GROSS MORPHOMETRY OF THE HUMAN PLACENTA AND UMBILICAL CORD WITH REFERENCE TO NEONATAL INDICES

A THESIS SUBMITTED IN PARTIAL

FULFILMENT OF THE

REQUIREMENTS FOR THE DEGREE OF

MASTER OF PHILOSOPHY IN HUMAN ANATOMY AND CELL BIOLOGY

IN THE

DEPARTMENT OF ANATOMY, SCHOOL OF MEDICAL SCIENCES,
COLLEGE OF HEALTH SCIENCES

BY

JOSHUA TETTEH

KWAME NKRUMAH UNIVERSITY OF SCIENCE & TECHNOLOGY, KUMASI

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MARCH, 2015

DECLARATION

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

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ABSTRACT

In recent years more attention has been focused on the morphology of the placenta and umbilical cord due to their vital roles in foetal development and neonatal survival. While extensive studies have been documented in this area in the developed world, there is very little published information about the morphological variations that occur in human placenta and umbilical cord in Ghana. Therefore this study was designed to evaluate the structural variations in placental indices, umbilical cord indices and neonatal outcome and also compare the data obtained with other samples for regional variation. A total of 236 placentae with attached umbilical cords were obtained from the Kwame Nkrumah University of Science and Technology Hospital in Kumasi between February and July 2013 for this study. Mean placental indices for weight, diameter and thickness were 578.81 g, 17.40 cm and 2.04 cm respectively. The mean neonatal indices were 3.24 kg, 34.27 cm and 50.64 cm for weight, head circumference and length respectively. Neonatal weight correlated significantly with placental weight, neonatal length and neonatal head circumference ($P < 0.05$). On the contrary, neonatal weight had no significant correlation with placental thickness and diameter. However, there was significant correlation between the umbilical cord length with umbilical cord diameter, umbilical cord artery A1 diameter, umbilical cord artery A2 diameter and volume of Wharton's jelly ($P < 0.001$). Based on the results of the present study, the placental weight, umbilical cord length and diameter and neonatal weight values compared with other sampled populations showed significantly lower values. These findings suggest that regional variations exist with these parameters which are likely to contribute to the high neonatal morbidity and mortality rate reported in Ghana. This study further affirms that the placenta and umbilical cord should be critically examined in order to effectively monitor and manage adverse neonatal outcome.

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ABBREVIATIONS

A1A	Umbilical cord Artery 1 Area
A1D	Umbilical cord Artery 1 Diameter

A1V	Umbilical cord Artery 1 Volume
A2A	Umbilical cord Artery 2 Area
A2D	Umbilical cord Artery 2 Diameter
A2V	Umbilical cord Artery 2 Volume
AWJ	Area of Wharton's jelly
BL	Body Length
BW	Birth Weight
BW/PW	Birth Weight to Placental Weight ratio
CCI	Cord Centrality Index
CPA	Chorionic Plate Area
dI	Distance of umbilical cord insertion from margin
HC	Head Circumference
Ldi	Long distance of umbilical cord insertion from margin
PD	Placental Diameter
PI	Ponderal Index
PW	Placental Weight
Sdi	Short distance of umbilical cord insertion from margin
UCA	Umbilical Cord Area
UCD	Umbilical Cord Diameter
UCL	Umbilical Cord Length
UCV	Umbilical Cord Volume
UCVA	Umbilical Cord Vein Area
UCVD	Umbilical Cord Vein Diameter
UCVV	Umbilical Cord Vein Volume
VWJ	Volume of Wharton's Jelly

CHAPTER ONE

INTRODUCTION

1.1 THE PLACENTA

The human placenta is a dynamic discoid organ which has two surfaces; the chorionic plate facing the foetus and having the umbilical cord attached, and the basal plate which abuts the maternal endometrium (Wang *et al*., 2004; Sørensen *et al*., 2013). It is the only organ in the body derived from two separate individuals, the mother and the foetus and is the primary metabolic regulator for the respiratory, nutritional, excretory, endocrine and immunological functions of the foetus necessary for foetal growth (Raghunath and Vijayalakshmi, 2011; Singal *et al.,* 2013). The normal human placenta at term has a dark blue red or maroon colour, weighs about 590 grams and is approximately 20–25 cm in diameter and 3 cm thick (Tissot van Patot *et al*., 2009; Heazell *et al*., 2010). These morphological measurements can vary considerably due to many factors including pathological and physiological factors (Janthanaphan *et al*., 2006; Kaplan, 2008). The umbilical cord inserts into the chorionic plate, or foetal side of the placenta, where the vessels branch into a network covered by a thin layer of cells (Chang *et al.,* 2012). Human pregnancies complicated by factors such as preeclampsia, intrauterine growth restriction (IUGR), maternal residence at high altitude, cigarette smoking, anaemia, diabetes mellitus or asthma affect foetal and placental weight as well as placental microstructure (Samson *et al*., 2011). Several studies have reported that factors such as maternal protein and iron restriction as well as changes in the maternal and/or foeto-placental vasculatures affect the growth and efficiency of the placenta (Veras *et al.,* 2008; Yampolsky *et al.,* 2011; Sandovici *et al.,* 2012). It has been documented that lighter and smaller than normal placentae are reflective of reduced

foetal movements (RFM) in-utero, hence such women have higher risks of stillbirth and intra uterine growth restriction (IUGR) (Heazell and Frøen, 2008; Heazell *et al*., 2010).

1.2 UMBILICAL CORD STRUCTURE

The human umbilical cord, which is also sometimes referred to as the funiculus umbilicalis is a connecting cord from the developing foetus to the placenta (Proctor *et al*., 2010; NuggedAlla, 2013; Jain *et al*., 2014). The umbilical cord is derived from contributions of the body stalk, vitelline duct, yolk sac and allantois and is physiologically and genetically part of the foetus. Structurally it is made up of two umbilical arteries which carry oxygen-poor blood from the foetus to the placenta and one umbilical vein which returns oxygen-rich blood to the foetus (Holzman *et al*., 2007; Marshall, 2014). These vessels are surrounded by an extracellular matrix of mucous embryonic connective tissue (Wharton's jelly), covered by an outer covering of amniotic epithelium, and inserted into the foetal surface of the placental disc (Proctor *et al*., 2010; Lacono *et al*., 2012; Jain *et al*., 2014). The Wharton's jelly gives flexibility, mobility and strength to resist compression and at the same time allows the foetus to move freely (Predanic, 2009).

The exterior surface of the cord is dull white in colour, moist, and has an average diameter of 0.8 to 2.0 cm and an average length of 55 cm at term and may range from no cord (achordia) to lengths of up to 300 cm (Holzman *et al*., 2007; NuggedAlla, 2013; Jain *et al*., 2014). It is helical in shape, with a chirality of about 1 coil per 5 centimetres of length (Ernst *et al*., 2013). Several umbilical cord abnormalities are known to cause adverse prenatal outcome (Sabnis *et al*., 2012; Barnwal *et al*., 2013) such as IUGR, intrauterine death (IUD) or Foetal distress (Sabnis *et al*., 2012).

1.3 NEONATAL PARAMETERS

Adequate placental function is necessary for foetal growth (Risnes *et al*., 2009). The ratio between placental weight and birth weight (foeto-placental ratio) could be a useful indicator for placental efficiency since placental weight alone cannot be used as a representation for its function (Thame *et al*., 2004; Salafia *et al*., 2006).

Ponderal index assesses whether an infant appears relatively fat or thin at birth by quantification of the dissociation of weight and length and is of great help to recognize wasted infants irrespective of their distribution on the percentile lines of birth weight for gestational age (Brutsaert *et al*., 2012). Low birth weight is defined as birth weight less than 2.5 kg (WHO., 2003; Wallace *et al*., 2012; Garg *et al*., 2015). The idea of IUGR, described as low birth weight for gestational age to be the key determinant of infant mortality is superseded by ponderal index, this is because low birth weight (<2.5 kg) alone cannot be taken as a full proxy marker for the measurement of foetal growth dysfunctions. Hence for efficient detection of intrauterine malnutrition, it is important to include body length and compute the ponderal index for gestational age (Colley *et al.*, 1991). The ROHRER's ponderal index is given by (P.I.) = (100 X weight divided by length cube) (Walther and Ramaekers, 1982; Landmann *et al.*, 2006; Brutsaert *et al*., 2012). Wasted infants will show a relatively small ponderal index irrespective of their distribution on the percentile lines of birth weight for gestational age.

Foetal head circumference provides information on intrauterine growth restrictions.

Traditionally, IUGR has been classified as symmetric and asymmetric growth restrictions. Symmetrically growth – restricted neonates possess low birth weight, yet they may not be thin or wasted, since they show an appropriate weight for their length. These neonates may have been adversely affected by genetic, infectious or teratogenic insult early in-utero, however, most of them are healthy normal infants (Landmann *et al*., 2006).

Birth weight on the other hand, is a straightforward measure of the outcome of birth and is affected by several factors (direct or indirect) necessary for perinatal survival (Misra *et al.*,

2009). Birth weight is probably the single most important factor that affects neonatal mortality, in addition to being a significant determinant of post-neonatal infant mortality and of infant and childhood morbidity.

1.4 THE PRESENT STUDY

It is estimated that the world wide occurrence of perinatal deaths is more than 7.6 million and 4.3 million of these are foetal deaths (Sornes, 2000). Ninety-eight percent of perinatal deaths have been said to take place in developing countries and the perinatal mortality rate is estimated to exceed 55 per 1000 births, which is five times higher than in developed countries (Salafia and Vintziloes, 1999). Several studies have been conducted in the developed countries and Asia which have suggested that placental indices have a significant role in foetal growth in terms of weight, body length, and cord length (Lurie *et al*, 1999; Salafia and Vintziloes, 1999).

Currently very little is known about the incidence of foetal deaths resulting from placental and umbilical cord malformation in Ghana. The occurrence of foetal compression risk based on cord location and placental malformations are also unknown (Salafia and Vintziloes, 1999**;** Valsamakis *et al*., 2006). In Ghana, little information exists on the qualitative morphometric assessment of placental and umbilical cord indices in relation to the neonate. Therefore this study is carried out to explore the gross qualitative and morphometric assessment of the human placenta and umbilical cord and their correlation with neonatal factors such as foetal weight, length and head circumference.

1.5 AIM AND OBJECTIVES

1.5.1 AIM

To generate detailed baseline data on the morphological variations of the placenta, umbilical cord and neonatal indices using quantitative methods.

1.5.2 OBJECTIVES

1. To determine the relationship between gross placental morphometry and neonatal anthropometry.
2. To determine the relationship between placental anthropometry and umbilical cord indices.
3. To determine the relationship between umbilical cord indices and neonatal anthropometry.
4. To compare the placental, umbilical cord and neonatal indices with published data.

CHAPTER TWO

LITERATURE REVIEW

2.1 MORPHOLOGY OF THE PLACENTA

The human placenta is a discoid organ which presents two surfaces; the chorionic plate facing the foetus and to which the umbilical cord is attached, and the basal plate which abuts the maternal endometrium (Wang *et al*., 2004; Sørensen *et al*., 2013). The placenta is a dynamic organ which is unique in its development and functions. It is the only organ in the body which is derived from two separate individuals, the mother and the foetus. It is the primary regulator for the respiratory, nutritional, excretory, endocrine and immunological functions of the foetus necessary to foetal growth (Raghunath and Vijayalakshmi, 2011; Singal *et al*., 2013). The placenta functions as a selectivity filter, directing the influx of oxygen, inorganic salts, sugars, amino acids, peptides and other biologically active molecules to foetal circulation and the efflux of foetal waste materials to the maternal circulatory system (Machin *et al*., 2000; Valsamakis *et al*., 2006).

The placenta therefore serves as the major link between a mother and her unborn neonate, the foetus. Owing to the delicate and important nature of the placenta it is sometimes referred to as the "mirror of the perinatal period, which has not been sufficiently polished" (Machin *et al*., 2000; Valsamakis *et al*., 2006). It provides an indirect link between the maternal circulation and that of the foetus and serves as the organ for exchange of nutrients, gases and waste products through diffusion (Salafia *et al*., 2005).

The placenta cannot be measured directly until after birth, but the dimensions of the delivered placenta reveal the cumulative development of the placenta from conception to delivery (Sepulveda *et al*., 2003; Salafia *et al*., 2005). Placental weight is one of several standard placental measurements by which placental growth can be characterized (Wang *et al*., 2004; Roh *et al*., 2005). Placental weight is a summary of different dimensions of growth, including placental thickness, shape, number of blood vessels, cord insertion and arborisation of the villous and vascular nutrient exchange surface, reflected in increasing thickness of the disk (Sepulveda *et al*., 2003; Roh *et al*., 2005). These standard placental measurements have been a routine part of gross placental pathologic examinations (Machin *et al*., 2000; Valsamakis *et al*., 2006). However, these simple measurements may have limitations in capturing the often much more variable chorionic plate growth of placentae from complicated pregnancies. The growth of the placenta is directly related to its functional efficiency as the sole foetal source of both nutrients and oxygen (Machin *et al*., 2000; Valsamakis *et al*., 2006).

Placental weight has also been reported to be the culmination of placental growth in the lateral chorionic plate expansion and in disk thickness (Machin *et al*., 2000; Valsamakis *et al*., 2006). It has been reported that early in the second trimester, the placenta approximates the foetus in size and continues to grow until term. As pregnancy advances, it becomes relatively smaller and by term the ratio of its weight to that of the foetus is about 1:6 to 1:7
(Veras *et al*., 2008). At term, the normal placenta weighs 350-600g with a mean of about

590g (15% of the normal neonatal weight), (Tissot van Patot *et al*., 2009; Borton, 2011). Therefore neonate weighs approximately seven times the placental weight. This ratio decreases earlier in gestation.

The term placenta is circular, semi-circular or oval and approximately 20–25 cm in diameter and 3 cm thick (Heazell *et al*., 2010; Salafia *et al*., 2012; Yampolsky *et al*., 2013; Gill *et al*., 2014). Generally, the shape of the chorionic disk is rarely truly circular; its shape commonly varies, from round to oval, bi- or multi-lobate, or irregular. Placental shape is thought to be determined by where it is implanted in the uterus, regional variations in the decidua (that may determine areas of atrophy), variations in maternal vascular supply (with placental infarcts resulting in altered shape) and perhaps even the "manner of its original implantation (Yampolsky *et al*., 2008). The combination of placental shape and cord insertion is hypothesized to affect placental efficiency (Salafia *et al*., 2009; Yampolsky *et al*., 2009). Abnormal placental shape generally reflects pathologic villous atrophy (Bowman and Kennedy, 2014).

At term the foetal surface of the placenta is shiny and consists of large blood vessels which are opaque in nature distributed on the dense opalescent surface of the thickened chorion normally, coursing to the edge of the chorionic plate (Yetter,1998). The arteries overlie the veins and supply the almost 200 placental lobules with blood. A placental lobule is defined as the villous area supplied by one artery and one vein. The maternal surface has the dark red colour of venous blood and usually has 12 to 20 subdivisions, referred to as cotyledons which are sometimes grouped into visible lobes (Kishwara *et al*., 2009). Each cotyledon contains a primary villous stem arising from the chorionic plate and supplied by primary branches of foetal vessels (Valsamakis *et al*., 2006). The primary stems divide to form secondary and tertiary stems from which arise the terminal villi, where maternal–foetal exchange takes place (Salafia and Vintziloes, 1999; Valsamakis *et al*., 2006). The placenta uses about 1/3 of all the

oxygen and glucose supplied by the maternal blood. Also, the rate of protein synthesis is higher in the placenta than the liver (Kaplan, 2008).

The umbilical cord inserts into the chorionic plate, or foetal side of the placenta, where the vessels branch into a network covered by a thin layer of cells. Similar to the root system of a tree, this vascular network must effectively and efficiently provide nutrients for the foetus as it grows larger (Chang *et al*., 2012). Placental lakes are part of the normal appearance of the placenta in the second and third trimesters (Hwang *et al*., 2012). Placental lakes may be numerous, few or even absent and may seem to be more evident with increasing placental thickness. Lakes contain maternal blood which can be seen swirling and have low velocity venous blood flow within them (Reis *et al*., 2005; Hwang *et al*., 2012). Placental lakes have little to no clinical significance and do not seem to indicate an increase in adverse pregnancy outcome (Reis *et al*., 2005). Some investigators have suggested that placental lakes serve as precursors of perivillous fibrin deposition or intervillous thrombosis, if venous flow decreases within the lake (Holzman *et al*., 2007). Several studies have reported that factors such as maternal protein and iron restriction as well as changes in the maternal and/or foeto-placental vasculatures affect the growth and efficiency of the placenta (Veras *et al*., 2008; Yampolsky *et al*., 2011; Sandovici *et al*., 2012). Other factors that affect foetal and placental weight as well as placental microstructure include human pregnancies complicated by preeclampsia, IUGR, maternal residence at high altitude, cigarette smoking, anaemia, diabetes mellitus or asthma (Samson *et al*., 2011).

Placental thickness, by contrast, marks the extent of arborisation of the villous capillary bed, the actual locus of maternal foetal exchange (Veras *et al*., 2008). Foetal stem arterioles are also principal sites of placental vascular resistance. Thus, they contribute to total foetal peripheral resistance and foetal heart work (Yampolsky *et al*., 2011).

2.2 PLACENTAL DEVELOPMENT

The placenta is the first organ to form during mammalian embryogenesis (Rossant and Cross, 2001). Early in gestation, the developing embryo is small and its nutritional and waste disposal needs are minor. At this point, the embryo absorbs nutrients from the mother's endometrial secretions and expels its waste into the endometrium (Rossant and Cross, 2001; Abdelrahman, 2013). As it progresses from embryonic stage to foetal stage, more nutrients are required and a much more sophisticated means of satisfying the nutritional and waste disposal needs must be established (Wilson, 2008; Abdelrahman, 2013).

After fertilization the zygote undergoes cleavage to form the morula. Continued division of cells of the morula gives rise to the blastocyst (Cross *et al*., 1994; Li *et al*., 2014). The blastocyst consists of single layer of cells, the trophoblast, surrounding a cavity called the blastocoele, into which protrudes the inner cell mass (Salafia and Vintziloes, 1999; Cross *et al*., 1994; Yagi *et al*., 2007; Home *et al*., 2012).

Human implantation depends on a series of specific interactions between the early trophoblast cells of the blastocyst and the endometrium. Implantation involves adhesion and endometrial invasion culminating in the differentiation of the endometrial stroma (decidaulization) (Golos *et al*., 2013). Despite the complex mechanisms involved there is always an initial direct interaction of the trophoblast cells of the blastocyst with the endometrial luminal epithelium and ends with the formation of a definitive placenta which establishes a means of supporting the embryo in the endometrium during gestation (Cross *et al*., 1994; Machin *et al*., 2000;Valsamakis *et al*., 2006; Golos *et al*., 2013).

Developing trophoblast cells exhibit two distinct properties; they become competent to show cell to cell and cell to matrix binding and they exhibit the ability to degrade components of the extracellular matrix (ECM) (Machin *et al*., 2000). The trophoblast has a nutritive role and also functions as an endocrine organ (Machin *et al*., 2000). Morphologically, the trophoblast

consists of two cell types, cytotrophoblasts and syncytiotrophoblasts (Salafia and Vintziloes, 1999).

By the eighth day after fertilization the trophoblast has differentiated into an outer multi nucleated syncytiotrophoblast and an inner layer of mononuclear cytotrophoblast cells (Golos *et al*., 2013). Very little has been reported of the events during the first few weeks of gestation in humans; however it appears that the mononuclear cytotrophoblast cells divide and fuse with the overlaying syncytium to form villi and expand the surface area of the developing placenta (Li *et al*., 2014). Two main structural types of villi have been observed in first trimester placentae; free (floating) and anchoring villi (Machin *et al*., 2000;Valsamakis *et al*., 2006).

Floating villi do not contact uterine tissue directly while anchoring villi connect the embryo to the uterus. This connection is established by proliferating cytotrophoblast cells protruding and breaking through the syncytiotrophoblast to form solid cores of mononuclear cells (cell columns) which fix the trophoblast to the endometrial stroma (Wilson, 2008). Once the anchoring villi are formed, some cytotrophoblast cells of these villi acquire a transiently invasive phenotype and invade the decidualized endometrium. These motile and invasive cells are referred to as extra villous/intermediate trophoblast cells while the cytotrophoblast cells, which remain attached to the villous basement membrane (BM), are known as villous cytotrophoblast cells (Mayhew, 2014). Thus cytotrophoblast cells follow one of two differentiation pathways. (i) Villous cytotrophoblast cells form a monolayer of polarized epithelial stem cells which eventually differentiate to form a syncytium layer which covers the entire villous surface (Goldman-Wohl and Yagel, 2014). (ii) Cytotrophoblast cells of anchoring villi either form syncytium or break through the syncytium at selected sites to form multilayered columns of non-polarized cytotrophoblast cells which are motile and highly invasive (Wilson, 2008; Abdelrahman, 2013).

Villi may easily be distinguished in the human placenta on about the twelfth day after fertilization. When a solid cord of trophoblast is invaded by mesenchymal cells, presumably derived from cytotrophoblast, secondary villi are formed. After angiogenesis occurs in situ from the mesenchymal cores, the villi that are formed are termed tertiary (Goldman-Wohl and Yagel, 2014; Mayhew, 2014).

Reis *et al*. (2005) reported that during implantation, maternal tissues and capillaries of the decidua basalis are disrupted by the invasive action of the blastocyst and eventually, the chorion is soon surrounded by a stagnant pool of extravasated maternal blood, tissue debris and secretions from disrupted uterine glands, i.e., embryotroph. As development continues, larger uterine vessels (arteries and veins) are disrupted and brought into communication with the lacunar spaces (Enders and Carter, 2012). With the establishment of the arterial and venous connections, maternal blood begins to circulate through the developing intervillous spaces of the chorion frondosum (Enders and Carter, 2012; Burton *et al*., 2007). The invading cytotrophoblastic cells in the chorionic villi ultimately form the cytotrophoblastic shell (Burton *et al*., 2007). When the cytotrophoblastic shell is complete, it encloses the entire conceptus including the chorionic villi and serves as the only physical attachment between the maternal tissues and those of the conceptus (Mihu *et al*., 2009; Longo and Reynolds, 2010). The shell is interrupted only at the sites where maternal blood vessels communicate with the intervillous spaces of the foetal placenta. Chorionic villi exhibit elaborate branching patterns within the blood filled intervillous spaces (Genbacev *et al*., 2003; Longo and Reynolds, 2010; Milovanov *et al*., 2012).

Most of the surface area available for metabolic exchange is provided by the branching villi. As the lacunar spaces within the thickened syncytiotrophoblast coalesce and increase in size, irregular strands of syncytium are produced which project into the rapidly developing vascular channels (Valsamakis *et al*., 2006). Almost immediately after their formation,

cytotrophoblastic cells grow into these syncytial strands to produce the primary chorionic villi which are composed of trophoblastic cells only, thus; centrally located cytotropholastic cells ensheathed by a layer of syncytial cells (Machin *et al*., 2000; Cross *et al*., 2003; Mihu *et al*., 2009). Primary villi are converted to secondary chorionic villi by the invasion of a mesenchymal core derived from the extraembryonic chorionic mesoderm; vascularization of the mesenchymal core produces the functional tertiary chorionic villus (Machin *et al*., 2000; Castellucci *et al*., 2000; Cross *et al*., 2003). Initially, the entire chorionic surface is covered with villi but those adjacent to the decidua capsularis degenerates to produce the smooth (nonvillous) chorion laeve. Villi adjacent to the decidua basalis persist and increase in size to produce the chorion frondosum which becomes the foetal portion of the placenta (Machin *et al*., 2000; Cross *et al*., 2003; Valsamakis *et al*., 2006). The placenta is fully formed and mature by the fourth month of development. The placenta forms very early in the foetus and problems associated with its formation and function underlie many aspects of early pregnancy loss and pregnancy complications in humans (Rossant and Cross, 2001; Mihu *et al*., 2009).

In some villi, in which there is lack of angiogenesis, there results a lack of circulation and the villi may distend with fluid and form vesicles. By the end of the third month, this side of the chorion is smooth, and the remaining bushy chorion frondosum develop into the definitive placenta. In humans, the chorion laeve and amnion forms an avascular amniochorion that nevertheless serves important functions that include solute and fluid transport as well as prostaglandin formation at the time of parturition (Valsamakis *et al*., 2006).

Each of the main villi and the ramification thereof constitute a placental cotyledon. The total number of cotyledons remains the same throughout gestation, but individual cotyledons continue to grow until term, although less actively in the final weeks (Milovanov *et al*., 2012). As the villi continue to branch and the terminal ramification become more numerous and smaller, the volume and prominence of cytotrophoblast in the villi decreases

although syncytiotrophoblasts are obvious in the placental floor. As the syncytium thins out and forms knots, the vessels become more prominent and lie closer to the surface (Machin *et al*., 2000; Valsamakis *et al*., 2006).

In the stroma of the villi there are also changes associated with ageing. In the placenta during early pregnancy, the branching connective tissue cells are separated by an abundant loose intercellular matrix; later, the stroma becomes denser and the cells become more spindleshaped and more closely packed (Valsamakis *et al*., 2006). These changes are suggestive of an increase in the efficiency of transport to meet the metabolic requirement of the growing foetus (Mihu *et al*., 2009).

2.3 TROPHOBLAST INVASION AND UTEROPLACENTAL BLOOD FLOW

Adequate trophoblast invasion is required to sustain foetal growth. When the blastocyst adheres to the uterus, foetal trophoblast cells differentiate into villous or extravillous cells (Machin *et al*., 2000; Valsamakis *et al*., 2006). Migration and invasion of extravillous cytotrophoblasts into the maternal uterine epithelium and uterine endothelium are processes that are essential for increased uteroplacental blood flow as pregnancy progresses (Valsamakis *et al*., 2006). The syncytiotrophoblast cell layer, which is differentiated from cytotrophoblast cells, is the site where hormones such as oestrogen, progesterone, human chorionic gonadotropin (HCG), human chorionic somatomammotropin (HCS), and placental growth hormone are produced to maintain the pregnancy (Valsamakis *et al*., 2006).

2.4 PLACENTAL WEIGHT

The weight of the placenta has been varied over the years but recent studies show that it has an average weight of about 590 grams with a range of 350 to 750 grams (Panti *et al*., 2012; Lakshmi *et al*., 2013). It has been shown that placental weight has a significant role in foetal growth in

terms of weight, body length, and cord length but it has no significant role in the presence of meconium-stained fluid (Lo *et al*., 2002). Little *et al.* (2003) reported that absolute measures of infant size and placental weight had mutual positive correlation. Maternal haemoglobin levels influence placental weight, as anaemia and iron deficiency during pregnancy are associated with large placental weight (Asgharnia *et al*., 2008).

Placental weight reflects placental development and functions and is correlated with maternal age, gestational age, history of maternal diabetes, preeclampsia, birth weight, parity, route of delivery, infants' gender and Apgar score and foetal distress (Bianco *et al*., 1998). Other factors influencing placental weight include maternal height and weight, and serum ferritin concentration (Asgharnia *et al*., 2008). Increase in placental size is significantly associated with maternal weight, and it is an independent predictor of birth weight.

Large placental size and low birth weight have been implicated as factors predicting high blood pressure in adulthood (Hindmarsh *et al*., 2000). Risnes *et al.* (2009) found that the placenta to birth weight ratio was positively associated with risk of death from cardiovascular causes and that the positive association was particularly strong for stroke. In addition, placental weight displayed a positive association with cardiovascular death after adjustment for birth weight (Risnes *et al*., 2009; Thame *et al*., 2000; Thompson *et al*., 2007). Blood pressure is also thought to follow the same course from birth through childhood to adulthood, raising the possibility that children who were small at birth and had higher blood pressure in childhood are at increased risk of hypertension in adult life (Thame *et al*., 2000). As the severity of hypertension increases, placental weight as well as mean birth weight of new babies decrease and the incidence of IUGR and still birth rises (Udainia and Jain, 2001).

It has been shown that maternal or foetal diseases such as gestational diabetes, severe anaemia, hypertension and hydrops foetalis influence foetal and placental weight (Asgharnia *et al*., 2008). Eriksson *et al.* (2000) demonstrated that higher blood pressures have occurred in later life for

men and women who had been small babies with large placentae. In contrast, other studies have shown less correlation between gestational diabetes, severe anaemia, hypertension and hydrops foetalis and placental weight and have reported that absolute measures of infant size and placental weight had mutual positive correlation (Little *et al*., 2003). Since placental size is correlated with birth size, the ratio between placental weight and birth weight could be a useful indicator for placental efficiency (Risnes *et al*., 2009). In addition, a comparatively large placenta relative to birth weight may be an expression of a relatively inefficient placenta with reduced ability to translate its own growth into foetal growth (Salafia *et al*., 2006 Risnes *et al*., 2009). Furthermore, a placenta that is large relative to birth weight may be a marker for reduced nutrient supply to the foetus (Risnes *et al*., 2009).

Placental hypertrophy and reduced foetal growth have been postulated to be an adaptation to maintain placental function in pregnant women with conditions such as malnutrition (Udainia and Jain, 2001). As such, pregnancy with impaired foetal growth, resulting in small for gestational age (SGA) neonates, should have an increased placental weight to birth weight ratio (placental ratio) compared to those with appropriate weight for gestational age (AGA) or large for gestational age (LGA) infants (Salafia *et al*., 2006 Risnes *et al*., 2009). However some studies have shown that this is not the case (Myatt, 2002). Heinonen *et al.* (2001) showed that the actual placental weight was lower in SGA infants than in AGA infants with the same birth weight. Asgharnia *et al*. (2008) suggested that low birth weight should be related to low functional tissue mass of placenta and may be associated with reduction in the area for exchange between mother and foetus, both at the villi and foetal capillary surface area. Thus, the ability of exchanging oxygen and nutrition from mother to foetus is curtailed. It is also known that suboptimal oxygen delivery is associated with relatively large placentae and a high placenta-to-birth-weight ratio (Risnes *et al*., 2009). It has been hypothesized that alterations in the functional morphology of the placenta could at least contribute to the reduced foetal weight associated with air pollution (Veras *et al*., 2008).

It has been documented that lighter and smaller than normal placentae are reflective of reduced foetal movements (RFM) in-utero, with such women with RFM having higher risks of stillbirth and IUGR (Heazell and Frøen, 2008; Heazell *et al*., 2010). Such women represent a group with increased possibility of having abnormal placental structure (Warrander and Heazell, 2011). It has been shown that reduced nutritional supply to the foetus may lead to compensatory growth of the placenta, without noticeable restriction of foetal growth (Godfrey and Barker, 2000).

The weight of the placenta can be altered by the umbilical cord, membranes, attached maternal clots or foetal blood within and pathologic conditions (Heazell *et al*., 2010). Therefore the standard method of weighing the placenta, without trimming the placental disk of membranes and umbilical cord, may also affect placental weight (Machin *et al*., 2000; Valsamakis *et al*., 2006).

2.5 PLACENTAL THICKNESS

Placental thickness in millimetres increases in a linear fashion with advancing gestational age (in weeks) and almost matching it from 11 - 35 weeks of gestation (Schwartz *et al*., 2012; Ravi and Pruthvi, 2013). At term, the placenta is approximately 3 cm thick (Heazell *et al*., 2010). It can be an additional indicator of estimating gestational age especially where the duration of pregnancy is unknown or uncertain (Ravi and Pruthvi, 2013; Ahmed *et al*., 2014). It has been observed that the relationship of placental thickness with gestational age falls marginally and the rate of growth of placental thickness decreases after 36 weeks of gestation (Ravi and Pruthvi, 2013). Determining placental thickness may be helpful in the diagnosis of some abnormalities; a thin placenta may be seen in cases of IUGR and thick placentae are noted in hydrops foetalis of varied causes. Placenta grows throughout pregnancy, initial growth being much more rapid than that of the foetus (Czikk *et al*., 2013; Ravi and Pruthvi, 2013). Placental thickness and volume have been used to predict chromosomal anomalies and diseases such as preeclampsia,

thalassemia, and other complications of pregnancy (Azpurua *et al*., 2010). Foetal growth parameters such as bi-parietal diameter (BPD) and abdominal circumference (AC) are used in the sonographic estimation of gestational age and weight of the foetus in the second and third trimesters. Femur length has been established as an accurate parameter for trimesters (Ziylan, and Murshid, 2003). While foetal weight can be estimated by Sherpard's method using only BPD and AC with a deviation of 295g from the actual birth weight (Hebbar, 2003). These growth parameters are adversely affected by insufficient nutrients reaching the foetus through the placenta. In these foetuses, the placenta is often thin (Czikk *et al*., 2013; Chhabra *et al*., 2013). A placental thickness of less than 2.5 cm is usually associated with intrauterine growth retardation (IUGR) (Kuhlmann and Warsof, 1996; Chhabra *et al*., 2013), whereas thick placentae are associated with maternal diabetes mellitus, foetal hydrops and intrauterine foetal infections (Malathi and Shanthi, 2010). Ohagwu *et al*. (2009) therefore suggested that placental thickness might have a certain relationship with foetal growth parameters especially BPD and AC. However, a thick placenta may reduce efficiency because of increased villous depth (Risnes *et al*., 2009). Blood perfusion of abnormally thick placentae is thought to be less efficient, and the oxygen demands required to maintain a large placenta may limit oxygen and nutrient availability to the foetus, causing the foetus to be growth restricted relative to the placenta (Risnes *et al*., 2009; Daskalakis *et al*., 2008). As placental thickness increases, the foetal weight also increases suggesting that the placental growth directly influences the foetal weight (Ravi and Pruthvi,2013; Czikk *et al*., 2013). Therefore placental thickness is one of many requirements of placental measurements by which the distinctive nature or features of placental growth can be determined (Roh *et al*., 2005).

2.6 PLACENTAL FUNCTION

The human placenta is the organ responsible for the supply of oxygen and nutrients as well as antibodies and hormones to the foetus and allows foetal waste to be disposed of via the maternal kidneys (Kaplan, 2008). The placenta protects the foetus from immune attack by the mother

and induces increased maternal blood flow to the foetus. Near the time of delivery, the placenta produces hormones that mature the foetal organs in preparation for extra-uterine life (Hunt *et al*., 2005; Wilson, 2008; Chen *et al*., 2012).

The placenta supports essential foetal respiratory functions before lung development, carrying oxygen and nutrients from the maternal blood across its membrane into the foetal circulation by diffusion and allowing carbon dioxide to pass in the opposite direction (Yarbrough *et al*., 2014). The placenta provides the foetus with water, inorganic salts, carbohydrates, fats, proteins and vitamins and carries foetal waste into the mother's circulatory system to be secreted via her urinary system (Kaplan, 2008; Abdelrahman, 2013). The placenta also protects the foetus by prohibiting some harmful microorganisms from entering the foetal circulation. The portion of the placental membrane that provides this protection is called the placental barrier (Wilson, 2008; Palmeira *et al*., 2012; Abdelrahman, 2013). Storage is another function of the placenta. The placenta stores carbohydrates, calcium, iron and proteins for release into foetal circulation (Wilson, 2008). In performing all these functions, the placenta serves as a filter controlling the inflow of all these substances into the foetal circulation and the outflow of waste into the maternal circulation (Valsamakis *et al*., 2006; Ohagwu *et al*., 2009). Though the placenta serves as a filter, some substances can breach this process and enter the foetal circulation without being filtered out. These include alcohol and some chemicals associated with smoking cigarettes (Rizzo *et al*., 2009; Sachdeva *et al*., 2009). Some viral types may also cross this barrier including the Human Cytomegalovirus, leading to various degrees of birth defects in the infant (Lanari *et al*., 2001).

The placenta is a major endocrine organ which in almost all mammals, synthesizes and secretes steroid hormones (Donnelly and Campling, 2014). The human placenta is responsible for the production of hormones such as, progesterone for the maintenance of pregnancy and oestrogen which is responsible for foetal weight (Ohagwu *et al*., 2009; Donnelly and Campling, 2014). It

also secretes human chorionic gonadotropin (HCG) (Wilson, 2008). HCG is secreted by the syncytiotrophoblasts of the placenta in early pregnancy. It maintains the function of the corpus luteum and stimulates progesterone production in the placenta (Wilson, 2008). The presence of HCG in the blood and urine of pregnant women, is the basis for most common tests used to diagnose pregnancy (Webster, 2013; Wang *et al*., 2014). In addition, the placenta secretes the hormone relaxin, which is thought to relax the joints of the pelvis and assist in dilating the cervix at parturition (Anand-Ivell and Ivell, 2014). Furthermore, it manufactures HCS which modifies the metabolic state of the mother during pregnancy to facilitate the energy supply of the foetus and has anti-insulin properties (Ohagwu *et al*., 2009).

2.7 PLACENTAL PATHOLOGY

The placenta is the most accurate record of the infant's prenatal experience therefore after delivery if the placenta is examined grossly as well as minutely it provides much insight into the prenatal health of the foetus and mother (Raghunath and Vijayalakshmi, 2011; Singal *et al*., 2013). For several decades, the benefits of the placenta have been outlined by researchers and these benefits are linked with the anatomical examination of the placenta, although it is discarded after parturition without any in-depth examination. The assessment of the placenta in utero as well as postpartum, gives good information about foetal and maternal wellbeing (Roberts, 2008; Raghunath and Vijayalakshmi, 2011; Singal *et al*., 2013). A healthy neonate at term is the product of three important factors; a healthy mother, normal genes and good placentation and growth (Azpurua *et al*., 2010). Some of the most common abnormalities associated with the placenta are; placental abruption, placenta praevia, placental insufficiency, cysts, haematomas, multiple gestation placentae and infarctions and malignancies and other tumours (Wilson, 2008; Roescher *et al*., 2014).

2.8 Placental Abruption

Placental abruption also known as ruptured placenta, is described as the separation of a normally located placenta after the twentieth week of gestation and prior to birth (Jabeen and Gul, 2004; Tikkanen, 2011). Placental abruption occurs in 0.4-1% of all pregnancies worldwide (Tikkanen *et al*., 2006; Holzman *et al*., 2007; Nilsen *et al*., 2008; Tikkanen, 2011). It is likely to be caused by bleeding into the decidua basalis. Formation of haematomas cause additional separation of the placenta from the uterine wall, causing compression that compromises the blood supply to the foetus. Blood behind the placenta can penetrate the uterus and extend into the peritoneum. This is referred to as couvelaire uterus (Wilson, 2008). When this occurs, the myometrium becomes weak and can rupture, especially during uterine contractions. This presents a life-threatening emergency for both the foetus and mother (Wilson, 2008; Tikkanen, 2011). The extent of foetal distress and survivability are determined by the amount of placental separation and also the gestational age. The amount of maternal haemorrhage determines the risk to the mother. Foetal and maternal deaths are caused by haemorrhage and coagulopathy (Ananth and Wilcox, 2001; Tikkanen, 2011). The perinatal mortality rate from placental abruption is approximately 15% (Wilson, 2008). Immediate caesarean delivery is performed to try to save the lives of both foetus and mother (Wilson, 2008; Tikkanen, 2011). Risk factors include tobacco smoking, hypertension, cocaine use, abdominal trauma, premature rupture of membranes, multi-foetal gestation and previous abruption (Holzman *et al*., 2007; Bodelon *et al*., 2009; Tikkanen *et al*., 2009).

2.9 Placenta Praevia

In placenta praevia, the placenta implants over or near the internal os of the uterine cervix. Placenta praevia usually is diagnosed prior to the twentieth week of gestation; serial sonography is performed to document the placenta's location throughout the pregnancy. In almost 90% of cases the diagnosis of praevia is resolved prior to term (Oyelese and Smulian,
2006; Rao *et al*., 2012). Placenta praevia is diagnosed in 9.3% of women or 1 in 533 deliveries. Several terms are used to classify the types of placenta praevia: complete or total, partial,

marginal and low-lying (Yetter, 1998; Wu *et al*., 2005; Warshak *et al*., 2006). The low-lying placenta is not technically a praevia because the placental tissue does not cover the os and is usually described as the placental edge being within 2 to 3 cm of the internal os (Oyelese and Smulian, 2006; Sakornbut *et al*., 2007; Bronsteen *et al*., 2013). Some studies suggest that, when the placenta to cervical os distance is greater than 2 cm, women may safely have a vaginal delivery. Local anaesthesia for caesarean delivery in women with placenta praevia is safe (Oyelese and Smulian, 2006; Bronsteen *et al*., 2013). A complete placenta praevia is diagnosed when the placenta completely covers the internal cervical os. A subgroup of complete praevia includes central praevia in which the cervix appears in the centre of the placenta (Holzman *et al*., 2007; Daskalakis *et al*., 2011). Partial placenta praevia is described when the placenta partially covers the internal os, but not completely. Marginal placenta praevia is described as the placenta that only reaches the edge of the internal os (Holzman *et al*., 2007; Bronsteen *et al*., 2013).

2.10 Placenta accreta

Placenta accreta is abnormal placental implantation in which the anchoring chorionic villi attach to the myometrium, rather than being contained by decidua. In placenta accreta, the normal decidua basalis and fibrinoid layer are defective and as a result the placental villi adhere to the myometrial layer and may penetrate through it to reach other structures (Gielchinsky *et al*., 2002; Holzman *et al*., 2007). This type of condition includes placenta accreta, placenta increta and placenta percreta. Placenta accreta is the most serious form, demonstrated by an abnormally firm attachment of the placenta superficially to the myometrium (Sentilhes *et al*., 2010; Merck, 2013). Placenta accreta accounts for the majority of all abnormal placental attachments. In placenta increta, the placenta has a deep attachment into the myometrium, while the placental attachment in placenta percreta involves the complete invasion of placental tissue through the myometrium (Wu *et al*., 2005; Merck, 2013). Any form of placenta accreta can cause an

incomplete separation of the placenta from the uterine wall at birth and can result in haemorrhage, infection or other serious complication (Merck, 2013; Sumigama *et al*., 2014). Since scaring of the uterus is one of the markers for placenta accreta, it has been reported that the incidence of placenta accreta is rising, primarily because of the increasing number of women opting for caesarean delivery (Gielchinsky *et al*., 2002; Oyelese and Smulian, 2006; Warshak *et al*., 2006; Sentilhes *et al*., 2010).

2.11 Placental Insufficiency

Placental insufficiency is described as the inability of the placenta to provide oxygen and nutrients to the foetus (Gagnon, 2003; Simonazzi *et al*., 2013). This leads to foetal hypoxia with resulting growth restriction. IUGR is second only to prematurity as the most common cause of foetal demise (Chaddha *et al*., 2004; Simonazzi *et al*., 2013). Placental insufficiency is a complication experienced in up to 6% of all pregnancies. Foetuses that survive can experience problems with cardiovascular, metabolic and neurologic development into adulthood (Gagnon, 2003; Chaddha *et al*., 2004).

2.12 Placental cysts

Placental cysts are described as typically round or oval in appearance. Cysts generally are isolated from placental circulation and contain a gelatine-like substance on histologic examination (Wilson, 2008; Proctor *et al*., 2010). There are two types of cysts associated with the placenta: septal and sub-chorionic. Septal cysts are located within the substance of the placenta, while sub-chorionic cysts are located beneath the foetal plate (chorion) (Wilson, 2008; Stanek, 2011). Placental cysts are usually detected sonographically and are often benign in nature and pose no significant risks to the foetus or mother. When a cyst measures 4.5 cm or larger or there are more than 3 cysts present, IUGR may be indicative (Brown *et al*., 2002; Wilson, 2008; Proctor *et al*., 2010).

2.13 Placental infarcts

Infarction or infarct refers to an area of cell death and tissue necrosis resulting from insufficient blood supply (Lima, 2014). Microscopic thrombi (blood clots) may form within blood vessels, impeding blood flow, and are a common cause of infarction. This is usually what occurs during a heart attack ("myocardial infarction") secondary to occlusion of a coronary artery. Constriction or closure of blood vessels (vasoconstriction) can occur for a variety of reasons, most commonly as a result of hypertension (Lima, 2014; Kondo, 2014). If necrosis causes liquefaction or bleeding, infarcts become visible with ultrasound. If liquefaction does not occur, infarcts may not be seen until pathological examination. Infarcts are usually irregularly shaped and do not contain swirling blood upon direct visualization. Small infarcts are seen in 25% of normal pregnancies and are common features of a normal "aging" placenta and appear to be of no clinical significance (Holzman *et al*., 2007; Kondo, 2014). However, if placental infarcts are large or extensive, placental function can be compromised (Holzman *et al*., 2007). Infarcts may occur as a result of maternal vascular disease, reduced foetal growth, older maternal age, more prior miscarriages, poor neonatal condition, preeclampsia, or poor placentation (Holzman *et al*., 2007; Blair *et al*., 2011). Perinatal morbidity is associated with infarcts of more than 5 percent of the placental mass or greater than 3 cm in diameter. Such a placenta may be described as having a “moth eaten” appearance. Unexplained elevated maternal serum Alpha-Fetoprotein (AFP) has been associated with extensive placental infarction (Holzman *et al*., 2007). More so, certain substances like cocaine, are "vasoactive" and are known to cause closure of blood vessels and subsequent infarction (Lima, 2014).

2.14 Multiple Gestation Placentae

In some countries especially the United States, one in approximately 100 births is a multiple birth, and this is due at least in part to assisted reproductive techniques (Wilson, 2008). The placenta plays an essential a role in multiple births as in single births. Placentae in multiple

gestations can exhibit all of the abnormalities common in single births, but also have unique pathologies of their own (Razia *et al*., 2011). Twin gestations are associated with higher percentages of perinatal morbidity and mortality (Razia *et al*., 2011; Steingass *et al*., 2013). The placentae can implant in different parts of the uterus and remain distinctly separate or implant next to each other and fuse. Even when the placentae fuse, the blood and nutrient supply to each foetus remains distinct and separate (Francois *et al*., 2003; Wilson, 2008). In monozygotic twins, there may be one or two amniotic sacs, chorions or placentae, depending on how early or late the fertilized egg divides. When identical twins share the same amnion, they are called monoamniotic twins (Wilson, 2008; Morcel *et al*., 2010).

2.15 Malignancies and Other Tumours

Placental tumours are described as solid masses located within the placenta (Kim, 2003; Wilson, 2008; Lurian, 2010). The two most common of these include the mole and the chorioangioma. The mole tumour also known as molar pregnancy, is a gestational trophoblastic disease (Kim, 2003; Chaudhry and Hussain, 2013). Molar pregnancies are rare, occurring in 1 in every 1,250 pregnancies. Most are benign and are contained within the uterus. These are called hydatidiform moles. Hydatidiform moles contain abnormal placental tissue with clusters of tissue swollen with fluid (villi) that resemble clusters of grapes (Wilson, 2008;

Lurian, 2010). Foetuses that coexist with moles, if they survive, often are born with multiple malformations. Moles occur when placental tissue grows abnormally and forms a mass that can extend beyond the uterus (Wilson, 2008; Vimercati *et al*., 2013). There are 3 types of molar pregnancies: complete, partial or incomplete, and coexisting mole and foetus. The complete mole normally does not contain any foetal tissue. In 15% to 25% of cases, a complete mole may develop into choriocarcinoma (Wilson, 2008).

2.16 MORPHOLOGY OF THE UMBILICAL CORD

The human umbilical cord, which is also sometimes referred to as the funiculus umbilicalis or birth cord, is a connecting cord from the developing foetus to the placenta (Proctor *et al*., 2010; Nugged Alla, 2013; Jain *et al*., 2014). The umbilical cord is physiologically and genetically part of the foetus, it conveys nutrients to the foetus from the placenta and carries waste products from the foetus to the placenta and is known as the foetal supplyline/lifeline (Baergen *et al.*, 2001; Predanic, 2009). In humans, two umbilical arteries carry deoxygenated blood from the foetus to the placenta, while oxygenated blood is returned via the larger umbilical vein (Holzman *et al*., 2007; Marshall, 2014). These vessels are surrounded by an extracellular matrix of mucous connective tissue (Wharton's jelly), covered by an outer covering of amniotic epithelium, and insert into the foetal surface of the placental disc (Proctor *et al*., 2010; Lacono *et al*., 2012; Jain *et al*., 2014). The Wharton's jelly gives flexibility, mobility and strength to resist compression and at the same time allows the foetus to move freely (Predanic, 2009).

The exterior surface of the cord is dull white in colour and moist with a diameter of approximately 2.0 cm and an average length of 55 cm at term (Holzman *et al*., 2007; NuggedAlla, 2013; Jain *et al*., 2014). It is helical in shape, with a chirality of about 1 coil per 5 centimetres of length (Ernst *et al*., 2013). Umbilical cord plays an important role in foetal wellbeing. Several umbilical cord abnormalities are known to cause adverse prenatal outcome (Sabnis *et al*., 2012; Barnwal *et al*., 2013). Abnormal cord length, thick or thin umbilical cords, hyper coiling or hypo coiling, marginal or velamentous insertion of cord may be associated with IUGR, intrauterine death (IUD) or foetal distress (Sabnis *et al*., 2012).

2.17 DEVELOPMENT OF THE UMBILICAL CORD

The umbilical cord is formed from contributions of the body stalk, vitelline duct, yolk sac and allantois and becomes covered with single layer of amniotic epithelium due to expansion of the amniotic sac (Predanic, 2009; Yang *et al*., 2012; Tantius *et al*., 2014). During the early stages

of development, the primitive umbilical cord contains allantois with allantoic vessels and vitelline ducts with omphalomesenteric vessels (NuggedAlla, 2013). The former allantoic vessels will provide two umbilical arteries and two veins, and a week later, umbilical veins will form the venous network with omphalomesenteric veins in the developing liver thereby establishing the umbilical-portal venous connection (NuggedAlla, 2013). By the eighth week of gestation, the right umbilical vein usually regresses, leaving one vein and two arteries. The remaining vein enlarges to accommodate the increasing blood flow (Predanic, 2009; Martinez *et al*., 2013). The umbilical vein enters the left portal vein directly and with development of the ductus venosus, a larger portion of blood enters directly into the systemic venous system by-passing the liver venous network (Predanic, 2009). The intra-abdominal portion of the umbilical arteries originating from the internal iliac vessels run at the sides of the foetal urinary bladder. The distal parts of the intra-abdominal portions of the umbilical arteries regress and degenerate postnatally as the lateral umbilical ligaments while the umbilical vein becomes the round ligament of the liver (ligamentum teres hepatis) (Wilson, 2008).

2.18 UMBILICAL CORD LENGTH

The umbilical cord length is one of the major morphological features that cannot be accurately assessed antenataly via conventional ultrasound. Umbilical cord length varies considerably. The average umbilical cord length is approximately 55 cm with abnormal extremes of cord length ranging from apparently no cord (achordia) to lengths of up to 300 cm (Holzman *et al*., 2007; Schmid *et al*., 2013; Lima, 2014). An abnormal umbilical cord length is a known risk factor for adverse perinatal outcome (Predanic, 2009; Jain *et al*., 2014). A short umbilical cord, less than 40 cm in length, is associated with congenital anomalies, reduced foetal activity, interference with heart rate patterns in labour, restriction of foetal descent and cord rapture (Yetter, 1998; Predanic, 2009; Jain *et al*., 2014). On the other hand, long cords equal or in excess of 70 cm in

length are described in association with foetal entanglement, true knots, torsion and prolapse (Baergen *et al*., 2001; Suzuki and Fuse, 2012).

2.19 UMBILICAL CORD THICKNESS (WIDTH)

The umbilical cord thickness depends on umbilical cord vessels' luminal diameters and amount of Wharton's jelly. The mean umbilical cord circumference at term is approximately 2 cm with a range of 0.8 to 3 cm (Collins, 2002; Jain *et al*., 2014). The umbilical cord thickness or the size of the cord's cross sectional area, was found to correlate with foetal biometry (Raio *et al*., 1999; Predanic, 2009). It has been reported that umbilical cord width cross sectional area below the 10^{th}percentile which is categorized as lean umbilical cord, considerably increases the risk of having a small for gestational age (SGA) foetus at delivery, foetal distress in labour and operative delivery (Raio *et al*., 1999). Similar observations have been found in patients with an early onset of preeclampsia where the umbilical cords were found to be lean with reduced amount of Wharton's jelly and smaller umbilical vein area (Predanic, 2009).

The umbilical cord diameter increases with gestational age and foetal growth. An abnormally narrow umbilical cord correlates with small infant size or low birth weight (Abdalla *et al*., 2014). Cord diameters of less than 0.8 cm in term infants correlate with utero-placental ischemia. The difference in cord diameters can be striking when examining a twin placenta with birth weight discordance (Eze *et al*., 2014; Abdalla *et al*., 2014). In a recent study, it was demonstrated that umbilical cord thickness correlates with estimated foetal weight but does not predict foetal growth deficiency recognized as small for gestational age at birth (Predanic, 2009).

A thin umbilical cord might be determined by a reduction of the amount of Wharton's jelly, by a reduction of the umbilical cord vessels' cross-sectional area or by both. The umbilical cord is subject to a variety of influences, such as the foeto-placental blood flow, the umbilical vessels' blood pressure, the composition and amount of amniotic fluid and genetic variations (Ghezzi *et*

al., 2005). Lean umbilical cord on prenatal ultrasound possesses a risk that the foetus will be small for gestational age at delivery and will have distress (Raio *et al*., 1999). It has also been demonstrated that a lean umbilical cord is associated with growth developmental disorders, preeclampsia and oligohydramnios during labour (Ghezzi *et al*., 2005).

Abnormal umbilical cord thickening has been attributed to the swelling of Wharton's jelly (Predanic, 2009; Predanic *et al*., 2013). Significantly large umbilical cords of foetuses in mothers with gestational diabetes has been attributed to increase in Wharton's jelly content (Raio *et al*., 1999). An association between aneuploidy in the first trimester of pregnancy and umbilical cord thickness has recently been described. It was noted that aneuploidy foetuses had thicker umbilical cords that is evident in the first and second trimesters of pregnancy (Predanic, 2009). Several studies have observed an alteration of extracellular matrix in foetuses affected by trisomies 13, 18 and 21 (Ghezzi *et al*., 2002; Predanic *et al*., 2013). These alterations were related to a different expression of structural proteins, polysaccharides and proteoglycans of the extracellular matrix, which result in abnormal fluid accumulation (Predanic *et al*., 2013). It has been suggested that similar pathophysiologic processes could be the possible cause of umbilical cord swelling as well as increased nuchal translucency observed in aneuploidy foetuses (Ghezzi *et al*., 2002).

2.20 WHARTON'S JELLY CONTENT OF THE UMBILICAL C ORD

Wharton's jelly is a derivative of the extraembryonic mesoblast. Its inclusion in the cord substance and subamnionic layers could probably explain their mucoid and compressible nature (Skulstad *et al*., 2006). Wharton's jelly binds and encases the umbilical vessels, protecting them from twisting and compression during pregnancy and delivery (Ghezzi *et al*., 2001).

It is composed of spongy collagen fibres forming a network of interlacing cavities, cavernous and perivascular spaces in which the ground substance of the jelly is stored and the vessels are

anchored (Ghezzi *et al*., 2001; Di Naro *et al*., 2001). This ground substance is mainly composed of hyaluronic acid and proteoglycans in an aqueous solution of salts, metabolites and plasma proteins. The most common macroscopic finding of the modifications of Wharton's jelly composition is variation in umbilical cord size (Skulstad *et al*., 2006). It has been demonstrated that some cells, similar to myofibroblasts are normally present in the Wharton's jelly and function in both fibrogenesis and cell contraction, participating in the regulation of umbilical cord blood flow (Di Naro *et al*., 2001).

Wharton's jelly is a metabolically active tissue involved in fluid exchange between amniotic fluid and the umbilical vessels (Barnwal *et al*., 2013). Lean umbilical cords are usually accompanied by torsion and fibrosis of Wharton's jelly and a thickening of the vascular wall which obstructs the foeto-placental circulation leading to anoxia and foetal death (Barnwal *et al*., 2013).

Umbilical cord anomalies, like absence of Wharton's jelly, may result in antenatal foetal death (Clausen, 1989). It is reported that accumulation of sulphated glycosaminoglycans (GAGs) in the extracellular matrix of Wharton's jelly affect the structure of umbilical cord tissue. High concentrations of GAGs and proteoglycans surrounding the collagen fibres affect the solubility of this protein (Bankowski *et al*., 1996). Such changes may make the collagen less soluble and the jelly more compact and this may affect the umbilical cord's mechanical properties and macroscopic appearance (Barnwal *et al*., 2013).

Changes or alterations of any of the Wharton's jelly components have been described or postulated in some pathological conditions such as hypertensive disorders, foetal distress, gestational diabetes and foetal growth restriction (Ali *et al*., 2000; Ghezzi *et al*., 2001).

2.21 UMBILICAL CORD VESSELS

The foetal heart pumps foetal blood through the umbilical arteries into the placenta, where tiny branches are bathed in maternal blood (Holzman *et al*., 2007; Predanic, 2009). These vessels are drained by the tributaries of the umbilical vein, which return the blood back into the cord and ultimately into the foetal heart (Holzman *et al*., 2007). As a result, used blood is pumped through arteries to the mother and refreshed blood is returned to the foetal circulation by veins. After birth, this role is performed by the lungs (Bhatt *et al*., 2013; Koos and Rajaee, 2014).

The umbilical cord normally contains 3 blood vessels (1 vein and 2 arteries). Two cord vessels, with only 1 artery, are found in less than 1% of pregnancies (more common in twins, and foetuses of mothers with diabetes) (Lima, 2014). Approximately 30% of all foetuses with 2 umbilical cord vessels have associated congenital anomalies. Additionally, foetuses with 2 umbilical cord vessels have a higher incidence of IUGR, and miscarriage (spontaneous abortion) (Lima, 2014). Cord abnormalities ("accidents") are capable of interfering with blood flow. Several abnormalities of the umbilical cord are capable of impairing blood flow between the placenta and foetus (Lima, 2014).

The umbilical arteries branch from the foetal iliac arteries and carry less oxygen-rich foetal blood from the foetus to the placenta (Holzman *et al*., 2007). There are usually two umbilical arteries in the umbilical cord. After the cord has been inserted into the placenta, the arteries separate to supply the placental lobes. These arteries divide into numerous smaller arteries which end at the centre of each cotyledon called end arteries (Di Naro *et al*. 2012). The two umbilical arteries usually have similar diameter and their sum nearly correlates with that of the umbilical vein. Umbilical arteries with disproportional diameters are associated with placental anomalies, difference in umbilical cord insertion and gestational diabetes (Raio *et al*., 1998). The disproportionate umbilical arteries are not only evident by diameter difference but it is also a sign of different umbilical artery blood flow indices. Smaller arteries have greater resistance to blood flow as compared to the larger ones (Predanic, 2009). However, from clinical view,

discordant umbilical arteries seem to be a benign condition that does not affect the development of the foetus. Nevertheless, discordant umbilical arteries are associated with anomalous placental insertions (Di Naro *et al*. 2012). A single umbilical artery (SUA) occurs when one of the umbilical arteries does not form or atrophies during foetal development (Holzman *et al*., 2007). SUA has been reported to occur in 1% of all deliveries and in 5% of twin deliveries (Holzman *et al*., 2007). There is no evidence of a familial or genetic tendency for SUA but its incidence has been reported to be dependent on race (Geipel *et al*., 2000; Holzman *et al*., 2007). The left artery is absent more often than the right one (70% versus 30%). The association with additional malformations appears equal for right and left arteries (Geipel *et al*., 2000; Heredia and Jeanty, 2002). SUA is frequently found in association with stillbirths, IUGR, foetal structural anomalies and aneuploidies (Heredia and Jeanty, 2002).

The umbilical vein carries more oxygen-rich blood from the placenta to the foetus. The umbilical vein becomes the ductus venosus (Holzman *et al*., 2007). In the human foetus, the blood flows into the left atrium through the foramen ovale from the ductus venosus via the caudal part of the right atrium over the crista divedans. Thereafter, oxygenated blood from the placenta is directed selectively towards the left heart, delivering the most oxygenated blood to the coronary arteries and the brain (Achiron *et al*., 2010). The umbilical vein carries oxygen and nutrient rich blood from the chorionic villi of the placenta to the foetus. More than 75% of the blood which enters the liver from the umbilical vein, while the remainder is shunted to the inferior vena cava through the ductus venosus, which returns to the right atrium of the foetus (Sabnis *et al*., 2012).

2.22 ABNORMALITIES OF THE UMBILICAL CORD

Umbilical cord abnormalities can be related to cord coiling, length, and thickness; the placental insertion site; in utero distortion; vascular abnormalities; and primary tumours or masses (Raio

et al., 1999; Holzman *et al*., 2007; Barnwal *et al*., 2013). The lean umbilical cords are usually accompanied by torsion and fibrosis of Wharton's jelly and a thickening of vascular wall which obstructs the foeto-placental circulation resulting in anoxia and foetal death (Barnwal *et al*., 2013). A localized absence of Wharton's jelly in the involved area of the cord is believed to be the aetiological factor in the constriction and subsequent torsion (Barnwal *et al*., 2013).

The reduction in Wharton's jelly area could be attributed to foetal starvation as a result of poor maternal nutrition. Umbilical cord anomalies, example absence of Wharton's jelly, may result in Antenatal foetal death. Lean umbilical cord on prenatal sonography possesses a risk that the foetus will be small for gestational age at delivery and will have distress during labour. (Raio *et al*., 1999).

2.23 BIRTH WEIGHT TO PLACENTAL WEIGHT RATIO

Adequate placental function is necessary for delivery of nutrients, oxygen, and hormones to the foetus (Risnes *et al*., 2009). Although placental weight alone may be a crude indicator for its function, placental size is correlated with birth size (Salafia *et al*., 2006) and the ratio between placental weight and birth weight could be a useful indicator for placental efficiency (Thame *et al*., 2004)**.** Hypertension during pregnancy leads to placental insufficiency which affects foetal growth and foeto-placental ratio (Krishna and Bhalerao, 2011). Hypertension is significantly more common in people whose history includes a placenta disproportionately large for their birth weight that is, those who had a high placental weight to birth weight ratio.

The ability of the foetus to grow and thrive in utero is presumed to be a function of the placenta. The ratio between the placenta and new born weight has been reported as 1:6 (Nayak and Sundari, 2009).

Comparatively large placenta relative to birth weight may be a reflection of utero-placental dysfunction which may be due to inadequate supply of nutrients and oxygen to support normal

aerobic growth of the foetus (Risnes *et al*, 2009; Krishna and Bhalerao, 2011). The normal birth weight may be affected by parental genetic contributions (Rice and Thapar, 2010). Placental proportions such as, deviation of the placental shape from round, and the relative thickness of the placenta, also modify placental functional efficiency and not the effect of genetics alone (Yampolsky *et al*., 2009).

If the cord inserts near the edge of the placenta, this is called an eccentric insertion. A Battledore placenta refers to a cord inserted on the absolute edge of the placenta, resembling a lollipop (Holzman *et al*., 2007). A velamentous or membranous cord insertion refers to vessels inserting into and surrounded only by foetal membranes, with no Wharton's jelly. A velamentous insertion may cause compromise to the integrity of the umbilical vessels because there is little support by the body of the placenta (Holzman *et al*., 2007). Velamentous insertion of the umbilical occurs in approximately 1% of pregnancies, but is more frequent with twins and triplets. Rarely, these unprotected vessels may rupture and result in foetal death from haemorrhage. Additionally, with velamentous insertion of the umbilical cord, some of the blood vessels traveling unprotected in the foetal membranes may cross the cervix, a condition termed vasa praevia (Lima, 2014).

2.24 PONDERAL INDEX (PI)

Ponderal index assesses whether an infant appears relatively fat or thin at birth by quantification of the dissociation of weight and length. Ponderal index is of great importance in the recognition of wasted infants irrespective of their distribution on the percentile lines of birth weight for gestational age (Brutsaert *et al*., 2012). Intrauterine growth restriction, described as low birth weight for gestational age appears to be the key determinant of infant mortality. However, it is superseded by ponderal index because low birth weight (< 2.5 Kg) alone cannot be taken as a

full proxy marker for the measurement of foetal growth dysfunction. Therefore to facilitate the detection of intrauterine malnutrition, it is important to include body length and ponderal index corrected for gestational age (Colley *et al.*, 1991).

Ponderal index defines body proportionality at birth, thereby differentiating between symmetric from asymmetric growth restriction and also serving as a measure of the severity of asymmetric growth restriction in neonates (Landmann *et al.*, 2006). Ponderal index as compared to birth weight is more informative about the nutritional status at birth, it is relatively independent of race, sex, birth rank, and gestational age at term (Tikellis *et al*., 2012). Infants with low birth weight suffer higher mortality and neonatal morbidity, exhibit lower intelligence quotient and poorer growth (Lundgren and Tuvemo, 2008). Howe *et al.* (2010) and Tikellis *et al*. (2012) explained that soft tissue growth measurement by indices such as ponderal index, which is associated with both body fat and muscle mass could give better prognostic values for short-term complications as compared to the measure of skeletal growth, as shown by body length and head circumference which could reveal considerable prognostic value for future growth and development of the neonate.

To facilitate the diagnosis of intrauterine malnutrition at birth it is useful to incorporate body length in the assessment and to calculate ROHRER's ponderal index (P.I.) = (100 X W/L3) (Walther and Ramaekers, 1982; Landmann *et al.*, 2006; Brutsaert *et al*., 2012). Wasted infants will show a relatively small ponderal index irrespective of their distribution on the percentile lines of birth weight for gestational age. Several authors have used the P.I. as a criterion to define the state of nutrition of their study groups and these studies have demonstrated that P.I. at birth is correlated with skinfold thickness, skeletal retardation, postnatal growth and behaviour problems and neurological dysfunction at pre-school age (Walther and Ramaekers, 1982; Lewis *et al*., 2012; Tikellis *et al*., 2012). It is known that small-for-gestational age (SGA) infants have a higher incidence of asphyxia, hypoglycaemia, hypothermia, and hyperviscosity in the neonatal

period. With respect to human performance, several studies have shown that small size at birth predicts decreased muscle strength suggesting increased muscle fatigability and poor strength gains (Walther and Ramaekers, 1982; Brutsaert *et al*., 2012).

2.25 HEAD CIRCUMFERENCE

The foetal head circumference provides information on intrauterine growth restrictions. Traditionally, intrauterine growth restriction has been classified as symmetric and asymmetric growth restrictions (Landmann *et al*., 2006). Symmetrical growth restriction is evidenced by low birth weight, yet the neonates may not be thin or wasted, since they show an appropriate weight for their length. Symmetrically growth – restricted neonates may have been adversely affected by genetic, infectious or teratogenic insult early in-utero. On the contrary, most of them are healthy normal infants (Landmann *et al*., 2006). Asymmetrical growth – restricted neonates exhibit disproportionately low birth weights for the body lengths and majority have suffered chronic hypoxemia and malnutrition in-utero (Soothill *et al.*, 1987). This occurs late in pregnancy as a result of placental insufficiency to meet the foetal demand. Consequently, foetal responds to this unfavourable condition by invoking adjustment that maximizes the chances of survival, which includes redistribution of blood flow with more to the brain and heart and less to liver and kidney as well as limiting unnecessary movements. It can be observed on sonography when there is increase in head circumference over the abdominal circumference. Both symmetric and asymmetric growth – restrictions are thus determined by the ratio of the foetal head circumference to abdominal circumference (Anarnath *et al.*, 2000).

2.26 BIRTH WEIGHT

Birth weight is a straightforward measure of the outcome of births and is affected by several factors (which could be direct or indirect) necessary for perinatal survival (Misra *et al.*, 2009).

Birth weight is probably the single most important factor that affects neonatal mortality, in addition to being a significant determinant of post-neonatal infant mortality and of infant and childhood morbidity. Low birth weight is defined as a birth weight less than 2.5 kg (WHO., 2003; Wallace *et al*., 2012; Garg *et al*., 2015)

Available evidence suggests that the influence of birth weight is felt throughout the entire life time of the individual, and could stimulate the risk of cardiovascular diseases such as hypertension, heart attack and stroke, diabetes and obesity, osteoporosis, breast and prostate cancers and neuro-developmental outcomes (Misra *et al.*, 2009). Birth weight is governed by two major processes: duration of gestation and intrauterine growth rate. Birth weight is therefore described as a surrogate factor which by itself does not determine, but rather gives indication of the things happening in the intrauterine environment (Godfrey, 1998; Jarvis *et al.*, 2006; Retnakaran *et al*., 2012). The key determinant of birth weight is the transfer efficiency of placental nutrients and oxygen that enable foetal growth and development which also leads to the pathway in explaining why birth weight is connected with mortality and morbidity in infants, children and adults (Misra *et al*. 2009).

Also, environmental and genetic factors may be the results of association between birth weight and body size later in life. With respect to the constitutional growth potential; maternal adiposity, maternal body mass index, weight gain during pregnancy, maternal height, parity, age, gestational age, marital status, lifestyle, heredity, neonatal gender, working hours and various socio-economic factors influence size at birth and adulthood (Mamelle *et al*., 2006; Amagloh *et at*, 2009; Retnakaran *et al*., 2012). In the developing parts of the world, it has been established that race, nutrition, low pre-pregnancy weight, short maternal stature, and malaria are the major contributing factors to LBW babies (Kramer, 1987). According to a WHO collaborative study of maternal anthropometry and pregnancy outcome, weight gained at second or early part of the third trimester was the most practical screening for LBW and IUGR (WHO., 2003).

CHAPTER THREE

MATERIALS AND METHODS

3.1 STUDY DESIGN AND AREA

A longitudinal cross-sectional study was conducted from February 2013 to July 2013 on delivered placentae and foetal anthropometry from the Kwame Nkrumah University of Science and Technology (KNUST) Hospital in the Kumasi Metropolis. The facility has an average of 60 deliveries per month with an estimated average of 720 deliveries annually.

3.2 STUDY POPULATION

A total of 236 pregnant women who attended prenatal care and delivered at the facility were enrolled to participate in the study. Two hundred and thirty six placentae were collected for this study with informed patient consent and Ethics Committee approval. Permission as well as cooperation was also obtained from the hospital authorities, the Midwife in charge and the Nursing staff of the maternity unit. The placentae from normal singleton pregnancies with known gestational age delivered at the maternity unit were collected and washed under running tap water to wash off blood smear and clots. The umbilical cord was cut, leaving a stump of 2.5 cm from its foetal site of insertion. The placentae were examined for bleeding at the labour ward. Clots on the maternal surface, particularly adherent centrally located clots, may represent placental abruption. All the specimens were tagged with numbers that corresponded with the numbers indicated in the register for neonatal indices. The samples were restricted to mothers with complete data on maternal socio-demographic characteristics, placental gross measurements and neonatal indices.

The specimens were then placed in plastic containers filled with formalin (10%) with an airtight lid and kept at room temperature before transporting to the Department of Anatomy laboratory at the School of Medical Sciences - KNUST. At the Department of Anatomy laboratory the samples were washed again and stored in a solution of 0.5% formaldehyde in saline for further detailed examination and measurements.

3.3 INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria were placentae obtained from women who were not hypertensive, diabetics nor had sickle cell disease with complete information on their socio-demographic characteristics, known gestational age, live birth neonate, singleton pregnancy, available antenatal care card, sample with the number sticker attached and was identifiable.

Exclusion criteria were placentae obtained from women who were hypertensive, diabetic or had sickle cell disease, had multiple pregnancy, unknown gestational age, unavailability of ANC card, Human Immune-deficiency Virus (HIV) positive mothers, and incomplete information on maternal socio-demographic characteristics, samples without number sticker or stickers that could not be read.

3.4 ASSESSMENT OF PLACENTAL VARIABLES

3.5 Placental Weight

Gross placentae (including umbilical cord and placental membranes) were weighed in grams in the laboratory using a highly sensitive mechanical kitchen scale (Zhongshan Camry Electronic Co. Model: KCH) graduated from 0 – 5000g (Fig 1).

Figure 1: Photograph showing placenta in a kitchen scale used to determine placental weight (x 0.1)

3.6 Placental Thickness

The toothpick method was used in the determination of placental thickness (Abaidoo *et al*., 2008). This was done by piercing the placentae from the chorionic plate to the basal plate at nine different points selected along two planes that bisect at right angle including the point of umbilical cord insertion with a toothpick (Fig 2). The values were transferred onto a clear ruler 30 cm/12 inches (Helix China Inc.) calibrated in centimetres and their averages computed to determine the placental thickness (Fig 2)**.**

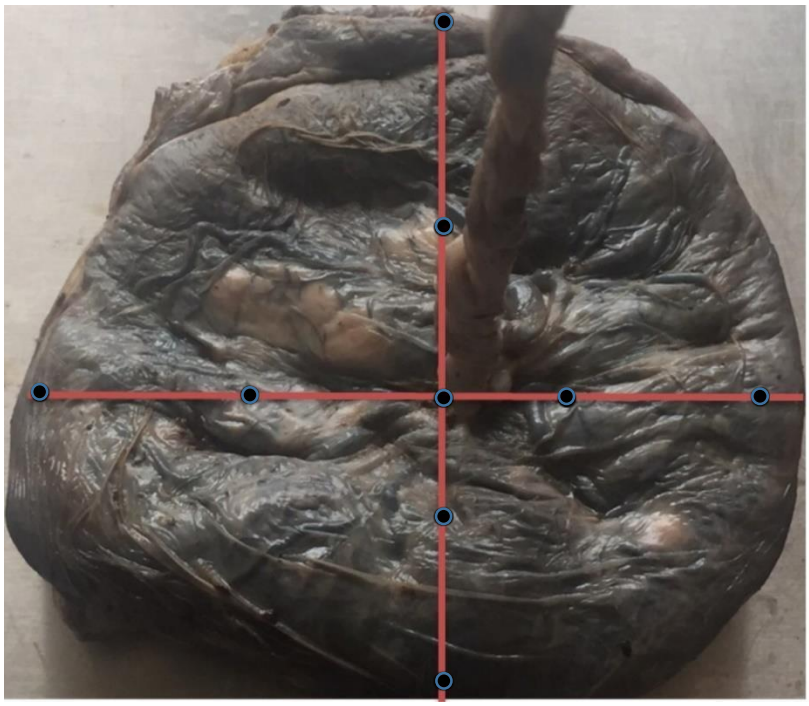

Figure 2: A photogragh showing the nine points on the placenta used to determine placental thickness (x 0.2)

3.6.1 Placental Diameter

The diameter of the placenta was measured using a Dritz C150 fiberglass measuring tape (Prym consumer USA Inc.). Four different angles of each placenta were measured and the mean determined (Fig 3). This was done in view of the fact that most the placentae upon gross examination were discoid or ovoid in shape making it impossible to take a single reading.

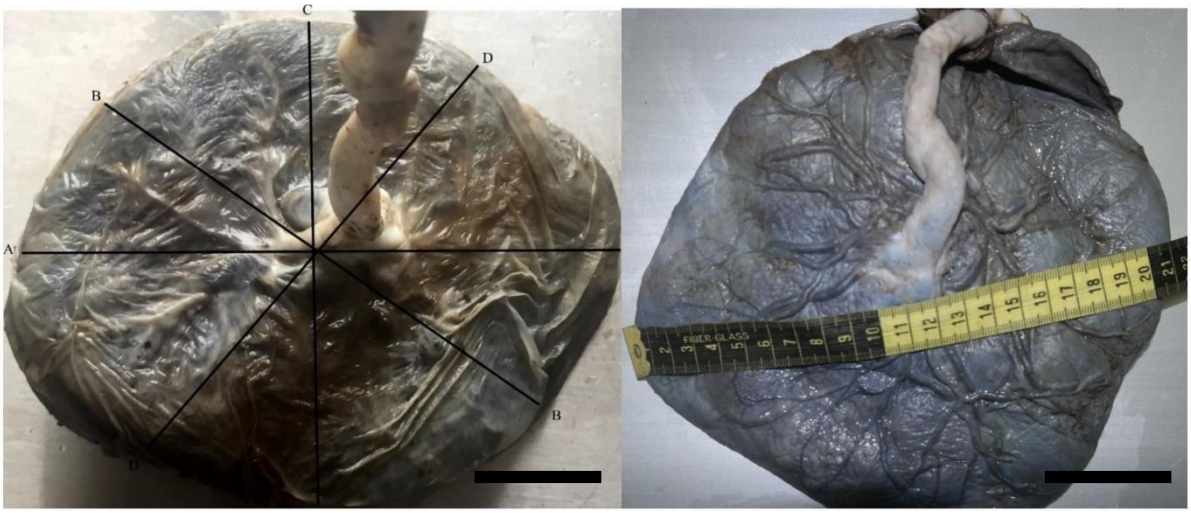

Figure 3: A photograph showing measurement of placental diameter (x 0.2)

3.7 Placental Shape

The foetal surface of the placenta was wiped dry and placed on a clean surface after which the shape of each placenta was observed and described as either round, oval irregular or bilobate.

3.8 Placental shape: Eccentricity

To confirm the shape of the placenta the eccentricity index was determined. Eccentricity is derived from the mathematical formula describing eccentricity for an ellipse/oval. This is the ratio of the distance between the foci to the length of the major axis. The value of an eccentricity should fall between 0 and 1, 0 indicates that the shape of placenta is circular while values towards 1 indicate an elliptical shape of the placenta.

$$EI = \sqrt{1 - \left(\frac{\text{Larger Diameter}}{\text{Smaller Diameter}}\right)^2}$$ (Pathak *et al*., 2010).

Chorionic plate area (square cm)

The chorionic plate area was estimated by calculation of the area of an ellipse from the measured (cm) major diameter and minor diameters of the chorionic disc using the formula:

$A = \frac{\pi * dL * dS}{4}$; Where A is the chorionic disc area, dL is the major diameter and dS the minor diameter of the placenta (Baptiste-Roberts *et al*., 2008).

3.9 Placental Completeness Determination:

This was done at the labour ward before fixation. The placenta which had been washed under running water was observed to see if there was any torn tissue to suggest retained tissue. The maternal surface was inspected to be certain that all cotyledons were present. The foetal membranes were then inspected along the edges of the placenta. Large vessels beyond the edges indicated the possibility that an entire placental (e.g. succenturiate lobe) has been retained.

3.10 Circumvallate Placenta Determination:

This was seen as a thick ring of membranes on the foetal surface of the placenta. A similar but a thin ring of membrane tissue represents cirmcumarginate placenta.

3.11 Amnion Nodosum Determination:

Naked eye observations were made on the foetal surface of the placenta. Amnion nodosum were seen as numerous small, firm, white or yellow nodules on the foetal surface of the placenta (Fig 4).

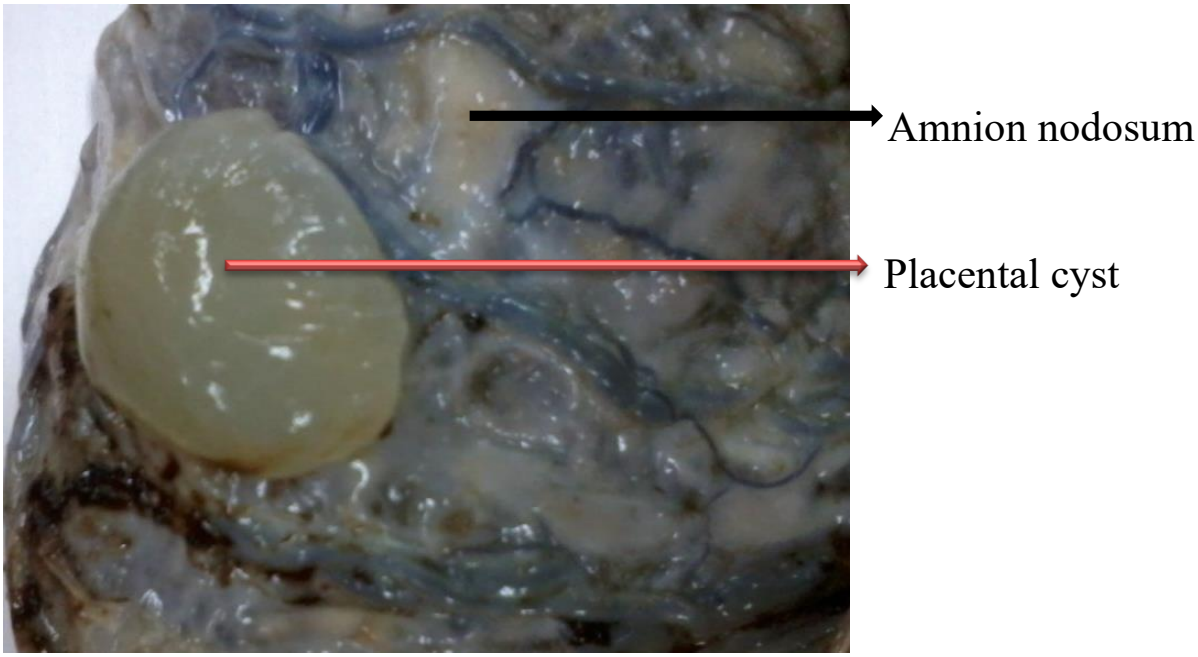

Figure plate of a placenta (x 0.9)4: A photograph of placental cyst and Amnion nodosum on chorionic

3.12 UMBILICAL CORD INDICES

3.13 Umbilical Cord Length and Diameter

Each 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. The umbilical cord length was measured in its entirety using

a standard non – elastic tape measure from the foetal end to its point of insertion into the placenta (see figure 5 below). The 2.5 cm stump was added to each measurement made. The umbilical cord length measurements were categorized into short, when the measured length was < 40 cm, normal, when the measurement was between 40 to 70 cm and long cord if the measurement was > 70 cm (Baergen *et al*., 2001). The umbilical cord diameter

(UCD) was measured with a pair of dividers placed outer - to - outer so that the Wharton's jelly was also included in only one measurement. All measurements were made in centimetres. The foetal end of the umbilical cord was sliced with a surgical blade before the diameters of the umbilical cord vessels were measured with a pair of divider and the result transferred onto a standard meter rule to the nearest millimeter.

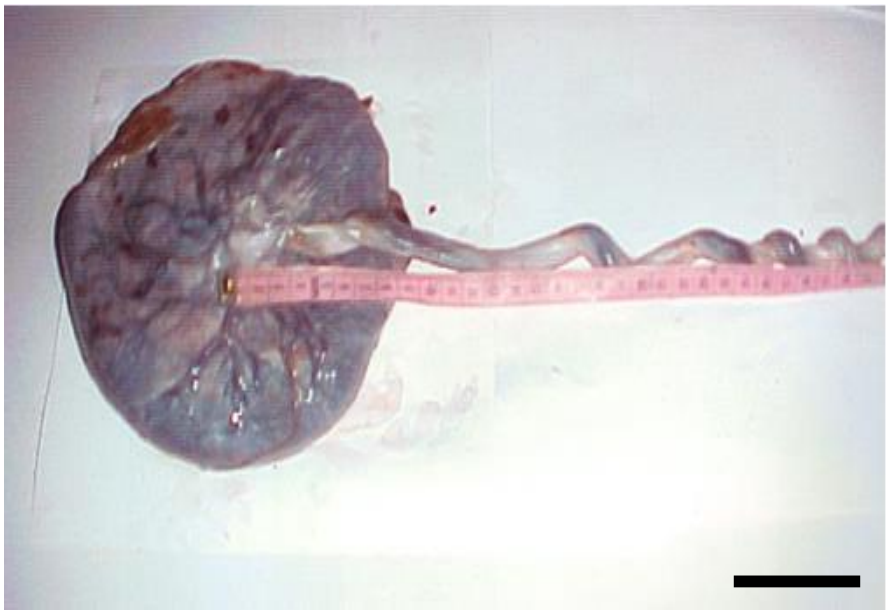

Figure 5: A photograph showing an umbilical cord attached to its placenta with a measuring tape to measure the length (x 0.1)

3.14 Umbilical Cord Insertion

Cord insertion into placenta was observed as being central (figure 6), eccentric (figure 7), marginal (figure 8) or velamentous (figures 9a and 9b)

Figure 6: Photograph of umbilical cord with central insertion (x 0.1)

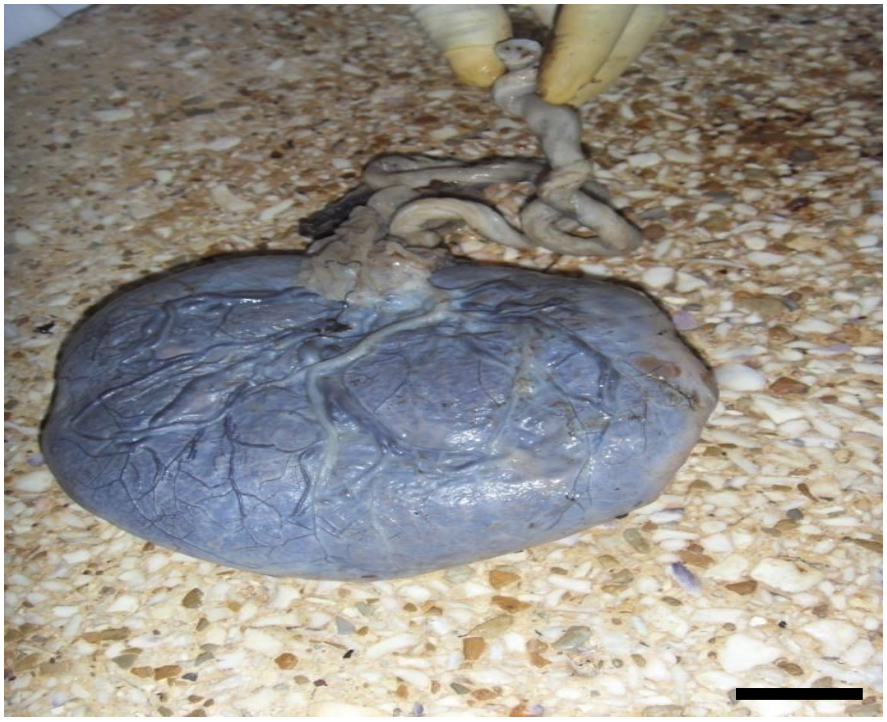

Figure 7: Photograph of umbilical cord with eccentric insertion (x 0.1)

Figure 8: Photograph of umbilical cord with marginal insertion (x 0.1)

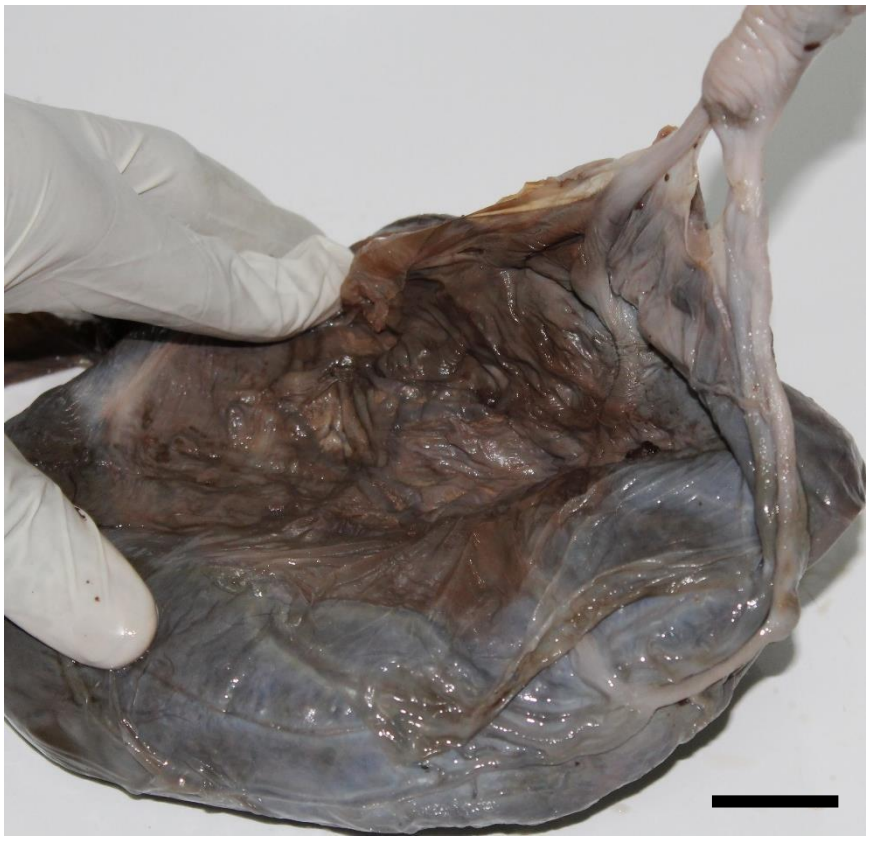

Figure 9: Photograph of umbilical cord with velamentous insertion (x 0.1)

Umbilical cord insertions were confirmed using Pythagorean Theory. Distance of umbilical cord insertion from placental centre was calculated mathematically according to the Pythagorean Theory (Figure 10). ‘a’ was calculated by subtracting ‘e’(shortest distance of umbilical cord

insertion to the chorionic plate margin on X-axis) from the half of 'C'(X-axis passing through the insertion of umbilical cord). 'b' was calculated by subtracting 'dc'(shortest distance of umbilical cord insertion to the chorionic plate margin on Y-axis) from half of 'D'(Y-axis passing through the insertion of umbilical cord). Since $dc^2 = a^2 + b^2$, where dc is the distance of umbilical cord insertion from the centre.

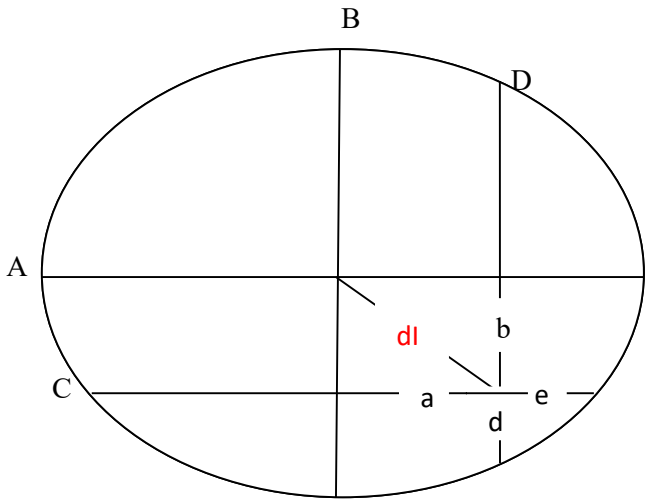

Figure 9: Diagrammatic representation of placental measurements **a = (½ C) - e, b = (½ D) - d, dI = distance of cord insertion from centre.**

The formula for calculating the distance of the cord insertion from the centre is:

$$dI = \sqrt{a^2 + b^2}$$

$$dc = \sqrt{\left(\frac{1}{2C} - e\right)^2 + \left(\frac{1}{2D} - d\right)^2}$$

(Pathak *et al*., 2010).

3.15 Cord centrality index (CI)

It is a ratio that describes the distance of the umbilical cord insertion from the chorionic plate margin. It will range between 0 and 1 (except in cases of velamentous cord insertion, where the value may be greater than 1 as the insertion may be further from the centre than half the longest diameter). The smaller the CI, the closer the umbilical cord insertion to the placental centre; the greater the CI, the further away the cord insertion:

$$\mathbf{CI} = \frac{\textbf{Distance of umbilical cord insertion from the centre}}{\textbf{Half the distance of the larger diameter of the placenta}}$$

3.16 Umbilical Cord Vessel Number

The number of umbilical cord vessels was observed by slicing both the foetal and placental ends of the cord and comparing the number of vessels seen at both ends (figure 11).

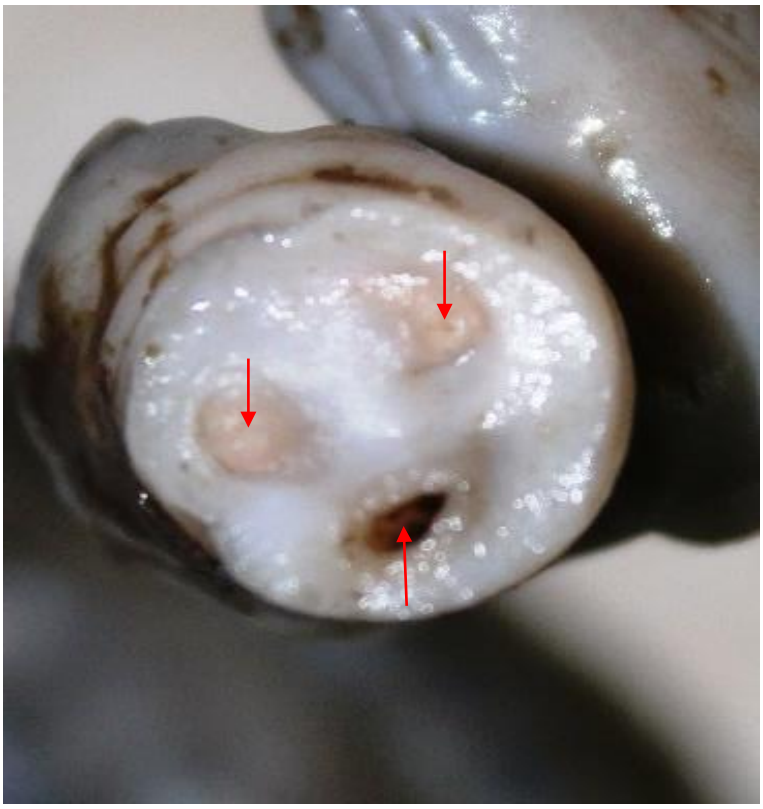

Figure 11: A photograph of the umbilical cord showing three blood vessels (x 3)

3.17 Cross sectional area and Volume

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:

$\boldsymbol{A = 2\pi r^2 L}$; Where $\boldsymbol{r}$ is the radius and $\boldsymbol{L}$, the length of cord vessel

The surface cross-sectional area of the Wharton jelly was computed by subtraction of the total vessel area from the cross-sectional area of the umbilical cord.

Volume of umbilical cord, umbilical arteries, and umbilical vein in a free loop of the umbilical cord were computed using the formula for calculating the volume of a cylinder:

$\boldsymbol{V = \pi r^2 L}$; Where $\boldsymbol{r}$ is the radius and $\boldsymbol{L}$ length of cord vessel

The volume of the Wharton jelly was computed by subtraction of the total vessels volume from volume of the umbilical cord.

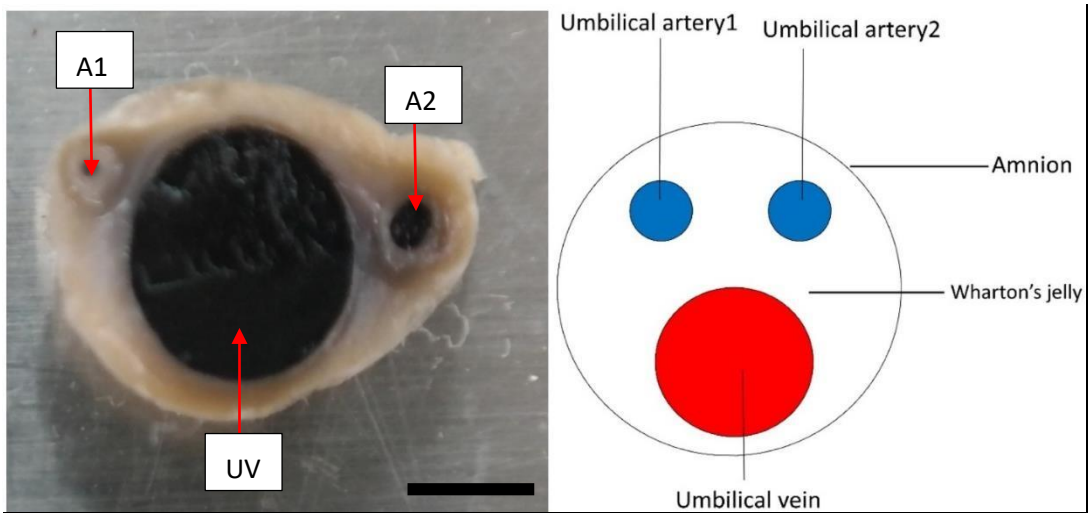

Figure 10: Pictorial and diagrammatic illustration of the umbilical cord vessels (x 2) A1= Umbilical Artery one, A2= Umbilical Artery two and UV=Umbilical Vein

$\boldsymbol{AWJ = UCA - (UCVA + A1A + A2A)}$, where $\boldsymbol{AWJ}$ is the area of Wharton's jelly, $\boldsymbol{UCA}$ is umbilical cord area, $\boldsymbol{UCV}$ is umbilical cord vein area, $\boldsymbol{A1A}$ is area of artery designated $\boldsymbol{A1}$ and $\boldsymbol{A2A}$ the area of artery designated as $\boldsymbol{A2}$ (figure 12). Similarly;

$\boldsymbol{VWJ = UCV - (UCVV + A1V + A2V)}$; where $\boldsymbol{VWJ}$ is the volume of Wharton's jelly, $\boldsymbol{UCV}$ is umbilical cord volume, $\boldsymbol{UCVV}$ is umbilical cord vein volume, $\boldsymbol{A1V}$ is volume of artery designated $\boldsymbol{A1}$ and $\boldsymbol{A2V}$ the volume of artery designated as A2 (A1 = smaller diameter, A2 = larger diameter).

3.18 NEONATAL INDICES

Infant indices including birth weight, body length, head circumference and sex were determined for all the babies. All measurements were done by the investigator with the help of the attendant within 24 hours after delivery.

Birth weight was measured with Seca 725 mechanical baby weighing scale (Seca Co. Ltd. USA) calibrated in kilograms when the infant is naked (Fig 13). Body length, head circumference and abdominal circumference were measured with Dritz C150 fiberglass standard tape measure (Prym consumer USA Inc.) to the nearest centimetre.

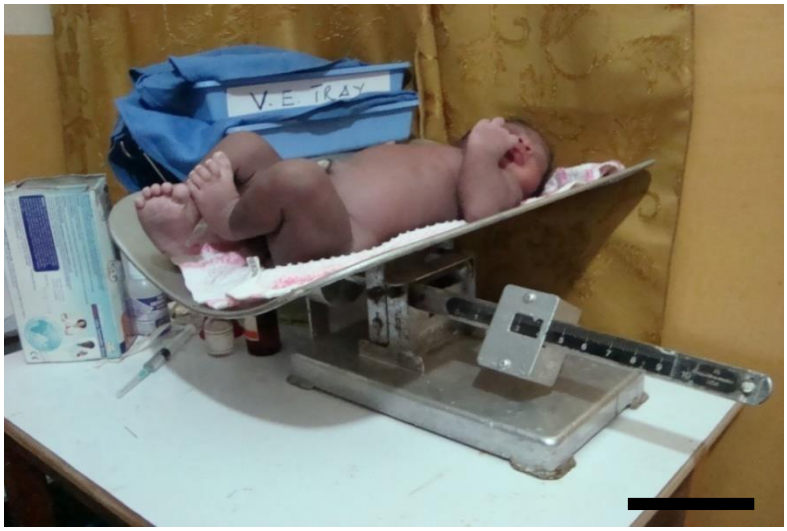

Figure 11: Photograph of Seca 725 Mechanical Baby Weighing Scale with a neonate

Ponderal index (PI) was computed as the ratio of birth weight in grams to the cube of body length in centimetres and multiplied by 100;

$$PI = \frac{BW}{BL_3} \times 100$$ (Landmann *et al.,* 2006),

Where BW is the birth weight in grams and BL is body length in centimetres.

Head circumference to Abdominal ratio was calculated by dividing the head circumference measured in centimetres by the abdominal circumference also measured in centimetres;

$$\frac{HC}{AC} = \frac{Head\ circumference\ (cm)}{Abdominal\ circumference\ (cm)}$$

3.19 STATISTICAL ANALYSIS

Statistical analyses were done using Microsoft Excel (2013 version) and the Statistical Package for the Social Sciences (SPSS) version 12 (SPSS Inc., Chicago, IL). Student t test was done using Microsoft Excel and Pearson's correlations were done using SPSS. All charts were drawn with Microsoft Excel. Statistical significance was defined as $P < 0.05$.

Data were entered and analysed using MS Excel and GraphPad Prism 6 Demo (GraphPad Software, Inc., San Diego, CA). Descriptive statistics (Mean and Standard deviation) were performed for continuous neonate, placenta, umbilical cord and vessels variables. The adopted level of statistical significant was $p < 0.05$. Spearman correlation matrix and coefficients were used to determine correlations among various placental and umbilical cord measurements with the neonatal anthropometric measures. Multiple linear regressions were used to assess the effect of correlations observed between maternal indices, placental indices, umbilical cord morphology, vessels morphometry and the neonatal anthropometric parameters. These were presented in graphs (Figures).

CHAPTER FOUR

RESULTS

4.1 NEONATAL INDICES

Among the 236 neonates studied, 49.15% (116) were females and 50.85% (120) were males. Neonatal characteristics studied are presented in Table 1. The mean birth weight was 3.24 Kg (SD = 0.51), ranging from 1.25 to 4.5 kg. The mean body length was 50.64 cm (SD = 3.43, range = 34 to 60 cm). The mean head circumference was 34.27 cm (SD = 1.95, range = 26 to 49 cm). The mean ponderal index was 2.53 (SD = 0.63, range = 0.9 – 8.1).

Table 1: Descriptive statistics of neonatal indices

Variable	Mean ± SD (N=236)	SE	Range	CoV
BW (kg)	3.24 ± 0.51	0.033	1.25 – 4.5	15.76%
BL (cm)	50.64 ± 3.43	0.224	34.0 – 60.0	6.78%
HC (cm)	34.27 ± 1.95	0.127	26.0 – 49.0	5.68%
PI	2.53 ± 0.63	0.041	0.9 – 8.1	25.04%

Data are expressed in Mean ± SD, Standard Error, Range with minimum and maximum limits, Coefficient of variation, SD=Standard Deviation, SE=Standard Error, CoV= Coefficient of Variation. BW=Birth Weight, BL=Body Length, HC=Head Circumference, PI=Ponderal Index.

4.2 PLACENTAL INDICES

Table 2 provides the descriptive statistics for the placental indices. The mean placental diameter was 17.40 cm (SD = 1.83; range = 11.75 – 23.0 cm). The mean placental weight was 578.81 g (SD = 121.60; range = 140.0 – 1050.0g). Mean placental thickness was 2.04 cm (SD = 0.45; range = 1.5 – 3.49 cm). The mean placental area was 240.29 cm^2 (SD = 50.04; range = 202.06 – 995.81 cm^2). The mean placental volume was 486.91 cm^3 (SD = 135.15; range = 108.38 – 415.27 cm^3).

2: Descriptive statistics of placental indices

Variable	Mean ± SD	SE	Range	CoV
PD (cm)	17.40 ± 1.83	0.12	11.75-23	10.54%
PW(g)	578.81 ± 121.60	7.92	140-1050	21.01%
PT(cm)	2.04 ± 0.45	0.03	1.5-3.49	21.95%
PA (cm^2)	240.29 ± 50.04	3.26	108.38 – 415.27	20.82%
PV(cm^3)	486.91 ± 135.15	8.80	202.06 – 995.81	27.76%

Data are expressed in Mean ± SD, Standard Error, Range with minimum and maximum limits, Coefficient of variation, SD=Standard Deviation, SE=Standard Error, CoV= Coefficient of Variation, PD= Placental Diameter, PW= Placental Weight, PT= Placental Thickness, PA=Placental Area, PV=Placenta Volume.

4.3 UMBILICAL CORD INDICES

The mean umbilical cord length was 41.74 cm (SD = 12.09; range = 16.0 – 80.50 cm) and umbilical cord diameter ranged from 0.65 – 2.0 cm with a mean of 1.19 cm (SD = 0.21). Umbilical cord area had a mean of 96.05 cm^2 (SD = 50.49; range = 20.56 – 427.18 cm^2). The mean umbilical cord volume was 48.03 cm^3 (SD = 25.24 range = 10.28 – 213.59 cm^3 (Table 3).

Table 3: Descriptive statistics of the umbilical cord indices

Variable	Mean ± SD (N = 236)	SE	Range	CoV
UCL (cm)	41.74 ± 12.09	0.97	16-80.5	28.97%
UCD (cm)	1.19 ± 0.21	0.014	0.65 - 2.0	17.78%
UCA (cm^2)	96.05 ± 50.49	3.29	20.56 – 427.18	52.57%
UCV (cm^3)	48.03 ± 25.24	1.64	10.28 - 213.59	52.57%

Data are expressed in Mean ± SD, Standard Error, Range with minimum and maximum limits, Coefficient of variation, SD=Standard Deviation, SE=Standard Error, CoV= Coefficient of Variation, UCL=Umbilical Cord Length, UCD=Umbilical Cord Diameter, UCA= Umbilical Cord Area, UCV=Umbilical Cord Volume

Table

4.4 UMBILICAL CORD LENGTH

The umbilical cord length was grouped into short (< 40 cm), normal (40 -70 cm) and long (> 70 cm). Out of the 236 umbilical cords studied, 50.85% (120), 46.61% (110) and 2.54% (6) were short, normal and long respectively (Figure 14).

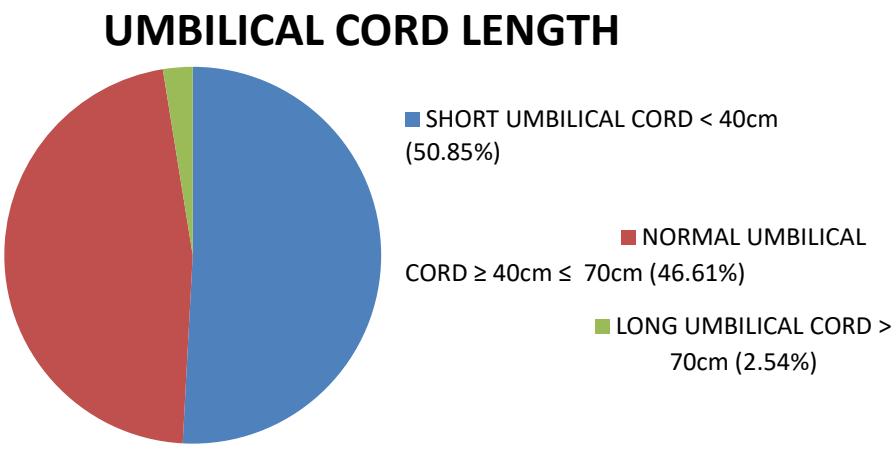

Figure 12: A pie chart showing percentage distribution of umbilical cord length

4.5 GROSS MORPHOMETRY OF UMBILICAL CORD VESSELS

The mean diameters of the umbilical cord arteries designated as A1 and A2 were 0.14 cm (SD = 0.04; range = 0.05 – 0.4 cm) and 0.18 cm (SD = 0.05; range = 0.09 – 0.4 cm) respectively. The mean area and volume of umbilical cord artery A1 were 1.49 mm^2 (SD = 1.34; range 0.16 – 11.30 mm^2) and 0.75 cm^3 (SD = 0.67; range = 0.08 – 5.65 cm^3) respectively. Similarly, the computed mean area and volume of umbilical cord artery A2 were 2.38 cm^2 (SD = 2.09; range = 0.39 – 13.92 cm^2), and 1.20 cm^3 (SD = 1.04; range = 0.20 – 7.64 cm^3) (Table 4).

4: Descriptive statistics of umbilical cord Arteries

Variable	Mean ± SD	SE	Range	CoV
A1 D (cm)	0.14 ± 0.04	0.003	0.05 - 0.4	31.03%
A2 D (cm)	0.18 ± 0.05	0.004	0.09 - 0.4	30.51%
A1 A (cm^2)	1.49 ± 1.34	0.09	0.16 - 11.30	89.53%
A2 A (cm^2)	2.38 ± 2.09	0.15	0.39 – 13.92	87.48%
A1 V (cm^3)	0.75 ± 0.67	0.04	0.08 – 5.65	89.53%
A2 V (cm^3)	1.20 ± 1.04	0.007	0.20 - 7.64	87.48%

Data are expressed in Mean ± SD, Standard Error, Range with minimum and maximum limits, Coefficient of variation, SD=Standard Deviation, SE=Standard Error, CoV= Coefficient of Variation, A1D=Umbilical Cord Artery 1 Diameter, A2D= Umbilical Cord Artery 2 Diameter, A1A=Umbilical Cord Artery 1 Area, A2A= Umbilical Cord Artery 2 Area, A1V= Umbilical Cord Artery 1Volume, A2V= Umbilical Cord Artery 2 Volume.

4.6 GROSS MORPHOMETRY OF UMBILICAL VEIN AND WHARTON'S JELLY

The mean umbilical vein diameter was 0.38 cm (SD = 0.16; range 0.17 to 0.88 cm). The umbilical cord vein area and volume had respective means of 11.66 cm^2 (SD = 11.84; range = 1.32 – 60.29 cm^2) and 5.83 mm^3 (SD = 5.92; range = 10.28 – 213.59 cm^3). Area of Wharton's jelly was 80.5293 cm^2 (SD = 45.78; range = 16.27 – 386.93 cm^2) and volume of Wharton's jelly was 40.26 cm^3 (SD = 22.89; range = 8.14 – 193.46 cm^3) as shown in table 5.

Table 5: Descriptive statistics of umbilical vein and Wharton's Jelly morphometry

Variable	Mean ± SD	SE	Range	CoV
UCVD (cm)	0.38 ± 0.16	0.01	0.17 - 0.88	42.51%
UCVA(cm^2)	11.66 ± 11.84	0.77	1.32 - 60.29	101.54%
UCVV(cm^3)	5.83 ± 5.92	0.39	10.28 - 213.59	101.54%
AWJ (cm^2)	80.52 ± 45.78	2.98	16.27 – 386.93	56.86%
VWJ (cm^3)	40.26 ± 22.89	1.49	8.14 -193.46	56.86%

Data are expressed in Mean ± SD, Standard Error, Range with minimum and maximum limits, Coefficient of variation, SD=Standard Deviation, SE=Standard Error, CoV= Coefficient of Variation, UCVD=Umbilical Cord Vein Diameter, UCVA=Umbilical Cord Vein Area, UCVV=Umbilical Cord Vein Volume, AWJ= Area of Wharton's Jelly, VWJ=Volume of Wharton's Jelly.

4.6 Umbilical cord Insertion

Table

Out of the 236 placentae, 19.49% (46) had central umbilical cord insertions, 66.95% (158) had eccentric umbilical cord insertions, 13.14%(31) had marginal umbilical cord insertions while the velamentous umbilical cord insertion was 1(0.42%) as shown in Figure 15.

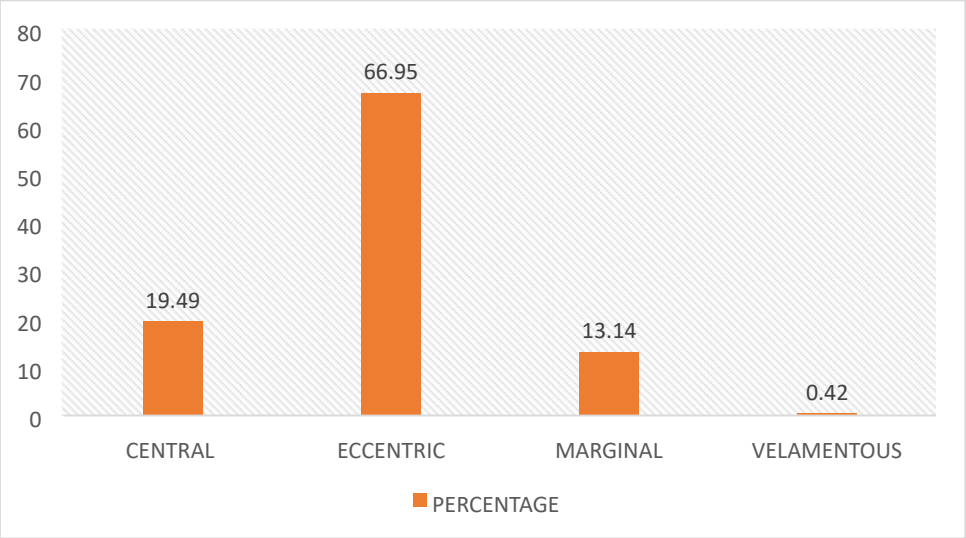

Figure 13: A bar chart showing percentages of umbilical cord insertions

4.7 UMBILICAL CORD INSERTION IN RELATION TO PLACENTAL WEIGHT

Approximately 2.54% of the placentae which weighed < 350 g had eccentric umbilical cord insertions. For the placental weight bracket 350-750 g, there was a prevalence of 17.80% (42), 61.86% (146), 11.44% (27) and 0 for central, eccentric, marginal and velamentous umbilical cord insertions respectively, whiles the prevalence for placental weight bracket > 750 g were 1.69% (4), 2.54% (6), 1.69% (4) and 0.42% (1) for central, eccentric, marginal and velamentous umbilical cord insertions respectively as shown in Table 6.

6: Umbilical Cord Insertion percentage in relation to placental weight.

		UMBILICAL CORD INSERTION				Total
		Central		Marginal	Velamentous	
Eccentric						
	<350	0	6 (2.54%)	0	0	**6(2.54%)**
PW (g)	350-750	42(17.80%)	146(61.86%)	27(11.44%)	0	**215(91.10%)**
	>750	4(1.69%)	6(2.54%)	4(1.69%)	1(0.42)	**15(6.36)**
Total		**46(19.49%)**	**158(66.95%)**	**31(13.14%)**	**1(0.42)**	**236(100%)**

PW= Placental weight

4.8 UMBILICAL CORD INSERTION IN RELATION TO SEX OF BABY

The prevalence of qualitative characteristics of the umbilical cord and its distribution among the male and female neonates in the study population are shown in Table 7. Central umbilical cord insertion was more prevalent in females (10.17%) than in the males (9.32%). Marginal umbilical cord insertion prevalence was higher in the female population (7.63%) than males (5.51%). On the contrary, eccentric umbilical cord insertion prevalence was high in the male population (36.01%) than females (30.93%). Only one velamentous umbilical cord insertion was observed in the female population constituting 0.42%.

Table 7: Umbilical Cord Insertion distribution in relation to sex.

			UMBILICAL CORD INSERTION						Total	
			Central	Eccentric		Marginal	Velamentous			
		Male	22	85	13	0	**120**	Female	24	73
	18	1	**116**							
Sex										
Total			**46**	**158**		**31**	**1**		**236**	

4.9 COMPARISON OF PLACENTAL WEIGHT, BIRTH WEIGHT AND SEX OF THE NEONATE

Table

Out of 236 neonates, majority (205) neonates had birth weight between 2 – 3 Kg whereas most (215) neonates had placental weight between 350-750 g (Table 8). Neonatal birth weight was grouped into low birth weight (< 2.5 Kg), normal birth weight (2.5 -4 kg) and high birth weight (> 4 Kg). For the male neonates, approximately 3.39% (8), 43.22 % (102) and 4.24 % (10) fell within the birth weight brackets < 2.5 Kg, 2.5 - 4 kg and > 4 Kg respectively. The trend was similar for the female neonates which showed 2.54 % (6), 43.64 % (103) and 2.97 % (7) for < 2.5 Kg, 2.5-4 kg and > 4 Kg weight brackets respectively. Placental weight of <350 g was more prevalent in male neonates 1.69% (4) than in the females 0.85% (2). Normal placental weight (350-750) prevalence was higher in the male neonatal population 47.46% (112) than females 43.64% (103). On the contrary, placental weight of >750 grams prevalence was high in the female population 6.36% (15) than males 1.69% (4).

Table 8: Distribution of placental weight and neonatal birth weight amongst male and female neonates.

Neonatal weight (kg)	**Sex of the neonate**		**Placental weight (g)**	**Sex of the neonate**	
	MALE	**FEMALE**		**MALE**	**FEMALE**
< 2.5	8	6	<350 grams	4	2
2.5 – 4.0	102	103	350-750 grams	112	103
> 4.0	10	7	>750 grams	4	15
TOTAL	**120**	**116**		**120**	**116**

4.10 BIRTH WEIGHT, PLACENTAL WEIGHT AND FOETO-PLACENTAL RATIO IN RELATION TO SEX

Considering birth weight in relation to sex, female neonates had a birth weight range from 1.25 to 4.40 kg with a mean birth weight of 3.20 kg. Their placental weight ranged from 240-1050

g with a mean of 600 g. In the male neonates, birth weight ranged from 1.30 to 4.50 kg with a mean birth weight of 3.27 kg and a mean placental weight 558 g (range 140 to 940 g). The foeto-placental ratio was 5.33 in females and 5.86.

4.11 Placental shape

Figure 16 shows the distribution of the different placental shapes. Approximately 29.66% (70), 56.36% (133), 12.71% (30) and 1.27% (3) of the placentae were round, irregular, oval and bilobate respectively.

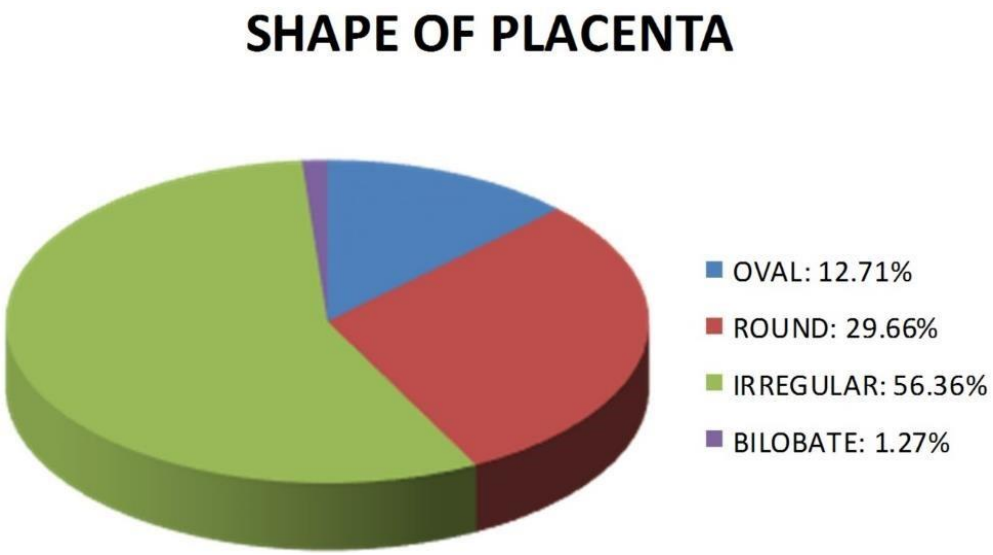

Figure 14: A pie chart showing Placental shapes and their percentages

4.12 LINEAR REGRESSION ANALYSIS OF FOETAL INDICES WITH PLACENTAL WEIGHT AND PLACENTAL VOLUME

Figure 17 below shows that the linear relation between placental weight and placental volume with birth weight were positive. Placental weight and placental volume showed significant correlation with birth weight. There was also a linear relation between placental weight and birth weight ($P = 0.0172$, $R^2 = 0.02402$) and between placental volume and birth weight ($P = 0.01488$, $R^2 = 0.0619$).

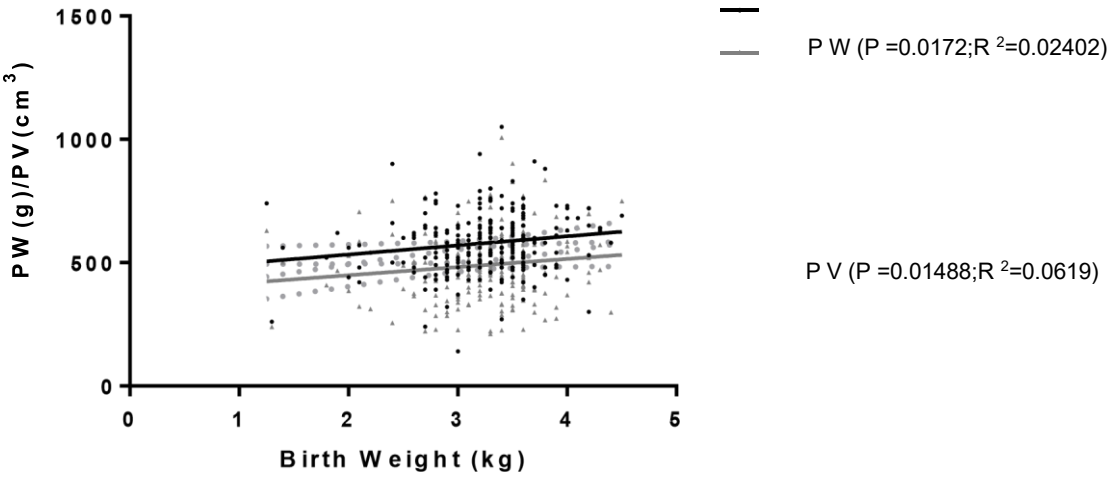

Figure 15: Linear regression graph showing placental weight and placental volume against birth weight

4.13 LINEAR REGRESSION ANALYSIS OF NEONATAL WEIGHT WITH HEAD CIRCUMFERENCE AND BIRTH LENGTH

Figure 17 below shows the linear relation between head circumference and birth length with birth weight. Head circumference and birth length exhibited significant correlation with birth weight. There was linear relation between both head circumference and birth length with birth weight with values of P = 0.001, R^2 = 0.09231 and P = 0.001, R^2 = 0.2473 respectively.

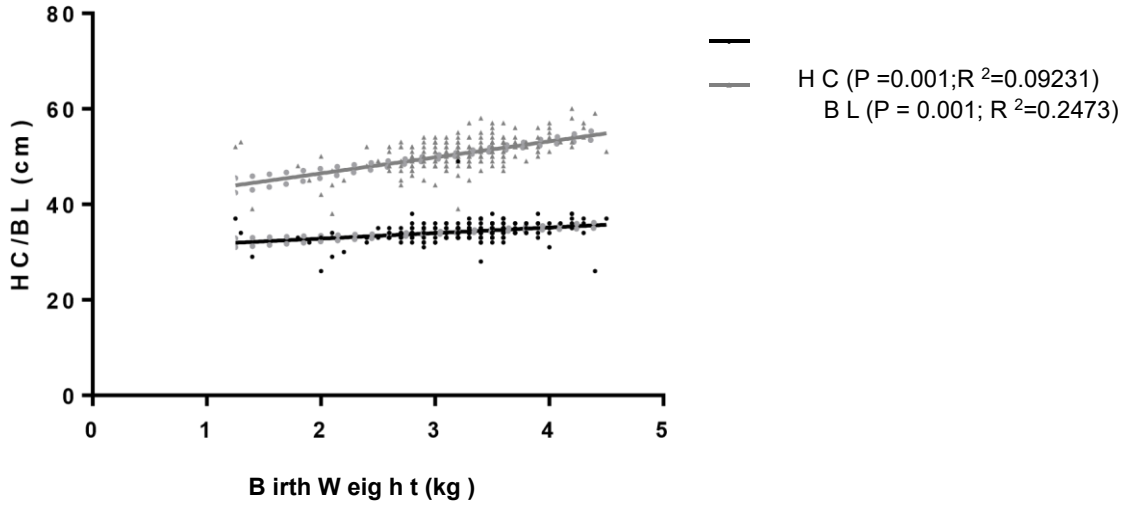

Figure 16: Linear regression graph of head circumference and birth length against birth weight

4.14 LINEAR REGRESSION ANALYSIS OF PONDERAL INDEX WITH BIRTH LENGTH, BIRTH WEIGHT AND HEAD CIRCUMFERENCE

A significant correlation was observed between ponderal index with birth length and birth weight as well as with head circumference. Further analysis with linear regression showed that all three were statistically significant. However birth length showed an inverse relationship with ponderal index (P = 0.0001, R^2 = 0.4582) whilst birth weight showed a positive relationship (P = 0.0006, R^2 = 0.04858) and head circumference also showed a positive relationship (P = 0.0011, R^2 = 0.04445) as illustrated in Figures 19 A, 19 B and 19 C.

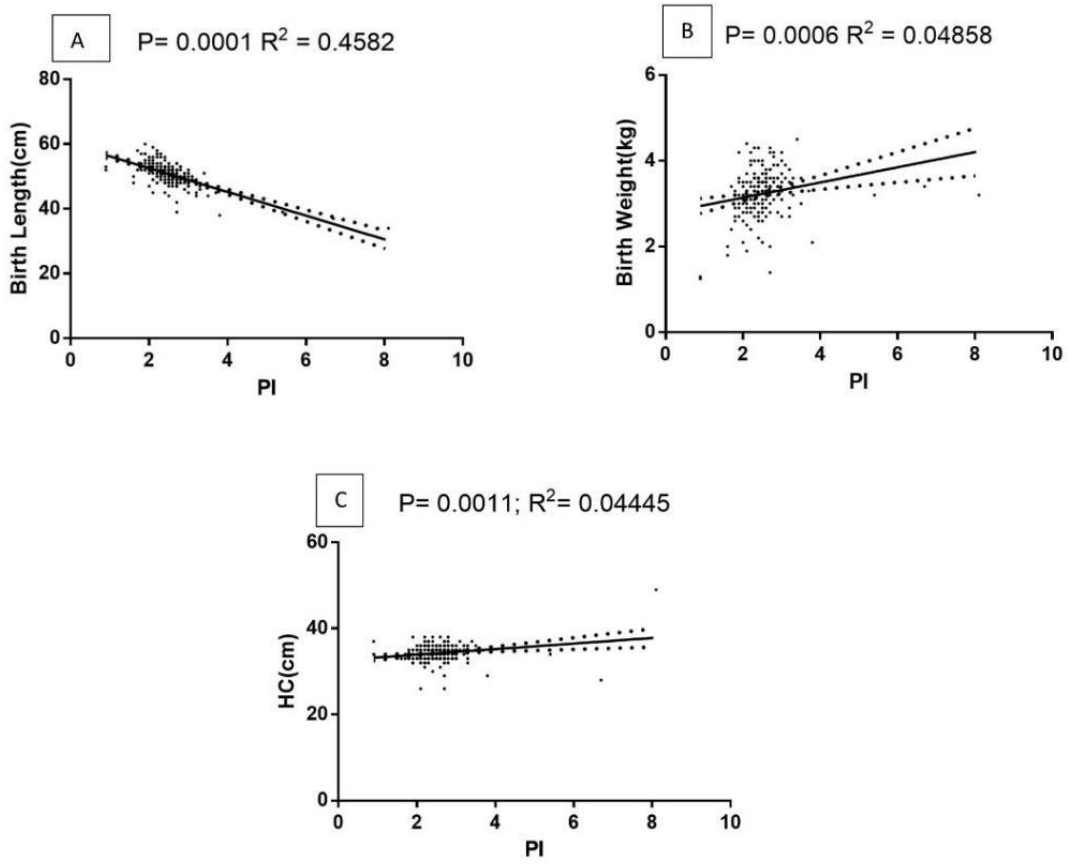

Figure 17: Linear regression graph of birth length, birth weight and head circumference against ponderal index

4.15 LINEAR REGRESSION ANALYSIS BETWEEN PLACENTAL DIAMETER AND UMBILICAL CORD LENGTH WITH PLACENTAL WEIGHT

Figure 19 below shows the linear relation between placental diameter and umbilical cord length with placental weight. The linear regression analysis showed that there was linear relation

between placental weight and placental diameter. ($P = 0.0001$, $r^2 = 0.3183$) (Fig 20 A) and between placental weight and umbilical cord length ($P = 0.0008$, $r^2 = 0.04712$) (Fig 20 B).

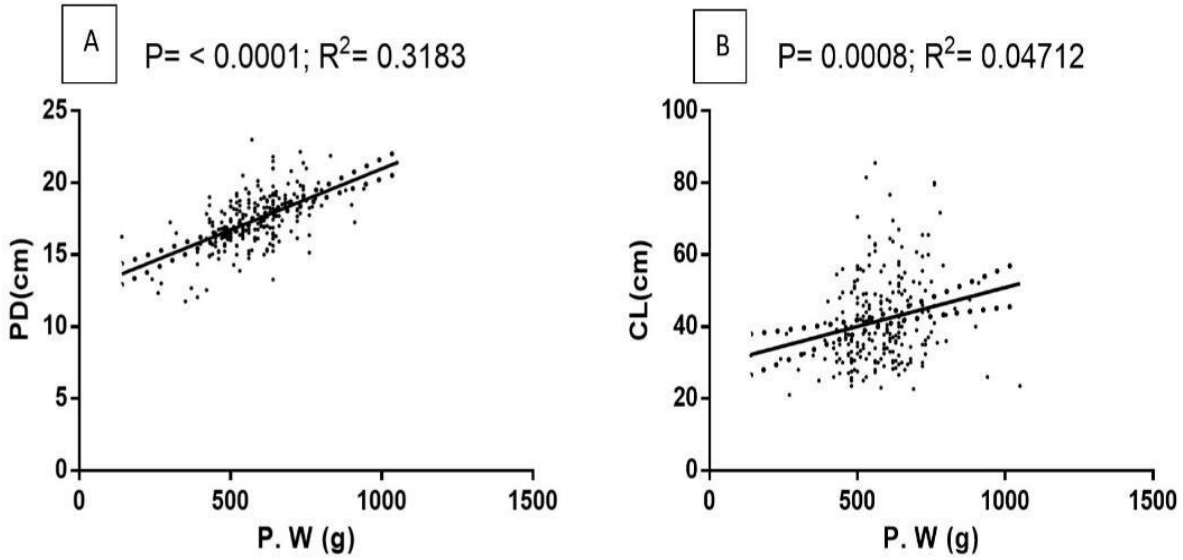

Figure 18: Linear regression graph of placental diameter and umbilical cord length against placental weight

4.16 PEARSON CORRELATION MATRIX OF FOETAL INDICES AND UMBILICAL CORD VESSEL MORPHOMETRY

Birth weight, head circumference and Birth length showed no significant correlation ($P > 0.05$) with the umbilical cord indices. Umbilical cord length had significant correlation with the following, umbilical cord diameter ($P < 0.001$, $r = 0.239$), umbilical cord artery1 diameter ($P < 0.001$, $r = 0.218$), umbilical cord artery2 diameter ($P < 0.001$, $r = 0.247$) and volume of Wharton's jelly ($P < 0.001$, $r = 0.235$). Umbilical cord vein diameter also showed positive correlation with the umbilical cord artery1 diameter ($P < 0.023$, $r = 0.148$) and umbilical cord artery2 diameter ($P < 0.011$, $r = 0.165$). Umbilical cord artery1 diameter showed a positive correlation with Umbilical cord artery2 diameter ($P < 0.001$, $r = 0.639$) (Table 9).

Table 9: Summary of Correlation analysis between neonatal indices and umbilical cord indices.

		BW	BL	HC	UCL	UCD	UCVD	UA1D	UA2D	VWJ
BW (kg)	Pearson Correlation	1								
	Sig. (2-tailed)									
BL (cm)	Pearson Correlation	0.497**	1							
	Sig. (2-tailed)	**0.001**								
	Pearson Correlation	0.304**	0.122	1						
	Sig. (2-tailed)	**0.001**	0.062							
HC (cm)	Pearson Correlation	0.01	-0.013	0.015	1					
	Sig. (2-tailed)	0.879	0.838	0.82						
UCL(cm)	Pearson Correlation	-0.027	-0.011	0.021	0.239**	1				
	Sig. (2-tailed)	0.681	0.871	0.742	**0.001**					
UCD(cm)	Pearson Correlation	-0.006	0.029	-0.109	0.114	-0.026	1			
	Sig. (2-tailed)	0.922	0.66	0.094	0.081	0.695				
UVD(cm)	Pearson Correlation	0.088	0.056	-0.019	0.218**	0.018	0.148*	1		
	Sig. (2-tailed)	0.177	0.388	0.766	**0.001**	0.787	**0.023**			
UA1D(cm)	Pearson Correlation	0.082	0.095	0.03	0.247**	0.033	0.165*	0.639**	1	
	Sig. (2-tailed)	0.211	0.146	0.648	**0.001**	0.618	**0.011**	**0.001**		
UA2D(cm)	Pearson Correlation	-0.03	-0.012	0.024	0.235**	0.999**	-0.034	0.013	0.026	1
	Sig. (2-tailed)	0.646	0.853	0.709	**0.001**	**0.001**	0.606	0.84	0.687	
VWJ(cm)										

**. Correlation is significant at the 0.01 level; *. Correlation is significant at the 0.05 level (2-tailed).

BW= birth weight, BL= birth length, HC= head circumference, UCL=umbilical cord length, UCD= umbilical cord diameter, UVD= umbilical cord vein diameter, UA1D= umbilical cord artery 1 diameter, UA2D= umbilical cord artery 2 diameter, VWJ= volume of Wharton's jelly

4.17 PEARSON CORRELATION MATRIX OF FOETAL INDICES AND PLACENTAL INDICES

Birth weight showed significant positive correlation with birth length (P < 0.000, r = 0.497), head circumference (P < 0.000, r = 0.304) and placental weight (P < 0.17, r = 0.115). Birth length had no significant correlation with the placental indices except with placental shape (P < 0.23, r = 0.148). Head circumference had no significant correlation with the placental indices. Placental thickness had significant correlation with the umbilical cord insertion (P < 0.004, r = 0.185) and placental weight (P < 0.000, r = 0.419). Placental weight also showed positive correlation with placental diameter (P < 0.000, r = 0.283) and placental volume (P < 0.001, r = 0.220). Placental volume showed a positive correlation with placental thickness (P < 0.001, r = 0.206) and placental diameter (P < 0, r = 0.920) (Table 10).

Table 10: Summary of Correlation analysis between neonatal indices and placental indices

		BW	BL	HC	PS	UCI	PW	PT	PD	PV
BW	Pearson Correlation	1								
	Sig. (2-tailed)									
BL	Pearson Correlation	0.497**	1							
	Sig. (2-tailed)	**0.000**								
HC	Pearson Correlation	0.304**	0.122	1						
	Sig. (2-tailed)	**0.000**	0.062							
PS	Pearson Correlation	-0.026	0.148*	0.005	1					
	Sig. (2-tailed)	0.686	**0.023**	0.933						
UCI	Pearson Correlation	0.048	0.047	-0.020	0.102	1				
	Sig. (2-tailed)	0.464	0.470	0.755	0.117					
PW	Pearson Correlation	0.155*	0.091	-0.007	0.043	0.090	1			
	Sig. (2-tailed)	**0.017**	0.163	0.910	0.507	0.166				
PT	Pearson Correlation	0.056	-0.018	0.108	-0.025	0.185**	0.419**	1		
	Sig. (2-tailed)	0.391	0.778	0.098	0.698	**0.004**	**0.000**			
PD	Pearson Correlation	0.058	0.024	0.022	0.135*	-0.046	0.283**	-0.059	1	
	Sig. (2-tailed)	0.379	0.709	0.732	**0.038**	0.484	**0.000**	0.365		
PV	Pearson Correlation	0.045	0.014	0.073	0.086	0.027	0.220**	0.206**	0.920**	1

Sig. (2-tailed)	0.493	0.827	0.262	0.186	0.677	0.001	**0.001**	**0.000**	

**.Correlation is significant at the 0.01 level; *. Correlation is significant at the 0.05 level (2-tailed).

BW= birth weight, BL= birth length, HC= head circumference, PS= placenta shape, UCI= umbilical cord insertion, PW= placenta weight, PT= placenta thickness, PD= placenta diameter, PV= placenta volume.

4.18 CORRELATION ANALYSIS BETWEEN PONDERAL INDEX AND NEONATAL INDICES

Analysis between ponderal index and neonatal indices showed a positive correlation ($P < 0.001$) between ponderal index, birth weight, birth length and head circumference, with coefficience of 0.022, -0.677 and 0.211 respectively.

4.19 ANALYSIS OF VARIANCE OF PRESENT STUDY AND SAMPLED VALUE

There was significant difference ($P < 0.0001$) between the present study and all the analysed samples except the Umbilical cord diameter between the present study and Sudan as shown in table 11.

	Present Study	**Asia**	**Nig. (Sokoto)**	**Israel**	**East Nig.**	**West Eur.**	**China**	**Japan**	**Sudan**	**USA**	**Britain**	**Sing**	**P***
UCL	**41.74**	**-**	**52.9**	**-**	**58.4**	**-**	**-**	**56.2**	**-**	**-**	**-**	**-**	< 0.0001
UCD	**1.19**	**-**	**1.4**	**-**	**-**	**-**	**-**	**-**	1.2	**-**	**-**	**-**	< 0.0001[a]
PW	**578.81**	**588**	**590**	**613**	**630**	**643**	**646.2**	**-**	**-**	**-**	**-**	**-**	< 0.0001
BW	**1.25**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**3.06**	**3.20**	**2.88**	< 0.0001

Table 11: Analysis of variance of present study and sampled values

UCL = Umbilical Cord length, UCD = Umbilical Cord diameter, PW = Placental weight, Birth weight, Nig. = Nigeria, Eur = Europe, Sing = Singapore. * = P value for the difference between present study and sampled values calculated by Analysis of Variance, followed by post Dunnett's Multiple Comparison Test. Statistically Significant

Difference ($P < 0.05$), a = present study versus Nigeria (sokoto), $P > 0.05$

CHAPTER FIVE

DISCUSSION

5.1 PLACENTAL WEIGHT

The mean placental weight was 578.81 g (SD = 121.60) with a range of 140-1050 g. The weight of the placenta was found to have a significant positive correlation with the weight of the neonate ($P < 0.017$, $r = 0.155$) but not with neonatal head circumference and neonatal length. The mean placental weight of 578.81 g in the present study was significantly lower than the sample means of 613, 630, 643 and 646.2 g reported in Israel (Barker *et al*., 1990), Eastern Nigeria (Adinma and Agbai, 1995), Western Europe (Lurie *et al*., 1999) and China (Lo *et al*., 2002) respectively. However, the value was not significantly different from the mean placental weights of 588 and 590 g reported in Asia and Sokoto in Nigeria respectively (Perry *et al*., 1995 and Panti *et al*., 2012).

Other investigators have reported normal placental weight to be within 400 - 600 g (Sanin *et al*., 2001; Borton, 2011). The weight of the placenta is used in the determination of the foetoplacental ratio which is a useful marker of foetal nutrition and utero-placental function. The weight of the placenta gives an idea of the amount of substance that is exchanged between the mother and the foetus. The low mean placental weight could have resulted from the factors

such as chronic intrauterine infections, maternal foetal transfusion, maternal anaemia, congenital neoplasms, maternal-foetal blood group incompatibility and foetal malformations. Other factors such as ethnicity, gestational diabetes, hypertension and hydrops foetalis have been reported to influence foetal and placental weight (Asgharnia *et al*., 2008; Leary *et al*., 2003; Van den Broek *et al*, 2005). However in the present study women with gestational diabetes, and hypertension were excluded from the study therefore these clinical conditions could not have contributed to the low placental weight. Also the variations in the mean weight of the placenta may be due to combination of factors such as regional variations, variations in the methodology and preparation of the samples, process of weighing the placenta and cord clamping time (Yao *et al*., 1969).

It has been observed that for each gram increase in placental weight, birth weight is increased by 2 g and this finding corresponds to earlier studies by Sanin *et al.* (2001) who found that for every 1 g increase in placental weight, the foetal weight increased by 1.98 g (SE = 0.25, $p < 0.01$). Since the weight of the placenta correlated positively with the weight of the neonate, it suggests that placental weight is an important predictor of neonatal weight. Therefore placental weight may serve as an indicator of nutritional and/or environmental factors. Such factors could include maternal size, maternal haemoglobin gain, altitude, paternal factors, maternal and paternal genetics, gestational age, maternal diabetes mellitus and smoking during pregnancy (L'Abée *et al*., 2011; Samson *et al*., 2011; Wallace *et al*., 2012). Chronic low utero-placental blood flow has been proposed as the most frequent cause of small placentae, but often the foetal weight is affected, so the ratio may be normal. Though the exact cause of placental enlargement does not seem clear, it is often revealed if the following are considered: maternal anaemia, maternal-foetal blood group

incompatibility, maternal-foetal transfusion, chronic intrauterine infection (syphilis), foetal malformations (especially of the lung), congenital neoplasms (e.g., neuroblastoma, teratoma,

and chorangiomas) and alpha- thalassaemia (Van den Broek *et al*., 2005; Haavaldsen *et al*., 2011).

5.2 PLACENTAL DIAMETER

The mean placental diameter was 17.40 cm (SD=1.83) with a range of 11.75 to 23.0 cm. The diameter of the placenta did not correlate with neonatal weight, neonatal head circumference or neonatal length. However, the diameter of the placenta did correlate significantly with placental volume ($P < 0.000$, $r = 0.920$) and placental weight ($P < 0.000$, $r = 0.283$). The diameter of the placenta may give an indication of the size of the placenta which in turn may give indirect information about the foeto-placental ratio. The diameter of the placenta affects the amount of nutrients, oxygen and carbon dioxide that will pass from the mother to the child and vice versa. Borton (2011) and Ohagwu *et al*. (2009) reported a term placental diameter range of 15 cm to 25 cm whilst Yetter (1998) reported a mean of about 22 cm. Comparing the mean placental diameter obtained in the present study with that of these investigators, the mean placental diameter is higher than that of Yetter (1998) but falls within the range of Borton (2011) and Ohagwu *et al*. (2009). However the upper limit was higher by 1.0 cm in the present study than that of Borton (2011) and 2 cm lower than that of Ohagwu *et al*. (2009).

The variations in the mean diameter may be due to racial, medical conditions or genetic since the study by Yetter, 1998 involved European women while the present study, that of Borton (2011) and Ohagwu *et al*. (2009) were in African populations. The individual placentae with larger diameter have a large surface area for the exchange of substances and is most likely to result in increased neonatal weight.

Though there was insignificant correlation between the placental diameter with the weight, head circumference and length of the neonate, the positive correlation with placental weight

indicates that foetal factors which directly affect the weight of the placenta will indirectly affect the diameter of the placenta and vice versa. The size of placental diameter may be affected by nutrition, maternal size, maternal and paternal genetic constitution and altitude.

5.3 PLACENTAL THICKNESS

In this study, the mean placental thickness was 2.04 cm (SD=0.45) with a range of 1.5 - 3.49 cm. Thickness of the placenta did not correlate significantly with neonatal weight, neonatal head circumference or neonatal length. However, there was significant correlation between the placental thickness and the weight of the placenta ($P < 0.000$, $r = 0.419$) and umbilical cord insertion ($P < 0.004$, $r = 0.185$). Ohagwu *et al.* (2009) reported an average placental thickness of 3.0 cm while Borton (2011) reported a range of 2 cm to 4 cm. Yetter (1998) gave the term placental thickness range of 2.0 cm to 2.5 cm. The average placental thickness for the present study is lower than that of Ohagwu *et al.* (2009) but in agreement with the reports of Yetter (1998) and Borton (2011). However, the minimum placental thickness is lower than the minimum value of Yetter (1998) and Borton (2011), while the maximum value is above that of Yetter (1998) but lower than that of Borton (2011).

The insignificant correlation between the placental thickness and the weight of the neonate could be due to race or sample size. The significant correlation between the placental thickness and placental weight and placental weight with neonatal weight suggests that factors that affect the thickness of the placenta may have an indirect effect on the weight of the foetus and foeto-placental ratio. Placental thickness may give an indication of the amount of substances (nutrients, gases) that are exchanged between the foetus and the mother. Factors that affect placental thickness include nutrition, maternal genetics, maternal haemoglobin concentration gain and altitude. Since there was no significant correlation between the placental thickness and the head circumference and the length of the neonate, it appears that an increase in any of these factors may not influence the thickness of the placenta significantly. Placentae less than

2.5 cm thick are associated with intrauterine growth retardation of the foetus whilst placentae more than 4 cm thick may be associated with maternal diabetes mellitus, foetal hydrops and intrauterine foetal infections (Malathi and Shanthi, 2010).

5.4 UMBILICAL CORD LENGTH

In the present study, the minimum cord length was 16 cm and the maximum was 80.5 cm with a mean of 41.74 cm ± 12.09. The percentage distribution of short, normal and long umbilical cord lengths were 50.85%, 46.61%, and 2.54% respectively. There was a significant correlation between umbilical cord length and placental weight ($P = 0.0008$, $r^2 = 0.04712$) but there was no significant correlation between neonatal weight, head circumference and neonatal body length with the umbilical cord length.

The categorization of umbilical cords in the present study was based on previous studies. Umbilical cords less than 40 cm in length were considered short and between 40 cm to 70 cm were classified as normal with those longer than 70 cm being long. Although reference standards for the length of the umbilical cord has been reported, variations exist in the classification of short and long umbilical cords (Naeye, 1985; Yetter, 1998; Mutihir and Pam, 2006; Abaidoo *et al.*, 2008). Classically, the umbilical cord continues to grow in length until birth with majority of umbilical cords nearly equally the same in length as the neonate. An observation made by Benirschke (2004) showed that human umbilical cords develop steadily with growing gestation and foetal crown-rump length; and measures approximately 55 cm long at term with human neonates exhibiting wider variations in terms of the length of their umbilical cords. Results of several studies support this finding (Nnatu, 1991; Stefos *et al*., 2003). In spite, of these reports which try to address the issues of umbilical cord development, the control mechanisms of the length of the umbilical cord is still unclear (Benirschke, 2004). However, umbilical cord length is believed to be influenced by environmental and genetic factors as well as exposure to certain sweeteners. Environmentally, Lyndon *et al*. (1994) observed that foetal

movement in the uterus in a way exerts influence on cord length as stated in the "tension theory". However, it is documented that the overall umbilical cord length assumes a narrow distribution with few abnormally short or long umbilical cords (Baergen *et al*., 2001). Benirschke (2004) observed that in excessive lengths, much of the cord develops early in gestation whiles sufficient space still remains available for easy foetal mobility. This assumption by Benirschke (2004) was validated with the reasons that the cords of foetuses with severely reduced movement such as thanatophoric dwarfism, osteogenesis imperfect and muscular dystrophy are evidently short. Again an early development of amniotic band which adhesively attaches the foetus to the placenta in early gestation will consequently lead to the formation of short umbilical cords. In other cases such as in multiple pregnancies (twins), as compared to singleton pregnancies, foetuses in the former have slightly shorter umbilical cords than the latter which may be from the fact that twins have relatively less space for movement. In addition, Benirschke (2004) reported that due to the fact that children with trisomy 21 generally have limited intrauterine motility such children have short umbilical cords.

In an intrauterine curarization experiment where there was loss of foetal movement in rodents, a significant correlation between the umbilical cord length and foetal movement was observed (Benirscke, 2004). Evidence of genetic predetermination of umbilical cord length was observed by Adinma and Agbai (1993) after it was found that the length of umbilical cord positively correlated with birth weight and placental weight. Infants with conditions such as skeletal dysplasia, Down's syndrome and long-term neurological abnormalities which are collectively known as reduced foetal motion syndromes, have short umbilical cords (Benirschke, 1994). Neonates with Beckwith-Wiedemann syndrome which is associated with excessive somatic growth have been reported to have excessively long umbilical cords and in this same experiment it became evidently clear that babies at high risk of having long umbilical cords are those of mothers with existing history of excessive long cord (Baergen, 2001). In a

study of umbilical cord length in an African population, a highly significant correlation between the length of umbilical cord and the weight of neonates and placenta was observed by Nnatu (1991) who concluded that umbilical cord length could serve as a predictive indicator for the outcome of foetal and placental weights.

In addition, the mean umbilical cord length had a lower numerical value (41.74 cm) which was significantly different ($p<0.0001$) from that of all compared sampled means of 52.9, 56.2 and 58.4 cm reported by Mutihir and Pam (2006), Suzuki and Fuse (2012) and Nnatu (1991) respectively. Also approximately 50% of the umbilical cords studied were short. The shortness of the umbilical cord may be due to cord loops or entanglement. However in the present study, umbilical cord entanglement was not observed but some of the cords appeared to be heavily looped. The pathogenesis of short umbilical cords remains uncertain. One prominent hypothesis to explain the ontogeny of the umbilical cord is the "stretch hypothesis," which attributes the development of a short umbilical cord to intrauterine constraint (Baergen et al., 2001). Short umbilical cords have been associated with antepartum abnormalities and risk factors for complications of labour and delivery (Krakowiak et al., 2004). About a decade ago, some investigators found that infants with short umbilical cords were more likely to be female, have a congenital malformation, and be small for their gestational age (Krakowiak et al., 2004). It is possible that the short cords reported in the present study were associated with increased risk for maternal labour and delivery complications, including retained placenta and operative vaginal delivery. However information on maternal labour and delivery were not readily available although in a few cases caesarean operation was indicated in the maternal records. Short umbilical cords have been associated with reduced foetal activity, interference with heart rate patterns in labour, restriction of foetal descent and cord rapture (Yetter, 1998; Predanic, 2009; Jain *et al*., 2014).

5.5 UMBILICAL CORD DIAMETER

The mean umbilical cord diameter in this study was 1.19 ± 0.21 cm with a range of 0.65 - 2.0 cm. The umbilical cord diameters obtained in the present study were similar to the findings of Collins (2002) who reported an average diameter of a normal cord to be 1.2 cm. From the results, it also appeared that the mean umbilical cord diameter (1.19 cm) was significantly disparate ($p<0.0001$) between the Ghanaian samples and the compared samples (1.2 and 1.4 cm) observed in Sudan and Nigeria respectively (Abdalla *et al*., 2014; Eze *et al*., 2014). However about 86.44% of the cords had diameters ranging from 1.0 cm to 2.0 cm. Based on previous studies by Eze *et al*. (2014) and Collins (2002), the mean umbilical cord diameter of 1.19 cm obtained in the present study appears to be within the normal range although 14% of the umbilical cords were thin. Earlier studies have documented that umbilical cords with diameters less than 0.8 cm in term infants correlated with utero-placental ischemia whiles in some patients thin cords were associated with an early onset of pre-eclampsia, reduced amount of wharton's jelly and smaller umbilical vein area (Eze *et al*., 2014). There is enough evidence in the literature to suggest that foetuses with thin umbilical cords are likely to be at risk of being small for gestational age at delivery and will have distress (Raio *et al*., 1999).

On the other hand, Collins (2002) observed that umbilical cord hernia, tumour, or oedema were associated with average umbilical cord diameter greater than 3 cm while those with diameter greater than 6 cm should prompt an examination of the umbilical cord and foetus. Umbilical cord diameter did not correlate positively with birth weight, neonatal length and head circumference.

5.6 UMBILICAL CORD VESSELS

All the 236 umbilical cords studied had three blood vessels. The mean umbilical cord artery A1 diameter was 0.14 cm ± 0.04 with a range of 0.05 - 0.4 cm and the umbilical cord artery A2 diameter was 0.18 cm ± 0.05 with a range of 0.09 - 0.4 cm whiles the umbilical cord vein diameter was 0.38 cm ± 0.16 with a range of 0.17 - 0.88 cm. Three umbilical cord vessels appear to be normal and adequate for proper foetal development and survival. In humans, the normal umbilical cord has a pair of arteries that is mildly helical around a straight vein (Pierce *et al*., 2001; Collins, 2002; Martinez *et al.,* 2007). In this study, the positive correlation between umbilical cord length and umbilical cord diameter, umbilical cord arteryA1 diameter, umbilical cord artery A2 diameter and the volume of Wharton's jelly suggest that factors that affect umbilical cord length would affect these parameters as well. It is therefore possible that an increase in Wharton's jelly volume would improve its protective capacity and this could impact favourably on foetal nutrition by enhancing foeto-placental circulation. This is because Wharton's jelly is a connective tissue which facilitates diffusion of water and growth metabolites through its interconnected cavities between the umbilical cord vessels and the amniotic fluid (Raio *et al*., 1999; Ghezzi *et al*., 2001).

Using the area and volume of the umbilical cord artery eliminates the problem of segmental reduction in umbilical cord artery as well as the fact that the vessel may not be absolutely circular in shape after birth. Also the use of volume has an added advantage over the area in that it gives a pictorial view of the total arterial space available for blood flow velocity determination at the various gestational ages. This is in line with the findings of Togni *et al*. (2007) in which a statistically significant correlation was found between the cross-sectional area of the umbilical cord arteries and gestational age. Morphologic and morphometric characterization of the umbilical cord components such as the umbilical vessels could greatly assist in improving on maternal and foetal outcome. Recent advancement in ultrasound technology has enhanced the study of morphometric variations of the umbilical cord vessel

association with foetal outcome at birth (Togni *et al*., 2007). For instance, evaluation of umbilical cord artery impedance to blood flow helps in identifying foetuses vulnerable to growth and developmental disorders (Raio *et al*., 2003). Various anatomic investigations have observed that umbilical cord in the face of foetal IUGR and hypertensive disorders with normal umbilical artery Doppler parameters exhibited reduced total vessel area and Wharton's jelly area in comparison with normal foetuses (Bruch *et al*., 1997; Inan *et al*., 2002).

Morphometric analysis of the vascular architecture of the umbilical cord provides functional interpretation. For instance, whereas an abnormal ratio of Doppler systolic/diastolic may indicate pathologic circulation of the neonate that leads to intrauterine retardation, normal values show foeto-placental circulation associated with small foetal size (Chang *et al*., 1993; McCowan *et al*., 2000). Neonatal body length relation with the area and volume of the umbilical cord vessels manifests the haemodynamic state of umbilical cord blood flow velocity. In cases of continuous diminution in the flow velocity of umbilical cord blood with increased foeto-placental obstruction, structural alteration in the umbilical cord vessels is induced and as a compensatory mechanism for the insufficient transfer of nutrients, foetal growth velocity is significantly decreased (Raio *et al*., 2003).

Earlier studies have reported umbilical cords with SUA, two-vessel cords as well as four-vessel cords (Collins, 2002; Martinez *et al.,* 2007). The present study found a positive correlation between the two umbilical cord arteries ($P = 0.001$, $r = 0.639$), which suggests that the functions of the two umbilical cord arteries may be interdependent hence the absence of one could compromise their function. This finding supports previous studies which reported an incidence of 3% - 20% SUA in stillbirths and an association between SUA and stillbirths. Malformations due to inadequate blood supply and brain damage occur in about 46% of babies with SUA (Schimmel and Eidelman, 1998; Martinez *et al*., 2007). It has been reported by Sornes (2000) that about 27% of live births with structural anomalies are associated with SUA. Four-

vesselcords have also been associated with foetal abnormalities and conjoined twining has been found to be associated with cases of five or more umbilical cord vessels (Schimmel and Eidelman, 1998; Martinez *et al*., 2007).

5.7 UMBILICAL CORD INSERTION.

The distribution of umbilical cord insertions in the present study was 13.14%, 0.42%, 19.49% and 66.95% for marginal, velamentous, central and eccentric umbilical cord insertions respectively. This gave a central/eccentric insertion of 86.44%. The 86.44% incidence for combined centric/eccentric insertion is comparable to results of Kouyoumdjian (1980), who observed that about 90% of all cord insertions are either central or eccentric. The results of this study though higher, are also comparable to the observations of Addai *et al.* (1994) where an incidence of 74% centric/eccentric insertion was reported. Umbilical cord insertion may be defined as how far the insertion point is located from the centre of the placenta, or how close the umbilical cord insertion is to the chorionic plate margin. The distance of umbilical cord insertion from the centre of the placenta has been suggested as a clinically useful marker of placental insufficiency. Abnormal umbilical cord insertion has been associated with a number of complications resulting from compression or rupture of poorly supported umbilical vessels (Benirschke, 2004). According to Benirschke, (2004) the prevalence rates of marginal cord insertions are 7-9% in singleton pregnancies and 24-33% in twins, whereas for the corresponding rates for velamentous insertions, are 2% in singleton pregnancies and 10-16% in twins. Benirschke (2004) also observed a prevalence rate of marginal insertion to be 5% among singleton pregnancies. Di Naro *et al*. (2001) linked velamentous insertions and to a lesser extent marginal insertions to foetal bradycardia, stillbirth and IUGR. One velamentous umbilical cord was observed in the present study. According to Kouyomidjian (1980), marginal

or the least frequent velamentous insertions which made up about 10% of the umbilical cord insertions is believed to result from disturbances during the process of implantation.

5.8 NEONATAL WEIGHT

The mean birth weight observed in this study was 3.24 kg (SD 0.51) with a range of 1.25 – 4.5 kg. This mean birth weight is similar to the 3.1 kg (SD 0.8) observed in Nigeria by Mutihir and Pam (2006). The low birth weight rate in this study was 5.93 % while 86.86 % were normal for gestational age and 7.20% were large for gestational age (>4.0 kg). Low birth weight is defined by Colley *et al*. (1991) as birth weight less than 2.5 kg. Nkyekyer *et al*. (2006) reported that low birth weight rate in West Africa is about 15.4% and that of Ghana to be around 11.0%. The low birth weight observed in this study is lower than in these previous studies. It has been documented that for every one gram increase in the weight of the placenta, the weight of the foetus is increased by approximately 2.0 g (Sanin *et al*., 2001). Both low birth weight (<2.5 kg) and high birth weight (>4.0 kg) are foetal conditions associated with increased risks of peripartum morbidity and mortality. Valsamakis *et al*.

(2006) suggested that low birth weight contributes to a range of poor health outcomes. Neonates born with low birth weight may face an increased risk of dying during their early months or years. Those who survive may have impaired immune function and increased risk of diseases. They are likely to be at risk of remaining undernourished, with increased muscle weakness, throughout their lives and such babies suffer a higher incidence of heart diseases and diabetes (Gupta *et al*., 2006). Birth weight greater than 4.0 kg is considered to be macrosomia. It affects 2 - 15% of all pregnancies, depending on maternal obesity, maternal pregnancy weight gain, maternal haemoglobin concentration, gestational diabetes mellitus, race, ethnic or socioeconomic composition of the population under study (Sornes, 2000).

Compared to the baseline of foetal macrosomia of 2 - 15% in the general population, the rate among mothers with poorly controlled gestational diabetes is elevated (20-33%). The 7.20% foetal macrosomia identified in the present study could be due to any of the above conditions or a combination of factors. Sanin *et al*. (2001) put the mean neonatal weight to be 3.38 ± 0.486 kg with a range of 2.18- 4.81 kg. Comparing this with the results obtained in the present study, the mean neonatal weight is lower than that of Sanin *et al*. (2001) however, the minimum foetal weight is lower than Sanin *et al*. (2001) and the maximum value is also lower than that of Sanin *et al*. (2001). This could be suggestive of differences in race and genetic makeup.

According to an experiment by Valsamakis *et al.* (2006), the most suitable birth weight range to minimize the risk of foetal and maternal morbidity and mortality is 3.0 - 4.0 kg. Comparing the mean birth weight of singleton babies in the United States, Great Britain and Singapore, Valsamakis *et al.* (2006) and Hershkovitz *et al.* (2001) found out that the mean neonatal weight in the United States, Great Britain and Singapore from 1975- 1992 were 3.06- 3.52 kg, 3.20- 3.75 kg and 2.88- 3.29 kg respectively. The mean neonatal weight of the present study fell within the range for all the three countries but the lower limit value (1.25 kg) was significantly lower than the lower limit values reported by these countries. Many factors, both internal and external can influence the weight of the neonate. These include maternal factors such as race, stature and genetics, paternal factors including paternal height and genetics. Environmental influences such as altitude, availability of adequate nutrition also affect the weight of the neonate. Other important factors are physiologic factors for example altered glucose metabolism, haemoglobin concentration, micro-vascular integrity. In addition pathologic factors such as hypertension, uterine malformation and complications of pregnancy including gestational diabetes mellitus and preeclampsia affect neonatal birth weight (Van den Broek *et al.*, 2005).

Of all these factors, gestational age at delivery is the most powerful determinant of foetal weight (Van Dijk *et al*., 2002; Van den Broek *et al*., 2005). However, the most compelling determinant of foetal weight in the present study appeared to be placental weight since the correlation between the neonatal weight and placental weight had a higher correlation coefficient. Other potential causes are collectively termed as intrauterine growth retardation. Causes of IUGR include intrauterine infections, genetic abnormalities, and chronic uteroplacental insufficiency.

5.9 NEONATAL HEAD CIRCUMFERENCE

The mean head circumference was 34.27 cm (SD 1.95) with a range of 26.0 to 49.0 cm. The head circumference of the neonate gives an indirect assessment of the weight of the neonate in that the bigger the head circumference, the heavier the neonate. The mean head circumference of 34.27 cm in this study is similar to the 34.2 cm (SD = 2.6) observed by Eregie (1993) in Benin-City, Nigeria and 34.49 cm (SD = 1.59) in Jos. These similarities can be attributed to race due to the fact that all these studies were conducted in West Africa. In a study conducted in India, Salafia and Vintziloes (1999) found the mean head circumference to be 32.20 cm.

There was no significant correlation between head circumference and weight of the placenta, placental diameter or placental thickness. The uniqueness of all the changes that occur in foetal life has been the deceleration in growth rate of the head. Measurements at various gestational ages showed that, at the onset of the 12^{th} week of gestation, the size of the head is half the crown-rump length, and at the beginning of the 20^{th} week of gestation the size of the head becomes one third of the crown-heel length and at birth it measures approximately one fourth of the crown-heel length (Loughna *et al*., 2009).

Head circumference can be influenced by factors such as anorexia nervosa and bulimia nervosa (Anarnath *et al.*, 2000). This present study found a positive link between head circumference

and weight of the neonate (P = 0.001, R^2 = 0.09231) which showed that increased head circumference increases the birth weight. Head circumference again had a strong Pearson correlation with ponderal index (P < 0.001, r = 0.211). The study of Franko *et al*. (2001) found that women with a history of an eating disorder had a higher rate of small for gestational age babies, babies with microcephaly, miscarriage, low birth weight neonates, premature labour and IUGR.

5.10 NEONATAL LENGTH

The mean length of the neonates was 50.64 cm (SD= 3.43) with a range of 34.0 – 60.0 cm. There was no positive correlation between the length of the neonate and the weight of the placenta, the diameter of the placenta nor the thickness of the placenta. The mean neonatal length obtained in the present study is similar to the value (48.8 cm) reported by Lo *et al*. (2002). Contrary to the results of the present study, Lo *et al*. (2002) had a positive correlation between the foetal length and the placental weight (r = 0.305, p<0.01).

Foetal growth and development are influenced by the genetic constitution of the parents as well as environmental factors. Maternal genes have an important specific influence over foetal growth. In particular, maternal height, which is a representation of uterine capacity and the potential for growth, is a major determinant of foetal size (Murphy *et al*., 2006). The genetic make-up of the parents can significantly influence the length of the neonate. Borton (2011) and Valsamakis *et al*. (2006) in their respective studies, reported that when both parents are tall, the neonate will inherit tallness from both parents and if one is short and the other tall, based on their genetic make- up, the neonate may be tall or short. This suggests that the babies that fell above the mean range may have parents who are tall or one short and the other tall and those babies that are short have short parents.

CHAPTER SIX

SUMMARY OF MAIN FINDINGS, CONCLUSION AND FUTURE WORK

6.1 SUMMARY OF MAIN FINDINGS

The present study recorded a high incidence of combined centric and eccentric insertions of the umbilical cord into the placenta (86.44%) suggesting that umbilical cord is commonly and best positioned central or eccentric. About 50.85% of the umbilical cords were short whiles 46.61% were found within the normal range of umbilical cord length. Approximately 91.10% of the placentae weighed between 350 – 750 g suggesting that normal placental weight should be within this weight bracket. Also, there was 86.86% of neonates in the normal weight bracket (2.5 – 4 kg) with about 5.93 % within the low weight bracket (< 2.5 kg). In addition, the foeto-placental ratio of 5.6 suggests that the foeto-placental ratio is in the normal range. The mean umbilical cord diameter of 1.19 cm suggests that it is in the normal range of 1-2 cm with thin umbilical cord prevalence of about 13.98 %.

The present study shows that umbilical cord length correlates positively with placental weight. There was also a strong correlation between neonatal weight and placental weight as well as placental volume which suggests that the healthy development of the foetus depends on how healthy the placenta is. The findings of this study suggest that the placenta is the single most appropriate sentinel for determining neonatal wellbeing. An effective and healthy placenta will provide a large surface area for transfer of substances between mother and foetus. This study further found that statistically significant regional variations existed between the placental weight, umbilical cord length, umbilical cord diameter and neonatal weight with compared samples.

6.2 CONCLUSION

In the present study, neonatal weight was found to be associated with placental weight and placental volume but not with placental diameter and placental thickness. Though umbilical cord length correlated with placental weight, it did not correlate with neonatal weight. Based on the studied sample, the placental, umbilical cord and neonatal values compared with other sampled populations showed significantly lower values. This finding therefore suggest that these regional variation that exist could be the reason for the high morbidity and mortality cases reported in Ghana.

6.3 FUTURE WORK

1. Future studies using larger sample sizes from health facilities with different geographical locations should be conducted.
2. Detailed light and electron microscopical morphometric assessment of placental and umbilical cord characteristics might be informative in studies tracing origins of prenatal and postnatal outcome of the neonate.

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