerian Population. *Rwanda Medical Journal*, **72**(3): 17 – 19.

Oluwafemi, O., Njokanma, F., Disu, E. and Ogunlesi, T. (2013). Current pattern of Ponderal Indices of term small-for-gestational age in a population of Nigerian babies. *BioMed Central: Paediatrics,* **119**:1-7.

Oluwole, A., Adegbesan-Omilabu, M. and Okunade, K. (2014). Preterm delivery and low maternal serum cholesterol level: Any correlation? *Nigerian Medical Journal,* **55**: 406-410.

Omorogiuwa, A. and Ozor, M. (2015). A longitudinal comparative study of lipid profile in third trimester of pregnancy and end of puerperium. *Pakistan Journal of Physiology*, **11**:3-5.

Onyiriuka, A. and Okolo, A. (2005). Small-for-gestational age, ponderal index and neonatal polycythaemia: a study of their association with maternal hypertension among nigerian women. *Annals of African Medicine*, **4**: 154 – 159.

Oshvandi, K., Jadidi, A., Dehvan, F., Shobeiri, F., Cheraghi, F., Sangestani, G., Koosha, B. M., Takarli, F. and Aghababaei, S. (2018). Relationship between Pregnancy-induced Hypertension with Neonatal and Maternal Complications. *International Journal of Paediatrics,* **6**: 8587-8594.

Ounsted, M., Moar, V. A. and Scott, A. (1986). Growth and proportionality in early childhood. III. Differences between babies of low birthweight in well-nourished and malnourished populations. *Early Human Development,* **14**: 167-178

Owiredu, W. K. B. A., Amidu, N., Gockah-Adapoe, E. and Ephraim, R. K. D. (2011). The prevalence of metabolic syndrome among active sportsmen/sportswomen and sedentary workers in the Kumasi metropolis. *Journal of Science and Technology (Ghana),* **31**(1):1-14.

Paiker, M., Gyan, P. M. and Perrna, A. B. S. (2016). Morphometric analysis of umbilical cord in normal vs hypertensive pregnancies in population of lucknow, Uttar Pradesh, India. *International Journal of Anatomy and Research*, **4**: 2618-2621.

Palomba, S., Russo, T., Falbo, A., Di Cello, A., Tolino, A., Tucci, L., La Sala1, G. and Zullo, F. (2013). Macroscopic and microscopic findings of the placenta inwomenwith polycystic ovary syndrome. *Human Reproduction,* **28**: 2838–2847.

Pankaj, S. and Kanchan, K. (2017). Correlation of Birth Weight with other Anthropometric Parameters of Newborns in Himachal Pradesh. *International Journal of Current Research and Review,* **9**: 49-54.

Pankaj, S., Pankaj, J., Jain, A. and Agarwal, G. (2015). Effect of gestational *diabetes mellitus* on gross morphology of placenta: a comparative study. *International Journal of Anatomy and Research,* **3**: 889-894.

Pardi, G., Marconi, A. M. and Cetin, I. (2002). Placental-fetal interrelationship in IUGR fetuses--a review. *Placenta*, **23**(Suppl A): S136 – S141.

Patel, D., Dawson, M., Kalyanam, P., Lungus, E., Weiss, H., Flaherty, E. and Nora, E. G. Jr. (1989). Umbilical cord circumference at birth. *American Journal of Diseases of Children*, **143**: 638-639.

Pathak, S., Hook, E., Hackett, G., Murdoch, E., Sebire, N., Jessop, F. and Lees, C. (2010). Cord coiling, umbilical cord insertion and placental shape in an unselected cohort delivering at term: relationship with common obstetric outcomes. *Placenta,* **31**: 963-968.

Pathak, S., Jessop, F., Hook, L., Sebire, N. J. and Lees, C. C. (2010). Placental weight, digitally derived placental dimensions at term and their relationship to birth weight. *Journal of Maternal – Foetal and Neonatal Medicine,* **23**: 1176-1182.

Petekkaya1, E., Deniz, M. and Yildiz, E. (2011). Analysis of the relationship between umbilical cord, placental morphology and anthropometric measurements of the newborn. *Pakistan Journal of Medical Science,* **27**: 569-573.

Phaneendra, R. R. S., Prakash, K. and Sreekumaran, N. N. (2001). Influence of prepregnancy weight, maternal height and weight gain during pregnancy on birth weight. *Bahrain Medical Bull*, **23**: 22-26.

Pietiläinen, K., Kaprio, J., Räsänen, M., Winter, T., Rissanen, A. and Rose, R. (2001). Tracking of Body Size from Birth to Late Adolescence: Contributions of Birth Length, Birth Weight, Duration of Gestation, Parents' Body Size, and Twinship. *American Journal of Epidemiology,* **154**: 21-29.

Pirnat, A., DeRoo, L., Skjærven, R. and Morken, N.-H. (2018). Women's prepregnancy lipid levels and number of children: a Norwegian prospective population-based cohort study. *British Medical Journal Open*, **8**:1-9.

Poon, L. and Nicolaides, K. (2014). First-trimester maternal factors and biomarker screening for preeclampsia. *Prenatal Diagnosis,* **34**: 618–627.

Potgens, A., Schmitz, U. and Bose, P. (2002). Mechanisms of syncytial fusion: a review. *Placenta,* **23**(suppl A): S107 – S113.

Prentice, A. (2011). The influence of maternal, fetal and child nutrition on the development of chronic disease in later life. In. United Kingdom: Scientific Advisory Committee on Nutrition, pp. 13-119.

Prieto, G. R., Ottone, N. E. and Bianchi, H. (2018). Morphological features of the human placenta and its free chorionic villi in normal pregnancies and those with diabetes and high blood pressure literature review. *International Journal of Morphology,* **36**: 1183-1192.

Proctor, L., Fitzgerald, B., Whittle, W., Mokhtari, N., Lee, E., Machin, G., Kingdom, J. and Keating, S. (2013). Umbilical cord diameter percentile curves and their correlation to birth weight and placental pathology. *Placenta,* **34**: 62-66.

Qaiser, D. and Omair, A. (2016). Anthropometrical Measurements of Healthy Newborn Babies in Karachi, and the Factors Affecting these Parameters. *Journal of the College of Physicians and Surgeons Pakistan*, **26**: 934-936.

Raghuram, P., Arjun, S., Prakash, K., Babita, G., Varshil, M., Kunal, B. and Aadhijaya, B. (2016). Evaluation of Lipid Profile in Second and Third Trimester of Pregnancy. *Journal of Clinical and Diagnostic Research,* **10**: QC12 – QC16.

Raio, L., Ghezzi, F., Cromi, A., Nelle, M., Durig, P. and Schneider, H. (2004). The thick heterogeneous (jellylike) placenta: a strong predictor of adverse pregnancy outcome. *Prenatal Diagnosis*, **24**: 182-188.

Raio, L., Ghezzi, F., Di Naro, E., Franchi, M., Maymon, E., Mueller, M. and Bruhwiler, H. (1999). Prenatal diagnosis of a lean umbilical cord: a simple marker for the foetus at risk of being small-for-gestational age at birth. *Ultrasound in Obstetrics and Gynaecology*, **13**: 176-180.

Raisanen, S., Sokka, A., Georgiadis, L., Harju, M., Gissler, M., Keski-Nisula, L., Kalviainen, R. and Heinonen, **S. (2013).** Infertility Treatment and Umbilical Cord Length–Novel Markers of Childhood Epilepsy. *PLoS ONE*, **8**: e55394.

Rebelo, F., Farias, D. R., Mendes, R. H., Schlüssel, M. M. and Kac, G. (2015). Blood pressure variation throughout pregnancy according to early gestational BMI: A Brazilian cohort. *Brazilian Archives of Cardiology*, **104**(4): 284-291.

Reichman, N., Hamilton, E., Hummer, R. and Padilla, Y. (2008). Racial and ethnic disparities in low birthweight among urban unmarried mothers. *Maternal and Child Health Journal,* **12**: 204-215.

Richards, M., Hardy, R., Kuh, D. and Wadsworth, M. (2001). Birth and cognitive function in the British 1946 irth cohort: longitudinal population based study. *British Medical Journal,* **322**: 199-203.

Roberts, D. (2008). Placental Pathology: A survival guide. *Arch Pathology of Laboratory Medicine,* **132**: 641-651.

Rohinidev, I. M., Jeyasingh, T. and Vimala, V. (2016). Morphological study of umbilical cord and its embryological significance. *International Journal for Anatomy Research*, **4**: 1806-1809.

Roland, M., Friis, C., Godang, K., Bollerslev, J., Haugen, G. and Henriksen, T. (2014). Maternal Factors Associated with Fetal Growth and Birthweight Are Independent Determinants of Placental Weight and Exhibit Differential Effects by Fetal Sex. *PLoS ONE*, **9**: 1-5.

Romanowicz, L. and Bankowski, E. (2010). Lipid compounds of human Wharton's jelly and their alterations in preeclampsia. *International Journal of Experimental Pathology*, **91**: 1-9.

Rondo, P., Ferreira, R., Nogueira, F., Ribeiro, M., Lobert, H. and Artes, R. (2003). Maternal psychological stress and distress as predictors of low birth weight, prematurity and intrauterine growth retardation. *European Journal of Clinical Nutrition*, **57**: 266-272.

Rostamzadeh, S., Kalantari, M., Shahriari, M. and Shakiba, M. (2015). Sonographic Measurement of the Umbilical Cord and Its Vessels and Their Relation with Fetal Anthropometric Measurements. *Iran Journal of Radiology*, **12**: e12230.

Rudman, D., Kutner, M. H., Blackston, R. D., Cushman, R. A., Bain, R. P. and Patterson, J. H. (1998). Children with normal variant short stature: Treatment with human growth hormone for six months. *New England Journal of Medicine*, **305:** 123-231.

Runkle, J., Flocks, J., Economos, J., Tovar-Aguilar, L. and McCauley, L. (2014). Occupational Risks and Pregnancy and Infant Health Outcomes in Florida Farmworkers. *International Journal of Environmental Research and Public Health,* **11**: 7820-7840.

Rupa, L., Shirol, V., Anita, M. and Tyagi, N. (2013). Clinical determinants of placental morphometry and birth weight. *International Organization of Scientific Research: Journal of Dental and Medical Sciences*, **10**: 22-27.

Sabir, H., Azhar, B., Monirujjaman, I. K., Afrin, S. and Abdullah-Al-Shoeb, M. (2013). Maternal Socio-demographic factors and anthropometric characteristics related to infant birth weight. *Journal of Pharmaceutical and Biomedical Sciences,* **29**: 788-797.

Sabita, S. and Gugapriya, T. (2014). A cross-sectional morphometric study of hypertensive with normal placentae and its correlation with foetal outcome. *International Journal of Anatomy and Research,* **2**: 437-442.

Sabnis, A., More, R., Mali, S. and Niyogi, G. (2012). Umbilical Cord Morphology and its Clinical Significance. *Medical Case Reports,* **3**: 30-33.

Sadler, T. W. (2012). *Langman's medical embryology*.12: Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins.

Salafia, C., Haas, E., Thorp, J., Eucker, B., Pezzullo, J. and Savitz, D. (2005). Measures of placental growth in relation to birth weight and gestational age. *American Journal of Epidemiology*, **162**: 991-998.

Salafia, C. M., Zhang, J., Charles, A. K., Bresnahan, M., Shrout, P., Sun, W. and Maas, E. M. (2008). Placental characteristics and birthweight. *Paediatric and Perinatal Epidemiology*, **22**(3): 229-239.

Salafia, C., Yampolsky, M., Misra, D., Shlakhter, O., Haas, D., Eucker, B. and Thorp, J. (2010). Placental surface shape, function, and effects of maternal and fetal vascular pathology. *Placenta*, **5**: 1-5.

Salameh, W. and Matrogiannis, D. (1994). Maternal hyperlipidemia in pregnancy. *Clinical Obstetrics and Gynaecology*, **37**: 66-77.

Salavati, N., Smies, M., Ganzevoort, W., Charles, A., Erwich, J. J., Plösch, T. and Gordijn, S. (2019). The Possible Role of Placental Morphometry in the Detection of Fetal Growth Restriction. *Frontiers in Physiology*, **9**: 1-12.

Sales, W., Dias, J. S., Kroll, C., Mastroeni, S., Silva, F. and Mastroeni, M. (2015). Influence of altered maternal lipid profile on the lipid profile of the newborn. *Archive of Endocrinology and Metabolism*, **59**: 123-128.

Salmani, D., Purushothaman, S., Somashekara, S., Gnanagurudasan, E., Sumangaladevi, K., Harikishan, R. and Venkateshwarareddy, M. (2014). Study of structural changes in placenta in pregnancy-induced hypertension. *Journal of Natural Science, Biology and Medicine*, **5**: 352-355.

Sanchez-Vaznaugh, E., Kawachi, I., Subramanian, S., Sa´nchez, B. and Acevedo-Garcia, D. (2009). Do Socioeconomic Gradients in Body Mass Index Vary by Race/Ethnicity, Gender, and Birthplace? *American Journal of Epidemiology*, **169**: 1102–1112.

Savitri, A. I., Zuithoff, P., Browne, J. L., Amelia, D., Baharuddin, M., Grobbee, D. E. and Uiterwaal, C. S. (2016). Does prepregnancy BMI determine blood pressure during pregnancy? A prospective cohort study. *British Medical Journal Open,* **6**: e011626.

Schreuder, Y., Hutten, B., van Eijsden, M., Jansen, E., Vissers, M., Twickler, M. and Vrijkotte, T. (2011). Ethnic differences in maternal total cholesterol and triglyceride levels during pregnancy: the contribution of demographics, behavioural factors and clinical characteristics. *European Journal of Clinical Nutrition,* **65**: 580–589.

Selemani, M., Mwanyangala, M., Mrema, S., Shamte, A., Kajungu, D., Mkop, A., Mahande, M. and Nathan, R. (2014). The effect of mother's age and other related factors on neonatal survival associated with first and second birth in rural, Tanzania: evidence from Ifakara health and demographic surveillance system in rural Tanzania. *BioMed Central: Pregnancy and Childbirth,* **14**: 240.

Shahnawaz, K., Choudhary, S., Sarker, G., Das, P., Pal, R. and Kumar, L. (2014). Association between maternal socio-demographic factors and low birth weight newborn in a rural area of Bihar, India. *South East Asia Journal of Public Health,* **4**: 30-34.

Shariff, E. and Prakash, S. (2019). Effect of maternal body size and socioeconomic status on the outcome of pregnancy. *National Journal of Physiology, Pharmacy and Pharmacology,* **9**: 28-32.

Shevade1, S., Arole, V., Bharambe, V. and Paranjape, V. (2015). Placental Morphology and Fetal Outcome in Preeclampsia And Normotensive Pregnancies. *International Organization of Scientific Research: Journal of Dental and Medical Sciences,* **14**: 11-15.

Sicard, M., Nusinovici, S. and Hanf, M. (2017). Fetal and postnatal head circumference growth: Synergetic factors for neurodevelopmental outcome at 2 years of age for preterm infants. *Neonatology,* **112**: 122–129.

Silver, R. K., Dooley, S. L., Tamura, R. K. and Depp, R. (1987). Umbilical cord size and amniotic fluid volume in prolonged pregnancy. *American Journal of Obstetrics and Gynaecology,* **157**: 716-720.

Singh, S., Kumar, P. and Thakur, B. (2018). Anthropometric measurements of a neonate vis-a-vis maternal nutritional status. *Thakur,* **5**: 640-644.

Sivarao, S., Vidyadaran, M., Jammal, A., Zainab, S., Goh, Y. and Ramesh, K. (2002). Weight, Volume and Surface Area of Placenta of Normal Pregnant Women and their Relation to Maternal and Neonatal parameters in Malay, Chinese and Indian Ethnic Groups. *Placenta,* **23**: 691-696.

Skulstad, S. M., Ulriksen, M., Rasmussen, S. and Kiserud, T. (2006). Effect of umbilical ring constriction on Wharton's jelly. *Ultrasound in Obstetrics and Gynaecology,* **28**: 692-698.

Sokal, D., Sawadogo, L. and Adjibade, A. (1991). Short stature and cephalopelvic disproportion in Burkina Faso, West Africa. Operations Research Team. *International Journal of Gynaecology and Obstetrics*, **35**: 347-350.

Spurway, J., Logan, P. and Pak, S. (2012). The development, structure and blood flow within the umbilical cord with particular reference to the venous system. *American Journal of Ultrasound Medicine*, **15**: 97 - 102.

Staley, J., Bradley, J., Silverwood, R., Howe, L., Illing, K., Lawlor, D. and Macdonald-Wallis, C. (2015). Associations of Blood Pressure in Pregnancy With Offspring Blood Pressure Trajectories During Childhood and Adolescence: Findings From a Prospective Study. *Journal of the American Heart Association*, **4**:1-12.

Stefulj, J., Panzenboeck, U., Becker, T., Hirschmugl, B., Schweinzer, C., Lang, I., Marsche, G., Sadjak, A., Lang, U., Desoye, G. and Wadsack, C. (2009). Human Endothelial Cells of the Placental Barrier Efficiently Deliver Cholesterol to the Fetal Circulation via ABCA1 and ABCG1. *Circulation Research*, pp. 600-608.

Stevens, J., Katz, E. and Huxley, R. (2010). Associations between gender, age and waist circumference. *European Journal of Clinical Nutrition*, **64**: 6–15.

Strauss, R. and Dietz, W. (1998). Growth and development of term children born with low birth weight: effects of genetic and environmental factors. *Journal of Paediatrics*, **133**: 67–72.

Strong, T. H. Jr., Sarno, A. P. and Paul, R. H. (1992). Significance of intrapartum amniotic fluid volume in the presence of nuchal cords. *Journal of Reproduction Medicine,* **37**: 718-720.

Suzuki, S. and Fuse, Y. (2012). Length of the umbilical cord and perinatal outcomes in Japanese singleton pregnancies delivered at greater than or equal to 34 weeks‘ gestation. *Journal of Clinical Gynaecology and Obstetrics,* **1**(4-5): 57-62.

Tabrizi, F. and Saraswathi, G. (2012). Maternal anthropometric measurements and other factors: relation with birth weight of neonates. *Nutrition Research and Practice,* **6**: 132-137.

Tahmasebi, M. and Alighanbari, R. (2011). Evaluation of umbilical cord thickness, cross-sectional area, and coiling index as predictors of pregnancy outcome. *Indian Journal of Radiology and Imaging,* **21**: 195-198.

Tarrade, A., Panchenko, P., Junien, C. and Gabory, A. (2015). Placental contribution to nutritional programming of health and diseases: epigenetics and sexual dimorphism. *The Journal of Experimental Biology,* **218**: 50-58.

te Velde, E., Exalto, N., Hesseling, P. and van der Linden, H. (1997). First trimester development of human chorionic villous vascularization studied with CD34 immunohistochemistry. *Human Reproduction*, **12**: 1577–1581.

Tetteh, J. (2015). Gross morphometry of the human placenta and umbilical cord with reference to neonatal indices. In: Anatomy. Kumasi: Kwame Nkrumah University of Science and Technology, p. 113.

Thame, M., Osmond, C., Bennett, F., Wilks, R. and Forrester, T. (2004). Fetal growth is directly related to maternal anthropometry and placental volume. *European Journal of Clinical Nutrition,* **58**: 894–900.

Thame, M., Osmond, C., Wilks, R., Bennett, F., McFarlane-Anderson, N. and Forrester, T. (2000). Blood Pressure Is Related to Placental Volume and Birth Weight. *Hypertension,* **35**: 662- 667.

Togni, F. A., Araujo, J. E., Vasques, F. A., Moron, A. F., Torloni, M. R. and Nardozza, L. M. (2007). The cross-sectional area of umbilical cord components in normal pregnancy. *International Journal for Gynaecology and Obstetrics,* **96**: 156-161.

Trinder, P. (1969). Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. *Annals of Clinical Biochemistry,* **6**(1): 24-27.

Tripath, I. A., Agarwal, D., Devi, R. and Cherian, S. (1987). Nutritional status of rural pregnant women and fetal outcome. *Indian Paediatrics*, pp. 703-712.

Tsegah, M. and Asante, D. (2018). Mode Of Umbilical Cord Insertion And Neonatal Weight, And Some Placental Factors. *International Journal of Anatomy and Research*, **6**: 5471-5576.

Tsu, V. (1992). Maternal height and age: risk factors for cephalopelvic disproportion in Zimbabwe. *International Journal of Epidemiology*, **21**: 941-946.

Ugwa, E. A. (2014). Maternal anthropometric characteristics as determinants of birth weight in North-West Nigeria: A prospective study. *Nigerian Journal of Basic and Clinical Sciences,* **11:** 8 – 12.

Upadhyay, S., Biccha, R., Sherpa, M., Shrestha, R. and Panta, P. (2011). Association between maternal body mass index and the birth weight of neonates. *Nepal Medical College Journal*, **13**: 42-45.

Uzun, H., Benian, A. and Madazli, R. (2005). Circulating oxidized low-density lipoprotein and paraoxonase activity in preeclampsia. *Gynaecology and Obstetric Investigations*, **60**: 195–200.

Vaano, J. (2014). Length and head circumference at birth: associations with birth outcome and morbidity in macrosomic Finnish infants. In: Faculty of Health Sciences, Public Health Nutrition. Finland: University of Eastern Finland, p 65.

Victora, C., Adair, L. and Fal, C. (2008). Maternal and child undernutrition: consequences for adult health and human capital. *Lancet*, **371**: 340–357.

Villar, J., Ismail, L., Victoria, C., Ohuma, E., Bertino, E., Altman, D., Lambert, A., Papageorghiou, A. T., Carvalho, M., Jaffer, Y. A., Gravett, M. G., Purwar, M., Frederick, I. O., Noble, A. J., Pang, R. C., Barros, F. C., Chumlea, C., Bhutta, Z. A. and Kennedy, S. H. (2014). International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. *Lancet*, **384:** 857–868.

Visentin, S., Grumolato, F., Nardelli, G., Di Camillo, B., Grisan, E. and Cosmi, E. (2014). Early origins of adult disease: low birth weight and vascular remodeling. *Atherosclerosis*, **237**: 391–399.

Visscher, T., Seidell, J., Molarius, A., van der Kuip, D., Hofman, A. and Witteman, J. (2001). A comparison of body mass index, waist – hip ratio and waist circumference as predictors of all-cause mortality among the elderly: the Rotterdam study. *International Journal of Obesity*, **25**: 1730–1735.

Vizza, E., Correr, S., Goranova, V., Heyn, R., Angelucci, P. A., Forleo, R. and Motta, P. M. (1996). The collagen skeleton of the human umbilical cord at term. A scanning electron microscopy study after 2N-NaOH maceration. *Reproduction and Fertilization Development*, **8**: 885-894.

Vogel, J., Souza, J., Mori, R., Morisaki, N., Lumbiganon, P., Laopaiboon, M., Ortiz-Panozo, E., Hernandez, B., Perez-Cuevas, R., Roy, M., Mittal, S., Cecatti, J. G., Tuncalp,

O. and Gulmezoglu, A. M. **(2014).** Maternal complications and perinatal mortality: findings the World Health Organization Multicountry Survey on Maternal and Newborn Health. *British Journal of Obstetrics and Gynaecology,* **121**: 76–88.

Wang, Y. and Zhao, S. (2010). Vascular biology of the placenta. Morgan & Claypool Life Sciences Editorial.

Wang, Y., Mao, J., Wang, W., Qiou, J., Yang, L. and Chen, S. (2017). Maternal fat free mass during pregnancy is associated with birth weight. *Reproductive Health,* **14**: 1-7.

Wang, Y., Tanbo, T., Abyholm, T. and Henriksen, T. (2011). The impact of advanced maternal age and parity on obstetric and perinatal outcomes in singleton gestations. *Archives of Gynaecology and Obstetric,* **284**: 31 - 37.

Weissman, A., Jakobi, P., Bronshtein, M. and Goldstein, I. (1994). Sonographic measurements of the umbilical cord and vessels during normal pregnancies. *Journal of Ultrasound Medicine,* **13**: 11-14.

Whittle, W., Chaddha, V., Wyatt, P., Huppertz, B. and Kingdom, J. (2006). Ultrasound detection of placental insufficiency in women with 'unexplained' abnormal maternal serum screening results. *Clinical Genetics,* **69**: 97-104.

Williams, B., Mancia, G., Spiering, W., Agabiti Rosei, E., Azizi, M., Burnier, M. and Kahan, T. (2018). 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). *European heart journal*, **39**(33): 3021-3104.

World Health Organization (2000). Obesity: preventing and managing the global epidemic. *Report of a WHO Consultation World Health Organization Technical Report Series*, **894**: 1-253.

World Health Organization. (2002). WHO antenatal care randomized trial: manual for the implementation of the new model (No. WHO/RHR/01.30). World Health Organization.

World Health Organization. (2016). WHO recommendations on antenatal care for a positive pregnancy experience. World Health Organization.

World Health Organization (2018). WHO recommendations on antenatal care for a positive pregnancy experience. In. Geneva, Switzerland, p.1-10.

World Health Organization Expert Committee (1995). Physical Status: The Use and Interpretation of Anthropometry. In: WHO Technical Report. Geneva: World Health Organization, pp.1-463.

Wilcox, A. (2001). On the Importance - and the unimportance of birth weight. *International Epidemiological Association,* **30**: 1233-1241.

Wilcox, A. and Rusell, I. (1990). Why small black infants have lower mortality than small white infants: the case for population - specific standards for birthweight. *Journal of Paediatrics*, **116**: 1233-1241.

Wilkin, J. (2002). Formation and Role of Placenta. In: Larsen's Human Embryology. Philadelphia: Lippincott Williams & Wilkins, pp. 20 – 44.

Witter, F., Caulfield, L. and Stoltzfus, R. (1995). Influence of maternal anthropometric status and birth weight on the risk of cesarean delivery. *Obstetrics and Gynaecology*, **85**: 947–951.

Wood, A., Raynes-Greenow, C., Carberry, A. and Jeffery, H. (2013). Neonatal length inaccuracies in clinical practice and related percentile discrepancies detected by a simple length-board. *Journal of Paediatrics and Child Health*, **49**: 199–203.

Woollett, L. (2005). Maternal cholesterol in fetal development: transport of cholesterol from the maternal to the fetal circulation. *Norman Kretchmer Memorial Award in Nutrition and Development Lecture*, pp. 1155-1161.

Woollett, L. (2011). Review: Transport of Maternal Cholesterol to the Fetal Circulation. *Placenta*, **32**: S218–S221.

Wright, D. and Chan, G. (2009). Fetal bone strength and umbilical cord length. *Journal of Perinatology*, **29**: 603–605.

Yampolsky, M., Salafia, C., Shlakhater, O., Haas, D., Eucker, B. and Thorp, J. (2009). Centrality of the Umbilical Cord Insertion in a Human Placenta Influences the Placental Efficiency. *Placenta,* **30**: 1058-1064.

Yampolsky, M., Salafia, C., Shlakhter, O., Haas, D., Eucker, B. and Thorp, J. (2008). Modeling the variability of shapes of a human placenta. *Placenta,* **29**: 790-797.

Ye, K. B. Q., Du, Q.- J., Zhang, D., Shen, Y. and Yan-Ping, H. (2015). Maternal serum lipid levels during late pregnancy and neonatal body size. *Asia Pacific Journal of Clinical Nutrition,* **24**: 138–143.

Yeboah, F., Fondjo, L., Sein, M., Debrah, O., Annan, B., Tagoe, E. A. and Bawah, A. (2018). Association between antenatal booking visit and occurrence of preeclampsia: A Ghanaian study. *Edorium Journal of Gynaecology and Obstetrics,* **4**: 1-9.

Yu, Z., Han, S., Zhu, J., Sun, X., Ji, C. and Guo, X. (2013). Pre-Pregnancy Body Mass Index in Relation to Infant Birth Weight and Offspring Overweight/Obesity: A Systematic Review and Meta-Analysis. *PLoS ONE,* **8**: e61627.

Zadroina, M., Nowak, B., Zohołnierek, M., Zamorska, L. and Niweliński, J. (2012). Human Placenta as a Biomarker of Environmental Toxins Exposure – Long-Term Morphochemical Monitoring. Slavka Krautzeka, Croatia: IInTech Europe.

Zain, N., Low, W.-Y. and Othman, S. (2015). Impact of Maternal Marital Status on Birth Outcomes Among Young Malaysian Women: A Prospective Cohort Study. *Asia-Pacific Journal of Public Health*, **27**: 335–347.

Zeng, Z., Liu, F. and Li, S. (2017). Metabolic Adaptations in Pregnancy: A Review. *Annals of Nutrition and Metabolism*, **70**: 59-65.

Zhang, R., Dong, S., Ma, W. W., Cai, X. P., Le, Z. Y., Xiao, R. and Yu, H. L. (2017). Modulation of cholesterol transport by maternal hypercholesterolemia in human full-term placenta. *PLoS One*, **12**(2): e0171934.

Zygmunt, M., Herr. F. and Munstedt, K. (2003). Angiogenesis and vasculogenesis in pregnancy. *European Journal of Obstetrics and Gynaecology and Reproduction Biology*, **110**: S10 – S18.