RELATIONSHIP BETWEEN THE MORPHOLOGY OF THE PLACENTA, UMBILICAL CORD AND PERINATAL OUTCOME

A THESIS SUBMITTED IN PARTIAL

FULFILLMENT OF THE

REQUIREMENT FOR THE DEGREE

OF

MASTER OF PHILOSOPHY

IN THE

DEPARTMENT OF THEORETICAL AND APPLIED BIOLOGY,

FACULTY OF BIOSCIENCES

BY

PETER KWABENA APPIAH

KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

June, 2009

DECLARATION

The experimental work described in this thesis was carried out at the Department of Anatomy, School of Medical Sciences and the Department of Theoretical and Applied Biology, Faculty of Biosciences, KNUST. This work has not been submitted for any other degree.

APPIAH PETER KWABENA	…….	……
Student	Signature	Date

CERTIFIED BY

DR MRS CHRISSIE S. ABAIDOO	……	……
Supervisor	Signature	Date
DR KOFI OWUSU DAAKU	……	…….
Co-supervisor	Signature	Date
……..	……	…….
Head of Department	Signature	Date

DEDICATION

To my loving wife, MRS LYDIA OBUBA APPIAH, my Sons, KWAME NANA YEBOAH APPIAH & KWAME OHENEBA AGYABINTI APPIAH, and my mother.

ACKNOWLEDGEMENT

TO GOD IS THE GLORY AMEN.

I wish to thank the ABAIDOO family for the help and love I received from everybody; NANA ESI, for her sisterly love, PROF. R. C. ABAIDOO, for his interest in me, DR MRS C. S. ABAIDOO, for being more than a supervisor but a MUM and KUUKUA, for her help. You will always be remembered, thank you and GOD bless you.

I also wish to thank DR. H. S. OPARE ADDO and all 2D staff as well as staff of the Magazine Clinic, Victory Maternity Home, K.A.T.H. A1 labour ward, and the KNUST hospital labour ward, my nephew OSCAR GYAMFI, my colleagues at work and everybody who contributed to the success of this work, GOD bless you all.

ABSTRACT

To determine the relationship between the placenta, umbilical cord and the well being of the foetus, 256 placentae with attached umbilical cords obtained from KNUST Hospital and Victory Maternity home between 2004 and 2008 were studied. Average cord length was 44.8 cm (SD12.9**,** range 19.5cm-88.5 cm**)**. Short cords, long cords and normal cords (40 to 70 cm) constituted 39.62%, 2.64% and 57.74% respectively. Majority (82.6%) of the cords had a diameter between 1.0 cm and 1.45 cm. Central, eccentric and marginal insertions constituted 60.75%, 21.14% and 18.94% respectively. Occurrence of furcate insertion of umbilical cord vessels into the placenta was 28% and non-furcate insertion was 72%. Placenta weight was 315g- 933g with a mean of 563.47g (SD= 132.31). Placenta diameter was in the range of 14 cm to 25 cm with a mean placenta diameter of 18.69 cm (SD= 2.05). The mean placental thickness was 2.65 cm (SD= 0.55) with a range of 1.3 cm to 6.0 cm. Foetal weight (birth weight) correlated significantly ($p<0.01$) with weight and diameter of the placenta, gestational age, maternal age, cord length and thickness of the placenta ($p<0.05$). Foetal length correlated significantly ($p<0.01$) with the weight and diameter of the placenta and the gestational age. Foetal head circumference also correlated significantly ($p<0.01$) with the weight and diameter of the placenta, cord length, cord diameter and thickness of the placenta ($p<0.05$). There was a higher incidence of short cords and marginal insertions among the study population compared to other literature. In addition, the umbilical cord was commonly positioned centrally or eccentrically. Furthermore, a normal cord must have length in the range of 40-70 cm, a diameter range of 1.0 to 2.0 cm and umbilical coiling index in the range of 0.08-0.19 coils/cm. There was no significant correlation between the intrauterine ultrasonographic measurements and the gross anatomical measurements ($p>0.05$) therefore intrauterine ultrasonography may be used as a guide for the determination of foetal well-being.

Table of content

List of Tables

List of Figures

CHAPTER 1

INTRODUCTION

1.1. THE RELATIONSHIP BETWEEN MORPHOLOGY OF THE PLACENTA AND THE FOETUS

The well being of the foetus is affected by many factors but a healthy placenta is the single most important factor in producing a healthy baby (Van den Broek et al., 2005; Kliman 1997). The placenta begins to form at about the seventh day after fertilization when the first cell layer of cytotrophoblast is observed. During pregnancy, a range of problems may occur that could lead to foetal abnormalities and death. Although these problems could arise from a variety of sources including chromosome and genetic disorders of the foetus (e.g. Down's syndrome), maternal illness or behaviour (e.g. pre-eclampsia, smoking), environmental factors (e.g. radiation) the most important of them all is placental abnormalities (Yetter, 1998). Information on placental size, shape, consistency, completeness of the placenta, presence of accessory lobes, placental infarcts, haemorrhage, tumors may be important to the care of both mother and infant (Yetter, 1998).

The placenta is a complex multifunctional organ of mainly foetal origin with pleiotropic roles during foetal growth. It has a portion derived from the developing embryo and a maternal portion formed by the modification of the uterine lining of the mother (Yetter, 1998). During the gestational period, it provides nutrition, gas exchange, waste removal, endocrine, immune support and a special circulation system (Pijnenborg et al., 1983) to the developing foetus. It separates the maternal and foetal circulation, with which it is in contact through different surfaces, i.e., the syncytiotrophoblast exposes the placenta to the maternal circulation and the foetal vascular endothelium is in contact with foetal blood (Desoye and Haugel-de, 2007). The placenta comprises a large number of functional units called villi which contains branched

terminals of the foetal circulation allowing transfer of metabolic products. The placenta is blue-red in colour and discoid in shape, 15- 22 cm in diameter, 2- 4 cm thick, weighs 400- 600g. (Yetter, 1998). It is classified as chorio- allantoic since it is vascularized by vessels homologous with allantoic vessels of lower mammals; haemo-chorial because of the nature of the placenta membranes; villous because of their villi (Foidart et al., 1992)

It has a maternal surface that is divided into lobules or cotyledons with irregular grooves or clefts; the foetal surface is smooth, shiny, translucent and covered in amniotic membrane (Borton, 2006). The foetal surface of a full term placenta is shiny, grey and consists of large opaque blood vessels distributed on the dense opalescent surface of the thickened chorion. The maternal surface has the dark red colour of venous blood. The placenta uses about 1/3 of all the oxygen and glucose supplied to the maternal blood and the rate of protein synthesis is higher in the placenta than the liver (Kaplan, 1995).

1.2. DEVELOPMENT AND MORPHOLOGY OF THE UMBILICAL CORD

After about four weeks of gestation the only link of the foetus to the placenta is the umbilical cord which begins to form around this time replacing the yoke sac. It develops from the extra embryonic mesoderm and becomes the channel for blood vessels, through which all exchanges and other activities of the mother and the foetus via the placenta are carried out. It is a cylindrical structure made up of a single layer of amniontic epithelium within which are two arteries and one vein embedded in a gelatinous Wharton's jelly which is mainly a mucopolysaccharides (Kulkarni et al., 2007). At term the normal umbilical cord is about 55-65 cm in length (Salafia and Vintziloes, 1999) with a diameter of 2.0-2.5 cm which normally insert centrally or eccentrically on the foetal side of the placenta.

It provides the means by which oxygen, carbon dioxide, steroids and other products are carried to and from the foetus, and it also allows free movement of the foetus within the uterus and protects the umbilical blood vessels from mechanical injury (Abaidoo et al., 2008).

Due to its peculiar role of being the link between the placenta and the foetus, any abnormality of this cord, be it in the length, the amount of Wharton's jelly, number of vessels or its amniontic epithelium may lead to abnormal foetal outcome (Leung and Robson, 1989). For example short cords are associated with less foetal activity, myopathic and neuropathic diseases, prolong second stage of labour, cord rupture, breech presentation, placenta abruption and Down's syndrome (Heifetz, 1996). In contrast very long cords which are due to hyperkinesis are associated with cord thromboses, entanglement, and torsion as well as knot formation (Yetter, 1998). Thus abnormalities in cord length associated with intrauterine factors could lead to abnormalities that are only detected later in life (Leung and Robson, 1989). Inadequate Wharton's jelly could lead to foetal death (Yetter, 1998; Heifetz, 1996), whiles in two vessel cords the foetal abnormality rate could be as high as 50% (Leung and Robson, 1989) and these defects could either be genitourinary or gastrointestinal.

1.3. ULTRASONOGRAPHY OF THE PLACENTA

Abnormalities of the placenta and the umbilical cord are the most culpable cause of most abnormal foetal outcome and even death with only a few being attributed to other causes such as behaviour and diseases affecting the mother (Hertzberg et al., 1992). Sadly however, since the placenta and the umbilical cord are delivered with the baby, obstetricians have very little appreciation of placental development in the uterus. The need to be able to diagnose some of these abnormalities made the evolution of ultrasonography very useful in obstetrics and has found application in placenta studies. Even more so is the advent of transperineal ultrasonography which makes ultrasonography of the placenta at any stage of pregnancy now possible (Kingdom et al., 2006; Hertzberg et al., 1992).

Ultrasonography of the placenta which usually forms part of the general pregnancy ultrasound to assess the wellbeing of the foetus has some significant correlation with the pathology of the foetus and the newborn (Hertzberg et al., 1992). Real time scanners are able to

produce a continuous scan of the foetus, the placenta and umbilical cord. The procedure uses high frequency sound waves generated by conversion of electrical energy to sound energy (waves) in the ultrasound machine which is then incident transabdominally by the use of the scan probe on the lower abdomen (Fox 1986). These have found very indispensable usefulness in the diagnosis of placenta praevia, abruptio placentae, gestational trophoblastic disease, and primary tumors like choriongioma associated with foetal hydrops, congestive heart failure, low birth weight, premature labour and placenta accreta which leads to haemorrhage due to rupture of uterus (Hertzberg et al., 1992). Placenta extrachorialis which includes circummarginate, and circumvallate leads to high incidence of premature labour, threatened abortions, perinatal mortality and haemorrhage (Hoffman-Tretin et al., 1992). All these conditions have variable manifestation on ultrasound which is useful in their diagnosis during ultrasound (Naumoff et al., 1981; Fox 1986; Guy et al., 1990, Hoffman-Tretin et al., 1992).

Abnormal cord insertion and vessel arrangement as well as succenturate lobes which must be diagnosed antenatally to prevent post partum and foetal blood loss can all be seen on ultrasound in various forms (Mollogy et al., 1983). The most consistent placenta abnormality in cases of Rhesus incompatibility, diabetes, anaemia and pre eclampsia, is variation in sizes seen both on ultrasound and gross anatomic examination.

1.4. THE PRESENT STUDY

It is estimated that more than 7.6 million perinatal deaths occur each year world wide; 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 placenta 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 fetal deaths resulting from placenta malformation in Ghana. The distribution of these indices in most developing countries is unknown. The occurrence of foetal compression risk based on cord location and placental malformations are also unknown (Salafia and Vintziloes, 1999**;** Valsamakis et al., 2006). Therefore the present study was designed to provide some information on the morphological variations of human placenta and umbilical cord via ultrasonographic and gross anatomical assessment and their correlation with foetal factors such as foetal weight and length.

1.5. AIM AND OBJECTIVES

1.5.1. AIM

To determine the well being of the baby in relation to the placenta and the umbilical cord.

1.5.2. OBJECTIVES

1. To determine the relationship between the weight, length and head circumference of the baby and the umbilical cord length, cord diameter and umbilical cord coiling index.
2. To determine the relationship between the weight of the baby and the weight, diameter and thickness of the placenta.
3. To explore the relationship between the length of the baby and the weight, diameter and thickness of the placenta.
4. To explore the relationship between head circumference of the baby and the weight, diameter and thickness of the placenta.
5. To explore the relationship between ultrasonographic measurements and the gross anatomic indices of the placenta.
6. To relate the foetal ultrasonographic indices with neonatal outcome, such us weight length and Apgar score.

7 To determine the relationship between the gestational age, maternal age and the weight, length and head circumference of the baby

CHAPTER 2

LITERATURE REVIEW

2.1. MORPHOLOGY OF THE HUMAN PLACENTA

The human Placenta is a discoid shaped organ which develops from the uterus and the developing embryo. The placenta is a highly vascularised organ which functions in the maintenance of pregnancy and promotes normal foetal development (Wang et al., 2004; Reagan and Salsberry, 2005; Sepulveda, 2006). 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 baby, 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). The placenta is usually regarded as a foetal organ (Van den Broek et al., 2005). 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 (Paria et al., 2000).

It has been reported that 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 (Rana et al., 1995; Quin, et al., 2002; Sepulveda et al., 2003). Placental weight is one of several standard placental measurements by which placental growth can be characterized (Quin, et al., 2002**;** 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 (Quin, et al., 2002 ; 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). The transfer aspect of the placenta is to receive nutrients, oxygen, antibodies and hormones from the mother's blood and passes out waste. It also forms a barrier, which filters out some substances which could harm the foetus (Wang et al., 2004; Roh et al., 2005; Valsamakis et al., 2006). Many substances cannot be filtered out (Valsamakis et al., 2006). These include alcohol and some chemicals associated with smoking cigarettes (Genbacex et al., 2000). Several types of viruses, such as Human Cytomegalovirus may also cross this barrier; this often leads to various degrees of birth defects in the infants (Lanari 2001).

In addition to the transfer of gases and nutrients, the placenta also has metabolic and endocrine activity: producing hormones such as progesterone which is important in maintaining the pregnancy; somatomammotropin which acts to increase the amount of glucose and lipids in the maternal blood; oestrogen, responsible for foetal weight; relaxin for relaxation of the cervix during parturition and human chorionic gonadotrophin (hCG) (Petraglia, 1996).

The umbilical-chorionic vessels bear the burden of rapid transfer of large volumes of foetal blood to and from the villous capillary bed. Secondly, the chorionic plate area measures the area of the uterine lining covered by the placenta and, in effect, how many maternal spiral arteries are potential suppliers of the placenta and potential veins (Rana et al., 1995; Wang et al., 2004; Valsamakis et al., 2006). Placental thickness, by contrast, marks the extent of arborisation of the villous capillary bed, the actual locus of maternal foetal exchange (Reagan and Salsberry, 2005; Sepulveda, 2006). Foetal stem arterioles are also principal sites of placental vascular resistance.

Thus, they contribute to total foetal peripheral resistance and foetal heart work (Gudmundsson et al., 2003).

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). Abnormal placenta shape generally reflects pathologic villous atrophy. This study was designed to evaluate the reliability of placental variables as indices for foetal development and also to test the relationship of placental weight with gestational age and birth weight. In addition, the standard method of weighing the placenta, without trimming the placental disk of membranes and umbilical cord, may also merit simplification (Machin et al., 2000; Valsamakis et al., 2006).

Early in the second trimester, the placenta approximates the foetus in size and continues to grow until term. As pregnancy advances, it become relatively smaller and by term the ratio of its weight to that of the foetus is about 1:6 to 1:7 (Reagan and Salsberry, 2005; Sepulveda, 2006). Term placenta is circular, semicircular or oval 15 to 20 cm in diameter, and 2 to 3 cm thick. The foetal surface of the term placenta is shiny and consists of large opaque blood vessels 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; with a lobule, 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 (Yetter, 1998). The functional unit of the placenta is the foetal cotyledon and the mature human placenta has about 120 cotyledons, which are sometimes grouped into visible lobes. 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, 1995).

At term, the normal placenta is blue-red in colour and discoid in shape and weighs 400-600g (15% normal neonatal weight), (Borton, 2006). The neonate weighs approximately seven times the placental weight. This ratio decreases earlier in gestation. The weight of the placenta can be altered by the umbilical cord, membranes, attached maternal clots or foetal blood within and pathologic conditions (Leibschang, 1983).

2.2. DEVELOPMENT OF THE HUMAN PLACENTA

After fertilization the zygote undergoes cleavage to form the morula. Continued division of cells of the morula gives rise to the blastocyst. 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). 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) (Tabibzadeh and Babaknia, 1995). 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 (Tabibzadeh and Babaknia, 1995; Machin et al., 2000;Valsamakis et al., 2006).

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) (Tabibzadeh and Babaknia, 1995). The trophoblast has a nutritive role and also functions as an endocrine organ (Tabibzadeh and Babaknia, 1995). Morphologically, the trophoblast consists of two cell types, cytotrophoblasts and syncytiotrophoblasts (Salafia and Vintziloes, 1999).

By the 8th day after fertilization the trophoblast has differentiated into an outer multi nucleated syncytiotrophoblast and an inner layer of mononuclear cytotrophoblast cells (Pijnenborg et al., 1980). 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 (Aplin, 1991). 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 (Aplin, 1991). 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 (Vicovac et al., 1995). 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 (Vicovac et al., 1995). (ii) Cytotrophoblast cells of anchoring villi either from syncytium or break through the syncytium at selected sites to form multilayered columns of non-polarized cytotrophoblast cells which are motile and highly invasive (Loke, 1990).

Villi may easily be distinguished in the human placenta on about the 12th 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 (Vicovac et al., 1995).

Maternal venous sinuses are invaded early; but until the 14th or 15th day after fertilization maternal arterial blood does not enter the intervillous space. By about the 17th day, both maternal and foetal blood vessels are functional and a placental circulation is established. The foetal circulation is completed when the blood vessels of the embryo are connected with chorionic blood vessels which are probably formed in situ from cytotrophoblast (Loke, 1990). 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. Although villi cover the entire surface of the chorion early in pregnancy, two separate regions begin to differentiate as pregnancy advances (Vicovac et al., 1995). The villi found in the foetal pole in contact with the deciduas basalis continue to grow, because the blood supply is most satisfactory in this area and forms the Chorion frondosum. The villi on the abembryonic side of implantation site in contact with the decidual capsularis forms the chorion laeve which will degenerate (Machin et al., 2000). 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).

Some villi of the chorion frondosum extend from the chorionic plate to the decidua and serve as anchoring villi. Most villi however end freely in the intervillous space without reaching the deciduas (Hanley et al., 2002). As the placenta matures, the short, thick early stem villi branch repeatedly, forming progressively finer subdivision and greater numbers of increasingly smaller villi. 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 (Hanley et al., 2002). 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 spindle-shaped 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 (Hanley et al., 2002).

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 (Hanley et al., 2002; 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, hCG, placental lactogen, and placental growth hormone are produced to maintain the pregnancy (Valsamakis et al., 2006).

Increased blood flow during pregnancy increases the flow of nutrients from the mother to foetus. In addition, the cross-sectional area of umbilical cord for counting umbilical vein and artery showed lower number in intra uterine growth retardation (IUGR) foetuses than normally grown foetuses (Valsamakis et al., 2006).

2.4. GROSS ABNORMALITIES OF THE PLACENTA AND ITS APPENDAGES

A number of classification schemes have been reported to relate placental morphology with its function (Kaplan, 1995). It has been reported that the shape of placentae vary from discoid, circular and discoid with accessory lobes structure which is the extension into the mother from the foetus (Kaplan, 1995). Discoid placentae have larger surface area for foetal absorption than the other shapes. Circular and bilobular shapes are considered to be due to disturbance of implantation or uterine abnormalities (Reagan and Salsberry, 2005; Sepulveda, 2006).

2.4.1. PLACENTOMEGALY

Unfixed placentae that weigh more than 600 g are pathologic, but more importantly may be the placenta/foetal ratio (Quin, et al., 2002**;** Wang et al., 2004; Roh et al., 2005). Chronic low uteroplacental blood flow is the most frequent cause of small placentae, but often the foetal weight is affected, so the ratio may be normal. The cause of enlargement may be unknown, but it is often revealed if the following are considered: overt or latent maternal diabetes, maternal anaemia, maternal–foetal blood group incompatibility, maternal–foetal transfusion, chronic intrauterine infection (syphilis), foetal malformations (especially of the lung), the twin transfusion syndrome, congenital neoplasms (e.g., neuroblastoma, teratoma, and chorangiomas) and alpha- thalassaemia (Quin, et al., 2002; Van den Broek et al., 2005).

2.4.2. MULTIPLE PLACENTAL DISCS

Accessory placental lobes may be found at various distances from the main disc. Depending on the continuity of the chorionic plate and the location of the umbilical cord insertion, these may be represented by: The succenturiate placenta; the lobe is completely separate from the main disc in which the umbilical cord is inserted, with communicating vessels running through the discs. (Wang et al., 2004; Roh et al., 2005). The accessory lobe may be retained in the uterus after delivery leading to postpartum haemorrhage. This is suspected if a

circular gap is detected in the membranes from which blood vessels pass towards the edge of the main placenta (Quin, et al., 2002**;** Wang et al., 2004; Roh et al., 2005). The bipartite placenta; similar to the succenturiate, but the chorionic plate is in continuity with the main disc (Van den Broek et al., 2005). If retained after birth, it can cause bleeding and septic complications (Borton, 2006). Placenta Fenestrata: A gap is seen in the placenta covered by membranes giving the appearance of a window (Quin, et al., 2002**;** Roh et al., 2005). The mechanism behind the development of these peculiarities of placental formation may be explained by the embryo's implantation site. If villous chorion comes into contact with more than one endometrial surface before or during implantation, more than one placenta may develop (Roh et al., 2005).

2.4.3. EXTRACHORIAL PLACENTAE

When the membranous chorion does not insert at the periphery of the villous chorion of the placental disc, there is either a circummarginate or circumvallate appearance (Van den Broek et al., 2005). Placenta Circumvallata; if the membranes arise from a cuplike fold that can be elevated at their insertion, they are called circumvallate (Gupta et al., 2006; Yetter, 1998). A whitish ring composed of decidua, is seen around the placenta from its foetal surface. This may result when the chorion frondosum is too small for the nutrition of the foetus, so the peripheral villi grow in such a way splitting the decidua basalis into a superficial layer (the whitish ring) and a deep layer. It can be a cause of abortion, antepartum haemorrhage, premature labour and intrauterine foetal death (Roh et al., 2005; Machin et al., 2000; Valsamakis et al., 2006). Placenta circummarginate: If the membranes arise without bulky folding or thickening, the insertion is called circummarginate (Van den Broek et al., 2005). Probably of no clinical significance, but may be associated with an increase in foetal malformations (Yetter, 1998).

2.4.4. PLACENTA MEMBRANACEA

A thin membranaceous placenta is formed and attaches to the entire interior uterine surface rather than to a localized area. Bleeding may occur in late pregnancy as the development of the lower uterine segment and effacement of the cervix cause the villi to separate from the deciduas in the vicinity of the cervix (Yetter, 1998; Sepulveda, 2006). A great part of the chorion develops into placental tissue. The placenta is large, thin and may measure 30-40 cm in diameter (Reagan and Salsberry, 2005; Sepulveda, 2006). Failure of the chorion laeve to atrophy means that placental cotyledons form an envelope around the greater part of the uterine wall. This is associated with ante and postpartum haemorrhage and retained placenta (Borton, 2006). During the third stage of labour, spontaneous separation of the membranous placenta may not be complete, manual removal may be difficult, and blood loss may be excessive. This placenta may result from very shallow implantation or persistence of the chorion laeve that invades the entire endometrium because of an endometrial hypoplasia or deficiency at the implantation site (Van den Broek et al., 2005).

2.4.5. INFARCTS AND PLACENTA ISCHAEMIA

Infarcts usually indicate uteroplacental vascular disease, such as a thrombosed or severely degenerate uteroplacental artery. A sub mucosal uterine fibroid or other focal lesion may be causative, and this is especially the case with common, marginally located infarcts (Reagan and Salsberry, 2005). Central infarcts are more significant. Recent lesions have a red colour, and remotely acquired infarcts are grey-white. If the uteroplacental blood flow is otherwise relatively normal, a foetus may suffer few ill effects with as much as 30% placental infarction. Shrinkage of the villi and knotting of syncytiotrophoblast are characteristic histological features of severe acute ischeamia. Replacement of villous tissue by fibrinoid material and X-cells are histological signs of chronic ischeamia or degeneration (Reagan and Salsberry, 2005; Sepulveda, 2006)

2.4.6. AMNION NODOSUM

Elevated amniotic nodules less than 5 mm in diameter are characteristic of amnion nodosum. Amnion nodosum is pathognomonic of oligohydramnios. Of the many syndromes in which pathogenic mechanisms lead to this finding, Potter's syndrome is a very important example because it occurs commonly (1 in 4000 births) and involves widely disparate abnormalities (Gupta et al., 2006) . Newborns with Potter's syndrome often have low- set ears and abnormal facies and may be difficult to ventilate because of severe lung hypoplasia. Here, a non-functioning kidney syndrome, such as renal agenesis or multicystic renal dysplasia, leads to the lack of nutrient amniotic fluid (Gupta et al., 2006). There is no relationship between the numerical extent of amnion nodosum and symptomatic disease in the associated newborn. The alternative cause of amnion nodosum is oligohydramnios resulting from prolonged leakage of amniotic fluid (Sepulveda, 2006).

2.4.7. AMNIOTIC BANDS

Considerable clinical problems develop when the integrity of the membranes is compromised in pregnancy other than at term. Early disruption of this protective medium may lead to foetal anomalies commonly known as amniotic band syndrome (amnion disruption complex) (Sepulveda, 2006). Once the amnion is disrupted, the combination of mesoblastic proliferation and oligohydramnios leads to strands of different size that entangle and entrap the developing foetus or foetal structures. As a consequence, deformation, malformation, and disruption occur in the foetus. After rupture, the amniotic sac ceases to grow in synchrony with the chorion. The offending mesoblastic bands are often inconspicuous and are not found extending to the placenta (Reagan and Salsberry, 2005; Sepulveda, 2006).

2.5. ORIGIN AND DEVELOPMENT OF THE UMBILICAL CORD

The umbilical cord begins to form between four and six weeks of gestation, as the embryonic disc takes a cylindrical shape (Collins et al., 2002). At first, the embryo is a flattened disc interposed between the amnion at the dorsal surface and the yolk sac at the ventral surface. By the end of the third week of development the embryo is attached to the placenta via a connecting stalk (Sepulveda, 2006). Because the dorsal surface grows faster than the ventral surface, in association with the elongation of the neural tube, the embryo bulges into the amniotic sac and the dorsal part of the yolk sac is incorporated into the body of the embryo to form the gut (Sepulveda, 2006).

As the embryo enlarges, the unenclosed area of the ventral surface of the embryo becomes relatively smaller and even undergoes some constriction (Sepulveda, 2006). This unenclosed region, at the junction of embryonic and extra-embryonic territories, is the primitive umbilicus (Collins et al., 2002). By the end of the 5th week the primitive umbilical ring contains 1) a connecting stalk within which passes the allantois (primitive excretory duct), two umbilical arteries and one vein; 2) the vitelline duct (yolk sac stalk); and 3) a canal which connects the intra- and extra embryonic coelomic cavities (Van den Broek et al., 2005). By the 10th week the gastrointestinal tract has developed and protrudes through the umbilical ring to form a physiologically normal herniation into the umbilical cord (Van den Broek et al., 2005). Normally these loops of bowel retract by the end of the third month. By about the middle of the third month, the expanding amnion obliterates the exocoelom, fuses with the chorion laeve, and covers the bulging placental discs and the lateral surface of the body stalk, which is then called the umbilical cord, or funis (Van den Broek et al., 2005). Thus, the umbilical cord comes into existence through the expanding amnion applying itself about the body stalk and yolk stalk as it crowds them together (Collins et al., 2002).

2.6. UMBILICAL CORD LENGTH AND DIAMETER

The length of the umbilical cord varies from no cord (achordia) to 300 cm, with diameters up to 3 cm (Valsamakis et al., 2006). At term, the typical umbilical cord is 55 to 60 cm in length, with a diameter of 2.0 to 2.5 cm (Yetter, 1998). About 5% of cords are shorter than 35 cm, and another 5% are longer than 80 cm (Berg and Rayburn, 1995). Though it is not fully understood what controls cord length, various authors correlate cord length with foetal activity and movement. It is suggested that sufficient space in the amniotic cavity for movement and the tensile force applied to the umbilical cord during foetal movements are two main factors that determine cord length (Benirschke, 2004).

An umbilical cord less than 40 cm is said to be short. Short umbilical cords are uncommon. They occur in approximately 6% of pregnancies (Van den Broek et al., 2005). This shortness can be real or apparent (due to cord loops or entanglement). The pathogenesis of short umbilical cords remains unclear. 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). The presence of a short umbilical cord has been associated with antepartum abnormalities and risk factors for complications of labour and delivery (Krakowiak et al., 2004). Krakowiak et al. (2004) in a recent study found out that infants with short umbilical cords were more likely to be female, have a congenital malformation, and be small for their gestational age. In this study, a short cord was associated with increased risk for maternal labour and delivery complications, including retained placenta and operative vaginal delivery.

Long umbilical cords, defined as total length over 70 cm (Baergen et al., 2001), are associated with a number of circumstances which can impact foetal life. Long cords have both maternal and foetal associations. Maternal factors include, systemic disease, delivery complications and increased maternal age. Foetal factors include cord entanglement, foetal

anomalies, vertex presentation, increased birth weight, respiratory distress and male sex (Muppala et al., 2007). Infants with excessively long umbilical cords are found to be at a significantly increased risk of brain imaging abnormalities and/or abnormal neurological follow-up (Muppala et al., 2007). In investigating the clinical significance of umbilical cord length in human pregnancies, Wu et al. (1996) found out that cord length was significantly related to birth weight. They however, found out that the umbilical cord length does not significantly correlate with maternal age, gestational age, parity, foetal outcome or intrauterine foetal well-being.

2.7 NUMBER OF UMBILICAL CORD BLOOD VESSELS

The umbilical cord normally contains of one umbilical vein and two umbilical arteries. Single umbilical artery (SUA), the most common anatomical abnormality of the umbilical cord, is found in 0.2-1.1% of singleton pregnancies (Itskovitz et al., 1987) and in 6-11% of multiple pregnancies. In this condition the umbilical cord is made up of two blood vessels, one vein and one artery, instead of the normal one vein and two arteries (van Dijk et al., 2002). It is believed to be caused by atrophy of previously normal artery or agenesis of one of the umbilical arteries (Valsamakis et al., 2006). The selection process of the missing (or existing) vessel is likely to be random, even though a right single artery is slightly more common (Blazer et al., 1997). Single umbilical arteries are associated more commonly with foetal anomalies than normal cords. Of infants with single umbilical artery 20% or more are reported to have associated foetal anomalies (Thummala et al., 1998) including cardiovascular abnormalities, gastrointestinal tract defect, esophageal atresia, a variety of renal defects and multiple anomaly syndromes (Martinez-Frias et al., 2006). A 5-20% perinatal mortality rate has been reported in association with single umbilical artery and includes foetuses with severe congenital anomalies and chromosomal defects (Valsamakis et al., 2006).

2.8. UMBILICAL CORD COILING AND COILING INDEX

The three blood vessels of the umbilical cord pass along the length of the cord in a coiled fashion. Several theories have been proposed to explain the umbilical cord twist including those that interpret the twist as inherent to the cord itself, and those that explain the twist as a result of active or passive rotation of the foetus. Regardless of its origin, umbilical coiling appears to confer turgor to the umbilical unit, producing a cord that is strong but flexible (Gupta et al., 2006). Umbilical cord coiling index (UCI) has been reported to be approximately 1 coil/5 cm of umbilical cord length or 0.20 (SD 0.07) (Machin et al., 2000). However, recent studies have shown it to be lower than this. De Laat et al. (2005) showed it to be 0.17 (SD 0.009) while Gupta et al. (2006) in his study found it to be 0.31 (SD 0.08) complete spirals per centimeter. The total number of coils for any particular cord is believed to be established early in the gestation (van Dijk et al., 2002). The pattern of coiling develops during the second and third trimesters, presumably due to snarls in the cord, and this coiling change as pregnancy advances. The presence of a mixed coiling pattern and even reversal of the coiling direction in third trimester have been shown (Quin et al., 2002). Despite the belief that umbilical vascular coiling occurs early in gestation, it is not yet known whether this coiling is a genetic or acquired event (Gupta et al., 2006). A sonographic evaluation of umbilical cord coiling in the second trimester, by Predanic et al. (2005), was found to correlate well with the true UCI at birth, although the sensitivity in predicting coiling patterns as hypocoiled and hyper coiled cords was less accurate. The helical disposition of the umbilical cord affords it an elastic property which enables it to resist external forces such as torsion, compression and tension that might compromise the umbilical vascular flow. The coiled umbilical cord acts like a semi erectile organ that is more resistant to snarling torsion, stretching and compression than non-coiled one (Strong et al 1993).

Hyper coiled cords often have more thrombi in placental surface veins because the flow is more sluggish, and when coiling becomes excessive, the foetus can strangle circulation in the

cord vessels (Benirschke, 2005). Metaanalysis by De Laat et al. (2005) pointed out the fact that hypo coiling is associated with increased incidence of foetal demise, intrapartum foetal heart rate deceleration, operative delivery, foetal distress and chorio-amnionitis. Rana et al. (1995) also noted that premature delivery and low birth weight were associated with hyper coiled cords. Kashanian et al. (2006) also showed that neonatal weight in normocoiled and hypocoiled cords were higher than that of hyper coiled cords.

2.9. UMBILICAL CORD INSERTION

The location of umbilical cord attachment to the foetus and placenta is also important. The umbilical cord insertion into the placenta is described as central, eccentric, marginal, or velamentous as it relates to the chorionic plate (Ben-Arie et al., 1995; Salafia and Vintziloes, 1999; Valsamakis et al., 2006). Central and eccentric both insert into the disc of the placenta; marginal is usually defined as insertion within 2 cm of the disc edge, whereas velamentous inserts directly into the placental membranes before entering the placental tissue (Baergen et al., 2001). Typically, the umbilical cord inserts at the center or near the center, also known as central or eccentric insertion respectively. About 90 % of cord insertions are central or eccentric and about 7 percent of umbilical insertions occur at the placental margin (Yetter, 1998). Marginal insertions, according to Yetter (1998), are generally benign. Marginal cord insertions are more common than velamentous cord insertion. It occurs in approximately 5 % of pregnancy (Benirschke, 2005). Marginal cord insertion has also been associated with foetal growth impairment (Davies et al., 1984) and preterm delivery (Machin et al., 2000; Valsamakis et al., 2006).

Though the factors that determine the site of insertion of the umbilical cord on the placenta are not entirely known, some researchers associate it to errors in implantation of the blastocyst into endometrium (Baergen et al., 2001). According to Collins et al. (2002), these abnormal cord insertions occur as a result of the ‘migration’ and ‘dissolution’ of the placenta from its original

site, a process called trophotropism, which sometimes occurs during its development. In this case, there appears to be a relocation of the placenta, which dissolves, leaving the amnion remaining, which can then be the insertion site of the umbilical cord. This results in the umbilical cord and placental end being connected at the edge of the placenta (marginal insertion) and a membranous insertion (velamentous insertion) (Baergen et al., 2001).

A velamentous insertion is reported to occur in approximately 1–2% of singleton Pregnancies (Machin et al., 2000; Valsamakis et al., 2006). However, the prevalence of this finding is higher in multiple gestations ranging from 13% to 21% for twins (Machin, 1997). It is more frequently identified in monochorionic twin gestations and has been associated with the twin-to-twin transfusion syndrome. Velamentous insertion has been diagnosed by ultrasonography with a sensitivity of 67% and specificity of 100% in the second trimester (Hasegawa et al., 2006); first trimester diagnosis is also possible (Sepulveda, 2006). Potential complications associated with velamentous insertion include miscarriage, prematurity, low birth weight, foetal malformation, perinatal death, low Apgar scores, and retained placenta (Sepulveda et al., 2003). However, the most relevant is vasa previa, a condition in which the velamentous vessels run in the lower uterine segment unprotected by the Wharton jelly (Sepulveda et al., 2003). These vessels are prone to compression and bleeding preferentially at the time of delivery and may cause unexpected foetal death due to hypoxia or exsanguinations (Oyelese et al., 2004).

2.10. APGAR SCORE AS AN INDICATOR OF FOETAL OUTCOME

Apgar score is a means of accessing the outcome of a baby immediately after birth and 5 minutes after birth and in instances of foetal instability a 10 minutes is desirable. Apgar which many think is the acronym for the parameters of the test; appearance, pulse, grimace, activity and respiration, is the name of the person who invented the score in 1952 (Beck, 2009). The score has recently had its usefulness questioned, by the American academy of pediatrics' committee on foetus and newborn, and the American college of obstetricians and Gynecologist's committee on

obstetric practice, it is still believed to be the most useful simple technique for prediction of neonatal outcome as it was fifty years ago, (Papile et al., 2001) an observation collaborated by Whelan (2006). The score is charted as shown below (table 1).

Table 1. Apgar score chart (Whelan, 2006).

SCORE	0	1	2
Apgar	Pale	blue	Pink
Pulse	Absent	<100	>100
Grimace	Limp	Some tone	Active, cry
Respiration	Absent	Irregular breathing	Regular and crying

A total scored of 0-10 is given according to a baby's observation at 1 minute, and 5 minutes a baby who is born pink, having a pulse >100, active and crying on or without touch and breathing normally would have a score of 10. Thus the Apgar score is used in the delivery room to establish the likelihood of neonatal mortality (Whelan, 2006), cerebral palsy (Moster et al., 2001), neurological outcome (Nelson et al., 1981) and the need for resuscitation (Haddad et al., 2000).

2.11. FACTORS CONTRIBUTING TO DIFFERENCES IN FOETAL WEIGHT

Foetal weight can be influenced by many factors, both endogenous and extrinsic factors. These factors include gestational age at delivery, maternal factors (race, stature, genetics), paternal factors (paternal height), environmental influences (altitude, availability of adequate nutrition), physiological factors (altered glucose metabolism, haemoglobin concentration, macro vascular integrity), pathological factors (hypertension, uterine malformation), and complications of pregnancy (gestational diabetes mellitus, preeclampsia) (Wang et al., 2004).

2.11.1. GESTATIONAL AGE AT DELIVERY

This is the most significant determinant of new born weight. Preterm delivery is the leading cause of low birth weight new born in the United States (Martin et al 2008). Other potential causes of low birth weight can be attributed to Intrauterine Growth Retardation (IUGR) (Shi-wen et al., 2006). Causes of IUGR include infections, congenital syndrome, genetic abnormalities, and chronic uteroplacental insufficient, (Shi-wen et al., 2006). In post date gestations, the rate of foetal macrosomia is 17-29% as compared with 2-15% for the general population delivering term pregnancies. The rate of foetal macrosomia increases steadily with advancing gestational age beyond 37 weeks of pregnancy (Shi-wen et al., 2006).

2.11.2. MATERNAL RACE

A systematic difference is observed in the mean birth weight of babies born to mothers of different races and ethnicities. Depending on the mother's race, mean birth weights differ by as much as 141-395 g at term (Nahum et al., 1993). Although some of this difference may be attributed to systematic differences in the mean gestational age of foetuses at delivery, to systematic racial differences in maternal characteristics (e.g., maternal height and weight), and to differences in the prevalence of various diseases and complications of pregnancy that occur in different populations, an additional disparity in birth weight is attributable to racial differences (Wang et al., 2004). The precise cause of this effect is unknown, but it may be related to genetic or metabolic differences in foetal-growth potential for women of different races. Because of this effect, proper characterization of the race of mothers is important for accurate prediction of birth weights. For example, African American and Asian women have foetuses that are smaller than those of Caucasian women when appropriately matched for gestational age (Sornes and Bakke, 1989). After gestational age and maternal race, major parental, environmental, and pregnancy-specific determinants of birth weight are relevant for mothers with otherwise uncomplicated pregnancies. These include the following: maternal height, maternal obesity, maternal pregnancy

weight gain, parity, foetal sex, ambient altitude, maternal haemoglobin concentration, paternal height, cigarette smoking, and glucose tolerance (Wang et al., 2004).

2.11.3. MATERNAL HEIGHT

Maternal height is an easily measurable physical characteristic that is positively correlated with term foetal weight (Nahum et al 2004). Although lifestyle choices can potentially modify other maternal physical features (e.g., maternal weight and BMI), maternal height is arguably the single best measure of native human-size potential. Barring special circumstances (e.g., malnutrition in childhood, scoliosis and intrinsic bone disease) adult height is a trait that has genetic underpinnings that are generationally transmissible. Family pedigree studies have shown that, on average, "big people have big babies and small people have small ones." One would be intuitively challenged to argue with this line of reasoning, and data from numerous studies have independently confirmed the direct relationship of maternal height to the birth weight of offspring (Zhou, 1990).

2.11.4. MATERNAL OBESITY

The level of maternal obesity independently influences foetal weight such that the more a mother weighs, the larger her foetus is likely to be. This occurs because maternal weight and foetal weight are directly related, and women with high BMIs are at increased risk for developing diabetes during pregnancy (Valsamakis et al., 2006).

2.11.5. MATERNAL PREGNANCY WEIGHT GAIN

Maternal pregnancy weight gain is important with regard to foetal growth, such that the greater the weight gain is, the larger the foetus is likely to be (Sornes and Bakke, 1989). Weight gain during pregnancy is generally proportional to the caloric intake of a mother and, the greater the number of calories consumed, the more is available for incorporation into the developing tissues of the foetus (Ward, 2008). In addition, increased pregnancy weight gain is associated

with an increased risk of developing gestational diabetes (Sornes and Bakke, 1989; Valsamakis et al., 2006).

2.11.6. PARITY

Parity is directly and independently associated with foetal size. The greater the maternal parity, the larger the foetus is likely to be. Maternal parity is closely linked to maternal age, but once maternal parity is specified, maternal age is not an independent predictor of foetal weight. At term, a foetus typically gains 0.2-0.5 g/day for each increase of 1 in maternal parity (Sornes, 2000).

2.11.7. PATERNAL HEIGHT

Paternal height independently accounts for 2% of the variance in birth weight (10 g/cm of foetal weight at term). Offspring of fathers with heights 2 SDs above or below the mean have a term birth weight that is increased or decreased by 125 g, respectively (Wang et al., 2004). Normal variability in paternal height explains an independent portion of the variance in term birth weight of up to 250g that other maternal, environmental, or pregnancy-specific factors do not account for. Paternal weight and BMI, which are acquired traits and which depend on lifestyle choices and behaviours, do not independently influence foetal weight. Paternal age also has no effect on birth weight up to at least the age of 60 years (Salafia, 1990).

2.11.8. DIABETES MELLITUS

Uncontrolled maternal diabetes mellitus is commonly associated with excessive foetal weight (Berk et al., 1989). Glucose is the primary substrate foetuses require for growth (Wang et al., 2004). When maternal glucose levels are excessive, abnormally high rates of foetal growth can be expected. Compared with the baseline rate of foetal macrosomia of 2-15% in the general population (depending on the group studied), the rate among mothers with poorly controlled gestational diabetes is elevated (20-33%) (Valsamakis et al., 2006).

2.12. PLACENTA AND ITS EFFECT ON THE WELL BEING OF THE BABY

A lot of work has been done to find out the effect the placenta has on the well being of the baby. Some studies conducted in this area revealed so many relationships between the placenta and the baby that come out of the placenta. According to the work done by Luz et al. (2001) on 300 live newborns with gestational age of 37 weeks or older, the mean of birth weight was 3,369 g with a standard deviation (SD) of 445 g. Placenta weight had a mean of 537 g (SD: 96 g). The relation between the weight of the placenta and the birth weight was significant, and it was found that for each gram increase in placenta weight, birth weight is increased by 1.98 g (SE = 0.25, $p < 0.01$) and this relation is not linear, since the quadratic term is significant. Placenta weight has a nonlinear relation to the birth weight and is an important predictor of birth weight. (Luz et al, 2001).

In a similar study by Lurie et al. (1999) mean maternal age was 28.6 years (range 17-50). Mean gestation age at delivery was 39.7 weeks (range 33-42). Mean newborn weight was 3,382.1g ± 486.7 g (range 2,180-4,810). Mean placental weight was 613.0 ± 123.8 g (range 319-1,266). Mean foetal-placental weight ratio was 5.6 ± 0.96 (range 2.9-10.6) (Lurie et al., 1999). In another study conducted by Lo et al. (2002) in China on 522 singleton babies, it was revealed that the mean value of birth weight was 3235 +/- 17 g, body length was 48.8 +/- 0.1 cm, placenta weight was 646.2 +/- 0.3 g, birth weight/body length was 66.2 +/- 0.3, and birth weight/placenta weight was 5.1 +/- 0.1. Placenta weight was positively correlated with Birth weight ($r=0.413$, $p<0.01$), Birth length ($r=0.305$, $p<0.01$), Birth weight/body length ($r=0.397$, $p<0.01$). These results indicate that placental weight has a significant role in foetal growth in terms of weight, body length, and cord length (Lo et al., 2002).

2.13. ULTRASOUNOGRAPHIC MEASUREMENTS OF THE PLACENTA

The evolution ultrasound brought to obstetric and gynecology also found great application in the studies of the placenta (Spirit et al., 1984). Ultrasound waves are high frequency sound

waves with frequency higher than audible sound waves i.e. >20Hz, these sound waves are generated as a result of conversion of electrical energy to mechanical (sound) waves in the ultrasound machine (Kremkau, 1983). Image formation is as a result of reflections of these sound waves from the surfaces of the different tissues in the body into the scan head which then sends the reflections into the processing unit for the image formation, the reflections are due to differences in the mechanical properties of the various tissues (Spirit et al., 1984). Sound travels at 1540m/s n tissues at 37^{o}C, hence the time taken for a reflection to be received for processing into image is proportional to the depth of the image. Medical ultrasound waves have a frequency of 2.5-15MHz (Woo, 2006). The strength of each reflected wave is represented by a dot, the position of the dot represent the depth from which the echo was received and the dots are combine to produce the image (Kremkau, 1983). Strong reflection give white dots e.g. diaphragm, gallstones and bones, weak reflections give grey dots e.g. most solid organs and thick fluids, no reflections are received from fluids within cyst, urine and blood and this gives black dots (Spirit et al., 1984).

2.13.1. ULTRASONOGRAPHIC GESTATIONAL AGE DETERMINATION

For a normal pregnancy of a 28 day menstrual cycle the pregnancy lasts for about 280 days, with early clinical assessment and a precise last menstrual period (LMP) it is possible to predict the onset of labor and have it fall within three weeks in 90% of cases (Seeds et al 1986) however irregular menstrual cycle and alteration of date due to medication have over the years made this technique (use of LMP) unreliable even though still very useful in those that can have their LMP accurately determined. This is what has led to the determination of gestational age by sonographic method necessary, and it has seen a gradual standardization of the methods used and a steady improvement in technical precision (Borvicelli et al, 1981, Hadlock et al, 1983, Kopta et al 1983). Accurate estimation of gestational age by sonographic method has now become very critical in planning management of high risk pregnancies e.g. IUGR and has also led to a

reduction in their incidence (Usher et al 1988, Mital et al 2002). Several methods are used with each having higher accuracy within a certain period of gestation with an acceptable error of two weeks (Hadlock et al 1982) the method use is also affected by the socio-economic ethnic and altitude of the population used to establish the technique (Seeds et al 1986). These include the Biparietal diameter, Crown-Rump, and the Femur and humerus length.

2.13.2. ULTRASONOGRAPHIC LOCATION OF THE PLACENTA IN THE UTERUS

Location of the placenta within the uterus during pregnancy is of critical importance especially in the diagnosis of placenta previa (Cho et al., 2008) and most recently in sex determination (Ismail et al., 2007). Placenta previa, which is a condition in which the placenta completely or partially covers the internal ostium of the cervix, occurs in about 1% of all deliveries (Iyasu et al., 1993). The position is always given in relation to the position of the internal ostium of the cervix which is just below the bladder angle (Seeds et al., 1986). The position of the placenta can change during pregnancy especially if the position was determine transabdominally before the 20th week of gestation (Hertzberg et al., 1992), for example Hertzberg et al. (1992) noted in a study that for 154 pregnant women thought to have low lying placentation, only 4.2% were confirmed during the third trimester of pregnancy, this is also collaborated by Cho et al. (2008) who indicated placenta migration especially for the low lying and previa placentation. This supposed placenta migration is improbable but the likelihood is that the rapidly expanding uterus causes the position of the internal ostium to alter leading to the apparent change in the position of the placenta (Artis et al., 1985), thus locating the placenta in the uterus is more accurate during the third trimester of pregnancy (Hertzberg et al., 1992) but this is difficult to achieve with transabdominal ultrasound especially if the placenta is low lying (Hertzberg et al., 1992)

2.13.3. ULTRASONOGRAPHIC MEASUREMENT OF PLACENTAL THICKNESS

Measurements of placenta size have a very useful tool in pregnancy management especially in cases of pre eclampsia and diabetes (Spirit et al., 1984). Gestational age can also be estimated using measurement of placenta thickness (Mital et al., 2002). Habib (2002) showed that a sonographic placenta thickness of 2cm at 36 week gestation is a predictor of IUGR. Mital et al. (2002) showed a mean placenta thickness at term of 3.75cm and 1.5cm at week eleven, thus during the cause of pregnancy the placenta thickness depending on the time of ultrasound ranges from 1.5-3.75 cm

2.14. OTHER PATHOLOGIC PLACENTAL CORRELATIONS ON ULTRASOUND

Ultrasonographic morphology of the placenta has both pathologic and normal correlation (Spirit et al., 1984). Though most of the sonographic manifestation has pathologic correlation, some however has no pathologic correlation e.g. sub chorionic fibrin deposition (Spirit et al., 1984), perivillous fibrin deposition (Fox, 1986). Ultrasonography of the placenta however has some significant correlation to the pathology of the newborn and the foetus; gestational trophoblastic disease is seen on ultrasound as solid material filling the uterus containing multiple anechoic vesicles of varying size (Naumoff et al., 1981). Primary tumors like choriongioma associated with foetal hydrops, congestive heart failure, low birth weight, premature labour, appears as well circumscribed solid intra placental mass lesions within which vessels may be seen on ultrasound (Spirit et al., 1984). Placenta accreta which leads to haemorrhage necessitates hysterectomy due to uterus rupture (Fox, 1986) appears as placenta without the usual retro-placenta hypo echoic zone of decidual /myometrium, these placentae are also characterized by an increase number of large intervillous space in which fluid may be seen (Guy et al., 1990; Hoffman-Tretin et al., 1992). Placenta extrachorialis which includes circummarginate, and circumvallate which appear as folds of the placenta leads to high incidence of premature labour, threatened abortions, perinatal mortality and haemorrhage. Abnormal cord insertion and vessel

arrangement, succenturate lobes which must be diagnosed antenatally to prevent post partum and foetal blood loss can all be seen on ultrasound in various forms (Kohler, 1987).

CHAPTER 3

MATERIALS AND METHODS

3.1. ULTRASONOGRAPHIC MEASUREMENTS

Sixty-six pregnant women attending the Komfo Anokye Teaching Hospital (KATH) and the Magazine Clinic (a private hospital at Danyame, a suburb of Kumasi, Ashanti Region) were recruited to the study with informed patient consent from October 2004 to June 2008. This included 20 from KATH and 46 from Magazine Clinic. During the initial visit a comprehensive medical and gynecological history was taken and a thorough physical examination was performed by the specialist Obstetrician/Gynaecologist. Their age ranged from 21 to 38 years.

The last menstrual period (LMP) was used to determine the gestational age and the period within which to have the ultrasound examination. A transabdominal scanner (**ALOKA ECHO CAMERA SSD - 620**) was used to determine foetal wellbeing, gestational age and the expected date of delivery and to measure the growth and thickness of the placenta, prior to macroscopic examination and measurements of the foetus and placenta. The ultrasound examination was performed through a full urinary bladder. A full urinary bladder produces three effects: firstly, it pushed the uterus out of the pelvis, thus removing it from the acoustic shadow caused by the symphysis pubis; secondly it provided an acoustic window through which the pelvic organs were visualized; and thirdly, it displaced the bowel (intestines) superiorly thus preventing gas in the intestines from scattering the ultrasound beam. During scanning, the pregnant woman was made to lie in the supine position with the protruding abdomen facing upwards; the probe was placed on the skin and a layer of a gel was applied to the skin above the pubic area as an acoustic couplant facilitating the transmission of the sound from the transducer to the patient and to aid in the smooth movement of the probe. Three (3) serial ultrasound scanning of the uteri of these women were carried out at defined periods of the first, second and third trimesters of gestation. All the women gave their informed consent to be serially studied.

Ultrasonography was performed by a specialist and his residents, who did not have prior asses to the gynecological history of the patient.

3.2. SPECIMEN COLLECTION AND PREPARATION

Sixty six placentae with their attached umbilical cords from the pregnant women who were followed sonographically were collected from the Magazine clinic and the Komfo Anokye teaching hospital. In the second part of the study, 265 placentae with umbilical cords attached were collected from the Kwame Nkrumah University of Science and Technology (KNUST) Hospital and Victory Maternity home. This included 171 umbilical cords attached to placenta from the KNUST hospital and 94 from Victory maternity home. In all cases, after separating the baby from the umbilical cord, the specimens were tagged with numbers that corresponded with the numbers indicated in the data of the perinatal outcomes and placed in a container of 10% formalin. Samples were picked up and washed clean of blood and stored again in a solution of 0.5% formaldehyde in saline for further detailed examination and measurements.

3.3. UMBILICAL CORD MEASUREMENTS

Umbilical cords were examined and measurements made whiles still attached to the placenta. Gross examination of the umbilical cords was done to determine the following: mode of cord insertion into the placental disc (as centric, eccentric or marginal), blood vessel insertion (furcate or non-furcate) and number of coils of the cord. Marginal insertion was defined as attachment within 2 cm of the placental disc. Number of vessels was determined by making a cross-sectional incision at the tip of the foetal end of the cord and counting the vessels from the surface. In counting the number of coils, a coil was defined as a complete 360^{o} spiral course of the umbilical vessels around the Wharton's jelly.

Metric measurements (in centimeters) on the cord included cord length and diameter. A cord was measured in its entirety including the length of the placental end of the cord and the umbilical stump on the baby, which was usually about 2.5 cm. On the basis of cord length, cords

were grouped into three; length less than 40 cm, between 40 and 70 cm and greater than 70 cm as short, normal and longer than normal respectively. Cord diameter was measured using a pair of dividers. All measurements were done in centimeters (cm) using a standard tape measure.

Cord coiling index (UCI) was determined from the cord length and the number of coils, as the number of complete vascular coils divided by the cord length. The percentile values for UCI were calculated. Hypocoiled cords were defined as those with UCI less than the 10^{th} percentile and hyper coiled as those with UCI more than the 90^{th} percentile and normocoiled cords as those with UCI from 10^{th} to 90^{th} percentiles.

3.4. DETERMINATION OF PLACENTAL WEIGHT AND SHAPE

The weight of each placenta was determined by an electronic balance (Camry 206; 0.0-120 kg) and recorded against its specific number. The shape of each placenta was observed and described as either discoid, discoid with accessory lobe or circular in shape.

3.5. DETERMINATION OF PLACENTAL THICKNESS

The indirect method was used for measuring the central thickness of the placentae because of the destructive nature of the direct method. A tooth pick was used to pierce the placentae from the chorionic plate to the basal plate and each thickness was measured against a plastic ruler in centimetres and recorded.

3.6. PERINATAL OUTCOME

Perinatal indices studied were gestational age, birth weight, baby length, head circumference and Ponderal index (PI). Gestational ages, birth weight and baby length were obtained from the centers. Ponderal index was calculated using the formula: birth weight (in grams)/ (length in cm) ^{3} × 100. Using gestational ages, newborns were grouped into two; those with gestational ages less than 37 weeks (preterm delivery) and those with gestational ages greater than or equal to 37 weeks (term). Also in terms of birth weight newborns were categorized into two as those with birth weight less than 2.5 kg (low birth weight) and those with

birth weight greater than or equal to 2.5 kg (normal birth weight). With the PI, newborns were grouped as those with PI less than 2.5 and those with PI greater than or equal to 2.5. The two categories of each of the perinatal outcomes were compared with one another in terms of cord length, UCI and cord diameter.

3.7. STATISTICAL ANALYSIS

Statistical analysis were done using Microsoft Excel (2003 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 $P < 0.05$.

CHAPTER 4

RESULTS

4.1. PILOT STUDY TO DETERMINE INTRAUTERINE ULTRASONOGRAPHIC MEASUREMENTS OF THE PLACENTA

In a total of 66 cases, ultrasonography was performed during the first, second and third trimesters. At each ultrasound appointment, the ultrasonographic gestational age, position of the placentae within the uterus and the thickness of the placenta were measured. In the first trimester 38.46% could have their placentae positions identified whiles 23.1% could have their placental thicknesses measured. In the remaining 37.44%, neither the placental position nor placental thickness could be measured. The observed placental attachment sites within the uterus were 46, 4, and 16 for upper, lower and fundal positions respectively. Thus during ultrasonography, the most observed placental position was that of the upper 69.7% (46), followed by the Fundal 24.2% (16) and the lower segment placentation of both the posterior and anterior part of the uterus having the lowest frequencies 6.1% as shown in figure 1.

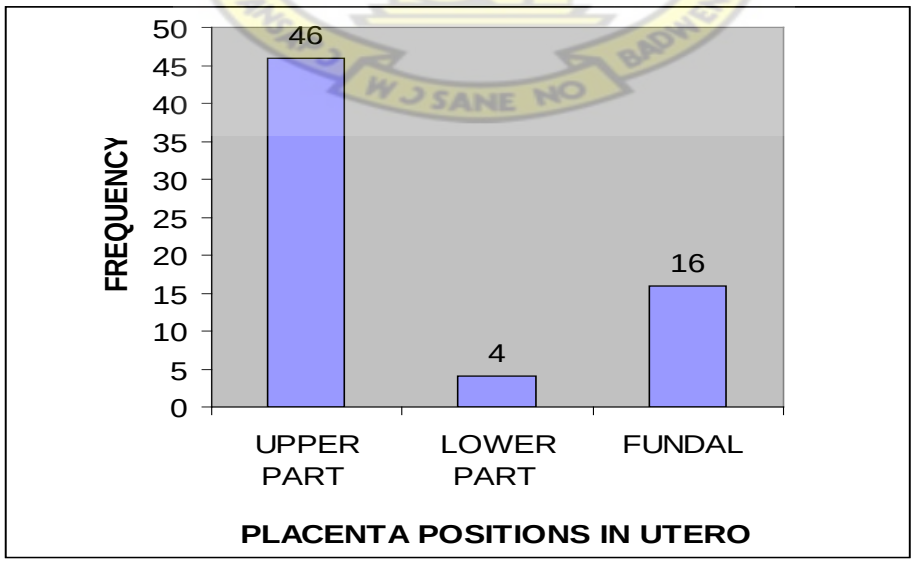

Figure1. The frequency distribution of placental positions in the uterus

Relating positions to birth outcome, there were 6.1% (4) cases of lower uterine segment placentation and of these 2 (50%) resulted in neonatal death compared to the other positions which had only 1.6% neonatal deaths.

4.1.1. ULTRASONOGRAPHIC MEASUREMENT OF PLACENTAL THICKNESS

The mean ultrasonographic placental thickness was 3.86cm ± 0.90. The ultrasound placental thickness showed no significant positive correlation with the Apgar score, baby length, length of the umbilical cord except the foetal birth weight (Table 2).

Table 2. Correlations between ultrasound placental thickness and Apgar score, baby length, cord length and foetal birth weight

ULTRASOUND PLACENTA THICKNESS	APGAR SCORE	BABY LENGTH	CORD LENGTH (cm)	BIRTH WEIGHT(kg)
	r=0.11	r=0.15	r= -0.14	r=0.32
PROBABILITY(P<0.05)	0.38	0.24	0.27	0.009

4.1.2. ULTRASONOGRAPHIC GESTATIONAL AGE DETERMINATION

The gestational age of thirty eight women who knew their exact last menstrual period (LMP) were randomly selected and compared with the calculated chronological date and the trimester within which the scan was taken according to the ultrasound report. These results are shown in the tables 3 and 4.

Table 3. Differences between chronological and sonographical gestational ages at the different trimesters of pregnancy

Trimester of ultrasound	Differences between chronological and sonographical gestational ages			
	< 1 week	1-2 weeks	>2weeks	Total number
FIRST	2	4	7	13
SECOND	2	7	4	13
THIRD	3	6	3	12

Table 4. Differences between chronological and sonographic gestational age and the range of weeks of pregnancy

Range of weeks of ultrasound	Differences between chronological and ultrasound gestational age			
	<1 week	1-2 weeks	>2 weeks	Total number
0-14 week	3	5	7	15
14-20 weeks	0	5	2	7
20-30 weeks	4	7	3	13
30-40 weeks	0	2	0	2

4.1.3. PLACENTAL INDICES

The mean placental thickness on gross measurements was 2.98± 0.65 (SD) with a range of 1.0 cm to 4.5 cm. The mean placental diameter was 16.25±1.81 (SD) with a range of 12.0 cm to 20.0 cm. The gross placental thickness measured showed a strong significant correlation (r=0.29 p=0.016) with the birth weight of the babies but no correlation with the ultrasonographic placental thickness, Apgar score, umbilical cord length placental diameter and length of the baby (P>0.05).

4.1.4. UMBILICAL CORD MEASUREMENTS

The mean umbilical cord length as measured gross anatomically was 36.73 cm ± 12.28 with a range 9.5 cm-70.0 cm. All the umbilical cords had three blood vessels. There was a

significant correlation (r=0.28, p=0.002) between the length of the umbilical cord and the length of the baby and the five minutes Apgar score (r =0.312, p= 0.011). The insertions of the umbilical cord were 89.39% 10.61%, for combined central-eccentric and marginal respectively in the first part of the study (table 5). All the cords had three umbilical blood vessels.

Table 5. Distribution of cord insertions

Umbilical cord insertions	**Number of placentae**
Central or eccentric	59 (89.39%)
Marginal	7 (10.61%)
Total	66

4.1.5. PERINATAL OUTCOME (PILOT STUDY)

As part of the pilot study the measured baby weight ranged from 1.1-4.9 kg with a mean birth weight of 3.026 kg ± 0.64. The mode was 3.2kg. Out of the 66 babies 24.24% had birth weight <2.5 kg and 1.52% had their birth weight >4.5kg. Apgar ranged from 3-9 with a mean of 6.38 ±1.65, whiles baby length ranges from 12-55 cm with a mean of 36.67±12.46, as shown in table 6. The birth weight distribution chart is as shown below in figure 2.

Table 6. Perinatal outcome (pilot study)

PARAMETERS	BABY WEIGHT(kg)	APGAR SCORE	BABY LENGTH(cm)
MINIMUM	1.1	3	12
MAXIMUM	4.9	9	55
MEAN	3.03	6.38	36.67
SD	0.64	1.65	12.46

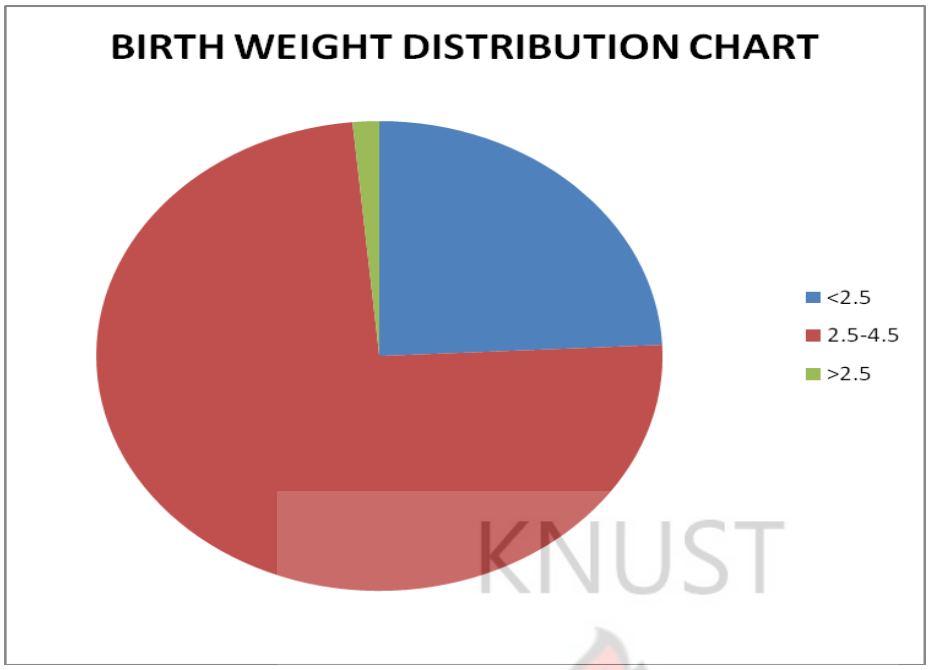

Figure 2. Distribution of birth weight (pilot study)

About 71.2% (47 out of the 66) delivered babies were within the normal birth range with 27.3% and 1.5% falling below and above the normal range respectively. The incidence of neonatal death in the 66 term births in relation to Apgar score were also analyzed and the results are indicated in table 7.

Figure 7. Occurrence of neonatal death in the 66 deliveries in relation to their five minutes Apgar score

5 minutes Apgar score	Number of births	Neonatal deaths	Rate per 100 births
0-3	5	2	40
4-6	26	2	7.7
7-10	35	0	0
total	66	4	6.1

The Birth weight ranges were then compared to the mean Apgar score for babies falling within each weight category (table 8).

Table 8. Birth weights in relation to 5 minutes mean Apgar score.

Birth weight (kg)	Mean 5 mins Apgar score	Expected score
0-2.6	5.83±1.95	10
2.7-4.5	6.57±1.39	10
>4.5	9	10

4.1.6. BABY LENGTH

The mean baby length was 36.67 cm ±12.46 cm with the standard baby length range at birth being 46.9 cm-54.6 cm (Valsamakis et al., 2006).), 78.79% were below normal, 18.18% normal and 3.03 above normal. Table 9 shows the distribution of baby length in the 66 term births.

Table 9. Baby length distribution

Baby length(cm)	Number of delivered babies
Below normal (<47.0)	52
Normal (47.0-55.0)	12
Above normal (>55)	2
TOTAL	66

4.1.7. Correlation between Birth Weight and Other Foetal and Placental Variables

When birth weight was compared with other foetal as well as other placental parameters using the Pearson's correlation there was a significant correlation between birth weight and 5 minutes Apgar score, baby length, gross placental thickness and ultrasound placental thickness as shown in table 10.

Table 10. Correlation between Birth Weight and Other Foetal and Placental Variables

BIRTH WEIGHT (kg)	5 MINUTES APGAR SCORE	BABY LENGTH(CM)	ULTRSOUND PLACENTAL THICKNESS (CM)	GROSS PLACENTAL THICKNESS (CM)
	r=0.37	r=0.37	r=0.32	r=0.29
PROBABILITY P<0.05	0.002	S0.002	0.000	0.016

4.1.8. Correlation between Baby Length and Other Foetal and Placental Variables

Whilst there was no correlation between baby length and the gross placental thickness as well as ultrasound thickness and placental diameter, there was a positive correlation between the length of the baby, the Apgar score and the weight of the baby as shown in table 11.

Table 11. Correlation between Baby Length and Other Foetal and Placental Variables

BABY LENGTH AT BIRTH (cm)	CORD LENGTH (cm)	5-MINUTES APGAR SCOER	UTRASOUND THICKNESS(KG)	GROSS THICKNESS (cm)	BIRTH WEIGHT (kg)	PLACENTAL DIAMETER (cm)
	r=0.28	r=0.34	r=0.14	r=0.08	r=0.37	r=0.18,
PROBABILITY (P<0.05)	0.021	0.007	0.24	0.51	0.002	p=0.14

4.2. UMBILICAL CORD LENGTH AND DIAMETER

The results obtained in the first part of the study suggested that ultrasonographic measurements were useful in the first trimester of pregnancy and the early part of the second trimester. Therefore in the second part of the study, no intrauterine ultrasonographic measurements were done. Postpartum umbilical cord, placentae and foetal measurements were

taken**.** A total of 265 placentae with their attached umbilical cords were collected from the Kwame Nkrumah University of Science and Technology Hospital and Victory Maternity Home, Ayigya from October, 2004 to January, 2008. Cord length ranged from 19.5 to 88.5 cm with a mean of 44.8 cm (SD12.9). Out of the 265 cords examined, 105 (39.62%) were short (cord length <40cm), 153 (57.74%) were of normal length (40-70cm) and 7 (2.64%) were longer than normal (>70cm) (Fig 3). Cord diameter ranged from 0.4 to 2.3cm with a mean of 1.2 cm (SD 0.3). About 82 % of the cords had diameters in the range of 1.0-1.45 cm (Fig. 4**).**

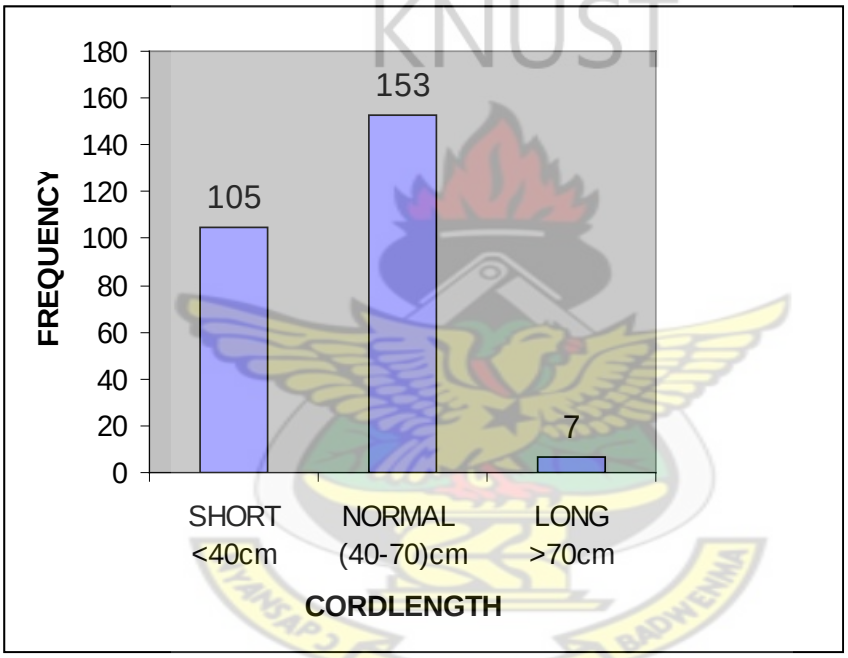

Figure 3. Frequency distribution of cord length

Cord diameter ranged from 0.4 to 2.3cm with a mean of 1.2 cm (SD 0.3). About 82% (217) of the cords had diameters in the range of 1.0-1.45 cm (Fig. 4**).**

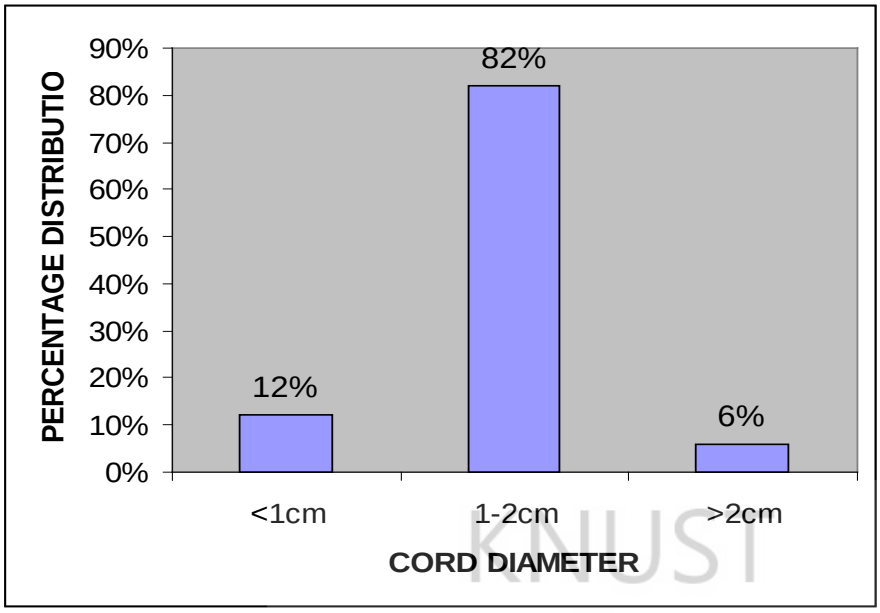

Figure 4. The percentage distribution of umbilical cord diameter

4.3. UMBILICAL CORD INSERTION, BLOOD VESSEL ATTACHMENT AND NUMBER OF BLOOD VESSELS

Of the 265 cords examined, 18.11% were of marginal insertion (Fig 5), 60.75% central (Fig 6) and 21.14% were eccentrically inserted (Fig 7). This gave a combined central and eccentric insertion of 81.94%. (Fig 8) Umbilical cord vessel attachments were found to be 28% and 72% for furcate and non-furcate vessels respectively (Fig 9). No velamentous umbilical cords were seen in this part of the study. The occurrence of 2-, 3- and 4-vessel cords were 1.13%, 95.85% and 2.64% respectively, indicating that a large majority of the cords had 3 umbilical cord vessels. Out of the 265 umbilical cords studied, one (0.38%) had a single umbilical artery.

Figure 5: **photograph of a marginal umbilical cord insertion**

Figure 6: a photograph of a central umbilical cord insertion

Figure 7: a photograph of an eccentric umbilical cord insertion

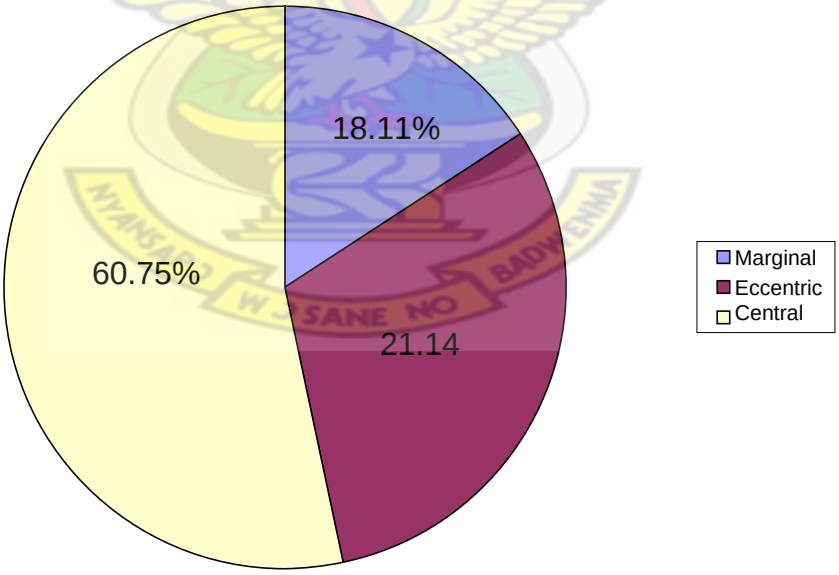

Figure 8. Distribution of types of cord insertion

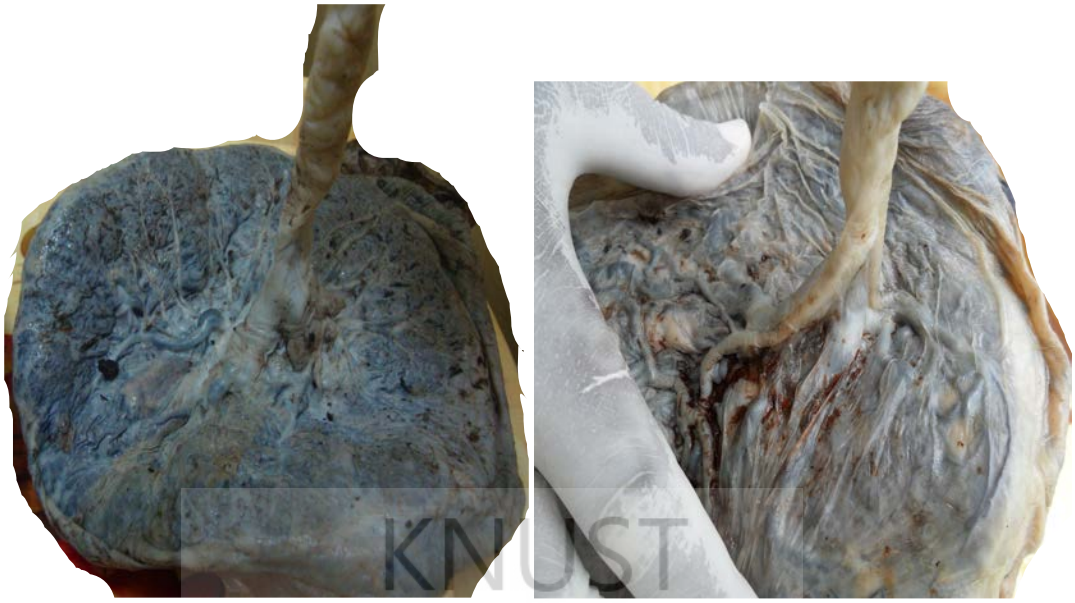

Fig 9. A photograph of two umbilical cords showing furcated attachment (right) and non furcated attachment (left).

4.4. UMBILICAL CORD COILING AND COILING INDEX

Cord coiling ranged from 1 to 14 coils with a mean of 5.65 coils (SD 2.54). The mean umbilical cord coiling index (UCI) was 0.19coils/cm (SD 0.01). When cords were grouped in terms of the coiling indexes as hypo coiling (UCI < 10^{th} percentile, i.e. 0.08), normocoiling (UCI from 10^{th} to 90^{th} percentile, 0.08-0.19) and hypercoiling (UCI >90^{th} percentile, i.e. 0.19), 5.3% were hypocoiled, 88.9% were normocoiled and 5.8% were hyper coiled (Fig. 10).

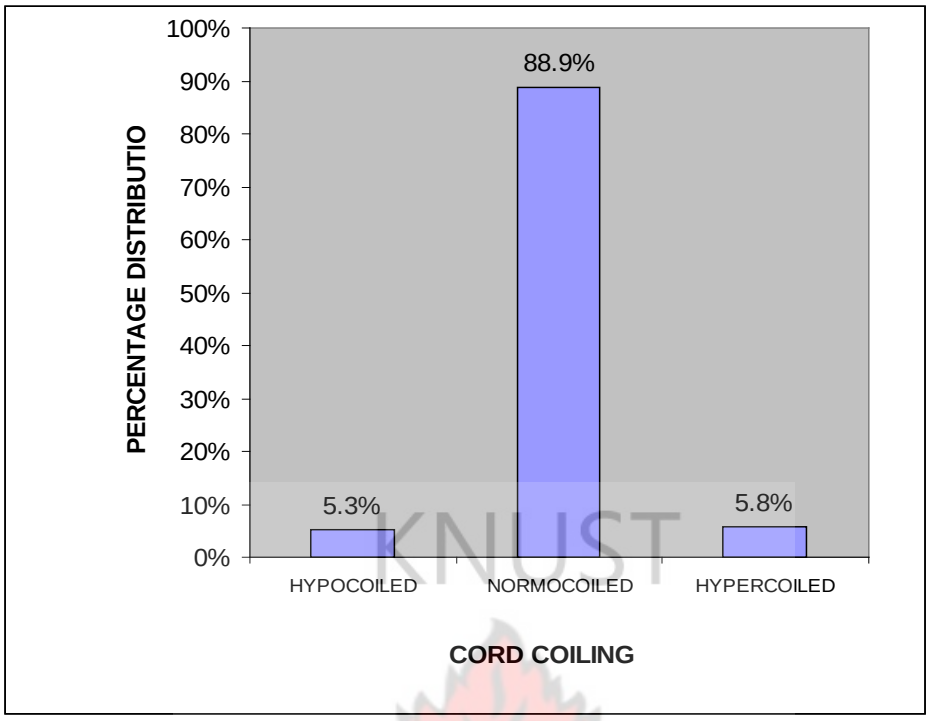

Figure 10. The Percentage distribution of cord coiling

4.5. FOETAL INDICES

Baby weight ranged from 2 to 5.2 kg with a mean of 3.07 kg (SD 0.51). Out the 265 babies, 22 (8.3%) had birth weight less than 2.5kg. Of these, 16 (72.73%) were preterm (GA < 37 weeks) and 6 (27.27%) were full term (GA greater than or equal to 38 weeks). Baby length also ranged from 40 cm to 55cm with a mean of 49 cm (SD 2.7). Head circumference ranged from 28 cm to 42 cm and a mean of 34.44 cm (SD 2.06). Gestational ages ranged from 32 to 42 weeks and a mean of 37 weeks (SD 2). Out of the 265 cords, 120 had gestational ages less than 37 weeks, representing a preterm delivery incidence of 45.28%. The maternal age ranged from 15- 48 years with a mean of 27.61 years (SD= 5.85) as shown in table 12.

Table12. Foetal and maternal indices

	WEIGHT OF BABY(kg)	LENGTH OF BABY(cm)	HEAD CIRCUMFERENC (cm)	GESTATIONAL AGE(weeks)	MATERNAL AGE/yrs
MINIMUM	2.00	40.00	28.00	32	15
MAX.	5.20	55.00	42.00	42	48
MEAN	3.07	48.79	34.43	37.34	27.61
STD DEV.	0.51	2.70	2.07	1.92	5.85
STD ERROR	0.04	0.21	0.16	0.15	0.4

4.6. CORRELATION BETWEEN UMBILICAL CORD VARIABLES AND PERINATAL OUTCOME

When cord parameters and perinatal outcomes were analyzed with Pearson's correlation to find out the association between them, There was a significant positive correlation between cord length and birth weight ($r= 0.21$, $p < 0.01$) and head circumference ($r= 0.23$, $p < 0.01$). Also, cord diameter had a positive correlation with birth weight ($r= 0.19$, $p <0.05$) and head circumference ($r= 0.12$, $p <0.05$). Only coiling index correlated significantly but negatively with pondered index ($r= -0.17$, $p <0.05$). None of the cord parameters correlated significantly with the gestational ages (Table 13).

Out of the 48 cords with marginal insertion, 5 had birth weight less than 2.5kg representing a low birth weight incidence among marginally inserted cords to be 10.42%. In finding out the association between marginal insertion and preterm delivery, it was observed that 18 (37.5%) out of the 48 marginally inserted cords had gestational ages less than 37 weeks.

The 110 infants with Ponderal index < 2.5 had a higher UCI of 0.14 coils/cm (SD 0.05) when compared to 0.12 coils/cm (SD 0.05) in 155 of the newborns with PI greater than or

equal to 2.5 (t 2.5, p<0.05). However, in terms of UCI, there was no significant difference between newborns of GA < 37weeks and ≥ 37 weeks; and those with birth weight < 2.5 kg and ≥ 2.5kg (Table 14). Also, in terms of cord length no significant differences were observed among these categories of birth weight, PI and GA (Table 15).

Table 13. Correlation of cord variables with perinatal outcomes

	BW		G A		P I		H C		B L	
Cord Parameters	r	p	r	p	r	p	r	p	r	p
Length	0.21	<0.01	0.08	NS	0.165	NS	0.23	<0.01	0.09	NS
Diameter	0.19	<0.05	0.09	NS	0.148	NS	0.12	<0.05	0.03	NS
UCI	-0.078	NS	-0.09	NS	-0.172	<0.05	0.16	NS	0.09	NS

NS=Not significant H C=Head circumference B L=Baby length
GA=Gestational age
BW=Baby weight
PI= Pondera index

Table 14. Comparison of the Categories of Perinatal Outcomes In Terms Of UCI

Perinatal outcome	**Number**	**MeanUCI (SD)**	**t**	**p**
Gestational ages:				
<37 weeks	122	0.13 (0.05)	1.1	NS
≥ 37 weeks	143	0.12 (0.04)		
Ponderal index:				
<2.5	110	0.14 (0.05)	2.5	< 0.05
≥2.5	155	0.12 (0.04)		
Birth weight:				
<2.5 kg	18	0.14 (0.01)	1.2	NS
≥2.5 kg	247	0.12 (0.01)		

NS- Not-significant **UCI= umbilical cord coiling index SD= Standard deviation**

Table 15. Comparison of the Categories of Perinatal Outcomes In Terms Of Mean Cord Length

Perinatal outcome	Number	Mean C L(SD)	t	P value
Gestational age:				
<37wks	122	45.7 (11.8)	0.78	NS
≥37wks	143	44.1 (13.7)		
Ponderal index:				
<2.5	110	43.5 (12.7)	0.26	NS
≥2.5	155	45.8 (13)		
Birth weight :				
<2.5kg	18	44.6 (11)	0.059	NS
≥ 2.5 kg	247	44.8 (13)		

4.7. PLACENTAL INDICES

The range of placenta weight obtained was 315g- 933g with a mean of 563.47g (SD= 132.31). The diameter of the respective placentae was in the range of 14cm to 25cm with a mean placenta diameter of 18.69cm (SD= 2.05). The mean placental thickness was 2.65cm (SD= 0.55) with a range of 1.3cm to 6.0cm.

4.8. CORRELATION BETWEEN BABY WEIGHT AND PLACENTAL INDICES

There was a significant positive correlation between the weight of the baby and the diameter of the placenta ($r = 0.34$, $p < 0.01$), the thickness of the placenta ($r = 0.16$, $p < 0.05$), the weight of the placenta ($r = 0.52$, $p < 0.01$) and the age of the mother ($r = 0.26$, $p < 0.01$, (table 16).

Table 16. Correlations between Baby Weight, Placental Indices and Maternal Age.

	WEIGHT OF PLACENTA	DIAMETER OF PLACENTA	THICKNESS OF PLACENTA	AGE OF MOTHER
WEIGHT OF BABY	R=0.52, p=0.000	R=0.34, p=0.000	R=0.16, p=0.017	R=0.26, p=0.000

R is the coefficient of correlation, p is the p value.

4.9. CORRELATION BETWEEN FOETAL HEAD CIRCUMFERENCE AND PLACENTAL INDICES

In the present study there was a significant positive correlation between the head circumference of the baby and the weight of the placenta ($r = 0.38$, $p < 0.01$), diameter of the placenta ($r = 0.25$, $p < 0.01$) and the age of mother ($r = 0.13$, $p < 0.05$).

4.10. CORRELATION BETWEEN BABY LENGTH AND PLACENTAL INDICES AND MATERNAL AGE

There was a significant positive correlation between the length of the baby and the weight of the placenta, diameter of the placenta and the thickness of the placenta; $r = 0.24$, $p < 0.01$; $r = 0.23$, $p < 0.01$ and $r = 0.16$, $p < 0.05$ respectively. However there was no correlation between the length of the baby and maternal age ($r = 0.03$, $p > 0.05$).

4.11. CORRELATION BETWEEN GESTATIONAL AGE AND FOETAL INDICES AND PLACENTAL INDICES

There was a strong positive correlation between the gestational age and the weight of the baby ($r = 0.47$, $p < 0.01$), the length of the baby ($r = 0.32$, $p < 0.01$), and the weight of placenta ($r = 0.19$, $p < 0.01$). However, there was no correlation between the gestational age and the thickness of the placenta ($r = 0.09$, $p > 0.05$), the diameter of the placenta ($r = 0.10$, $p > 0.05$) and maternal age ($r = 0.074$, $p > 0.05$).

4.12. REGRESSION BETWEEN FOETAL LENGTH AND PLACENTAL INDICES

For every unit increase in the Length of the baby, the weight of the placenta, the diameter of the placenta, the thickness of the placenta and the increased by 0.01mm, 2.85mm, and 7.85mm, respectively (see table 17).

Table 17. Regressions between baby length and placental indices.

	WEIGHT OF PLACENTA/kg	DIAMETER OF PLACENTA/cm	THICKNESS OF PLACENTA/cm
LENGTH OF BABY/cm	0.001	0.285	0.785

4.13. REGRESSION BETWEEN FOETAL HEAD CIRCUMFERENCE AND PLACENTAL INDICES

For every unit increase in the weight of the placenta, the diameter of the placenta, the thickness of the placenta and the head circumference of the baby increased by 0.07 mm, 0.04 mm and 5.09 mm respectively.

4.14. REGRESSION BETWEEN FOETAL WEIGHT AND PLACENTAL INDICES

Also, for every unit increase in the weight of the placenta, the diameter of the placenta, and the thickness of the placenta, the weight of the baby increased by 0.02 mm, 0.18 mm and 17 g respectively.

CHAPTER 5

DISCUSION

5.1. ULTRASONOGRAPHIC GESTATIONAL AGE ESTIMATION

In the pilot study, there was a 75% sonographic gestational age determination falling within the maximum two weeks difference from chronological age in the third trimester. This was found to be higher than the percentages in the second (69.2%) and first (46.2%) trimesters, suggesting that gestational age determination using the biparietal diameter measurement tend to be more accurate in the third than in the first and second trimesters (Table 3). However most of the third trimester ultrasonographs (11) were taken before the 31st week of gestation (Table 4). This observation agrees with Hadlock et al. (1982) who suggested that the best period for biparietal ultrasound gestational age estimation was between 12-28 weeks. Thus sonographic gestational age determination by the biparietal diameter method could be erroneous if estimated in the first trimester of pregnancy and this agrees with Kurtz et al (1980) who suggested 14-42 weeks as the best period with accuracy reducing as the pregnancy progresses. It could therefore be suggested that the best period to estimate gestational age using the biparietal diameter is likely to be between 14-28 weeks of gestation.

5.2. ULTRASONOGRAPHIC LOCATION OF THE PLACENTA IN THE UTERUS

Locating the position of the placenta is of utmost importance especially for the diagnosis of placenta previa. Even though it has a very low incidence (1%) (Iyasu et al 1993), it is a life threatening condition. In the present study there was a 6.1 % incidence of low lying placentation, but none of this low lying placentation turned out to be previa at delivery. This observation supported by the study of Hertzberg (1992), indicates a zero percentage incidence of placenta previa.

5.3. ULTRASONOGRAPHIC PLACENTAL THICKNESS

The mean placental thickness measured ultrasonographically was 3.68 ±0.9; this is close to the 3.75 obtained by Mital et al (2002). Also comparing the mean ultrasound placental thickness to that of the measured gross of 2.98± 0.65, there was no significant correlation between the sonographic placental thickness and the gross thickness measured showing that the sonographic measurement could only be used as a guide because the correlation even though not significant was positive. The ultrasound placental thickness however showed a positive correlation with birth weight indicating that during ultrasonography the likely outcome in terms of weight of a baby could be estimated.

5.4. UMBILICAL CORD LENGTH

In the second part of the present study the minimum cord length was about 19.5 cm and the maximum was 88.5 cm with a mean of 44.8 cm ± 12.0 This is lower than most of the reported averages in the literature but similar to the 44.3 cm (SD 9.2) and 47.04cm ± 12.8 obtained by Gupta et al. (2006) and Abaidoo et al. (2008) respectively. A large majority of the cords were between 41.5 cm and 55.00 cm in length. A mean cord length of 40.00cm as reported in the literature was used as a marker to differentiate between short cords and long cords (Gupta et al., 2006). Cords less than 40.0 cm were classified as short, whilst those greater than 40.0 cm were categorized as long. The prevalence of short cords in the present study was 39.80%. Although reference standards for cord length have been reported, variation exists in the definition of short cords. The umbilical cord at term has been reported to have an average length of 55 to 60 cm and normal length in the range of 40-70 cm (Yetter, 1998) and cords of length up to 300cm have also been reported (Valsamakis et al., 2006). A study in Nigeria by Mutihir and Pam (2006) also indicated an average cord length of 52.9 cm (SD 7.3). Naeye (1985) adopted a cord length of 40 cm and Yetter (1998) adopted a cord length less than 40 cm. Considering the reported prevalence of Naeye (1985) who used comparable reference

standard as the present study, it can be said that the 39.80 % prevalence in the present study is very high.

This study also indicated that 57.86 % (153) of the umbilical cords fell within the range of 40-70 cm (Figure 3) whereas 2.34% were long (>70 cm). This supports the assertion that normal cord length must be in the range of 40-70 cm (Yetter, 1998). Although it is not fully understood what controls cord length, various authors correlate cord length with foetal activity and movement. It is suggested that sufficient space in the amniotic cavity for movement and the tensile force applied to the umbilical cord during foetal movements are two main factors that determine cord length (Yetter, 1998; Benirschke (2004). According to Benirschke (2004), cords of foetuses that have severely diminished motions are remarkably short and twins have slightly shorter cords probably due to a reduced space for movement.

In studying umbilical cord length as a correlate of perinatal outcomes, this study showed that cord length correlates significantly with birth weight ($r = 0.21$, $p < 0.01$) and head circumference ($r = 0.23$, $p < 0.01$) (Table 13). Cord length did not, however, correlate significantly with gestational age, Ponderal index and birth length. This is in agreement with the finding by Wu et al. (1996) who also found that only birth weight correlates significantly with cord length with no association between cord length and gestational period, birth length and Ponderal index.

5.5. UMBILICAL CORD DIAMETER

The mean cord diameter was 1.2 cm (SD 0.3) with a range of 0.4 to 2.3 cm. This is similar to the finding of Collins et al. (2002), who reported that, on the average a normal cord has a circumference of 3.7 cm (diameter of 1.2 cm) and a range of 3 to 5 cm (diameter of 0.95 to 1.59 cm). According to Collins et al. (2002), cord diameter range of 1 to 3 cm can suggest oedema, tumor or hernia and that, cords with circumference greater than 6 cm (D= 1.9cm)

should prompt an examination of the umbilical cords and foetuses. The present study showed that about 82% of the cords had a diameter in the range of 1.0 to 1.45 cm (Figure 4). Yetter (1998), however, reported a diameter range of 2 to 2.5 cm. Cord diameter also correlated positively with birth weight and head circumference but not baby length and gestational age (Table 13).

5.6. UMBILICAL CORD INSERTION AND BLOOD VESSEL ATTACHMENT

The rates of cord insertion in the order of marginal, central and eccentric in the present study were 18.06%, 60.87% and 21.07% respectively (Figure 8). This gave a combined central/eccentric insertion of 81.94 %. An abnormal placental cord insertion site has been associated with a number of complications of pregnancy that may result from compression or rupture of poorly supported umbilical vessels (Benirschke, 2005). Intrapartum hemorrhage, foetal bradycardia, stillbirth, intrauterine growth restriction (retardation), twin-to-twin transfusion syndrome, and preterm labour have all been linked to velamentous and, to a lesser extent, marginal cord insertions (Di Salvo et al., 1998). Prevalence rates of marginal cord insertions are 7-9% in singletons and 24-33% in twins, whereas for velamentous insertions the corresponding rates are 2% and 10-16% respectively (Benirschke, 2005). Benirschke (2005) observed a prevalence rate of marginal insertion to be 5% among singleton pregnancies. Although all subjects in this study were singleton, the prevalence rate of marginal insertion of 18.06% is high compared with previous studies.

The association between marginal insertion and preterm delivery was observed in this study. About 43.7 % of the marginally inserted cords in this study had gestational ages less than 37 weeks as against a preterm delivery rate of about 9.3 % among Ghanaians observed at the Korle Bu Teaching Hospital (Nkyekyer et al., 2006), and the 15% among blacks reported by Anath et al. (2001). Thus there was a significant increase in the preterm delivery rate

among the marginally inserted cords in this study. Benirschke (2005) also observed such an association. This is not in agreement with previous studies such as that of Liu et al. (2002) who observed that only 7.3% (7 out of 96) of newborns with marginal insertion were found with preterm delivery against a preterm delivery rate of 9-11 % and therefore concluded that no significant increase in preterm delivery rates exists in association with marginal cord insertion.

There was no association between marginal insertion and low birth weight in the present study. The low birth weight incidence of 11% observed among the marginal cord infants in the present study was lower than the low birth weight incidence of 15 % in sub-Saharan Africa and the same as the 11% reported in Ghana (Nkyekyer et al., 2006). This does not indicate a significant increase in the low birth weight incidence among marginally inserted cord infants. This agrees with the study by Van den Broek et al. (2005) who found no association between the mode of insertion of the umbilical cord to the placenta and birth weight.

The incidence of umbilical vessel attachments was found to be 28% and 72% for furcate and non-furcate respectively. The occurrence of non-furcate vessels was significantly higher than furcate ones probably suggesting that non-furcate vessels are normal vessel attachments whereas furcate vessels could result in injury and haemorrhage due to lack of adequate protection for these vessels. Pierce et al. (2001) reported that the mode of umbilical cord insertion has no significant effect on the examined components, and such differences are probably the effect of biological variations during normal placental and foetal development. However, more recently it has been reported that the occurrence of foetal compression risk based on cord insertion and location is still unknown (Sornes, 2000).

No velamentous cords were seen in the present study, but it has been reported in a study conducted by Wright and Ridgway (1990) that velamentous cord insertions occur in about 1.1% of singleton pregnancies and 8.7% of twins. This type of cord vessel attachment is associated with an increased risk of foetal hemorrhage, from the unprotected vessels as well as vascular compression, thrombosis and foetal malformations (Wright and Ridgway, 1990).

The occurrence of 2, 3 and 4 vessels were 1.13%, 95.85% and 2.64% respectively indicating that a large majority of the cords had 3 umbilical cord vessels. Three umbilical cord vessels appear to be normal and adequate for proper foetal development and survival. It is well documented that in humans, the "normal umbilical cord" has an arterial pair that is mildly helical around a straight vein (Cohen et al., 1992; Martinez et al., 1995; Pierce et al., 2001). Therefore differences in umbilical cord vessel morphology may be a risk factor for the foetus and may predispose the foetus to umbilical cord accidents.

Out of the 265 umbilical cords studied, one (0.38%) had a single umbilical artery (SUA). Cords with a single umbilical artery, two-vessel cords and four-vessel cords have been reported (Martinez et al., 1995). SUA has been associated with stillbirths, with an incidence of 3% - 20%. Malformations due to inadequate blood supply and brain damage among foetuses with SUA have been reported to be as high as 46% (Martinez et al., 1995; Schimmel & Eidelman, 1998). In a report by Sornes (2000) it was found that about 27% of live births with structural anomalies were associated with SUA while in specimens obtained from early abortions, foetal deaths and autopsies, SUA was seen in 66.3%. Four-vessel-cords have also been associated with foetal abnormalities (Martinez et al., 1995; Schimmel & Eidelman, 1998). Cases of five or more cords are the numerous variations associated with conjoined twining (Martinez et al., 1995).

5.7. UMBILICAL CORD COILING INDEX (UCI)

The mean UCI observed in this study was 0.19 (SD 0.01) coils/cm. This means that on the average every 1 cm of a cord studied had 0.26 complete vascular coils around the Wharton's jelly. Compared to 0.2 (SD 0.1) reported by Ercal et al. (1996), 0.21 (SD 0.07) by Strong et al. (1994), and 0.13 coils /cm (SD 0.8) by Gupta et al. (2006). A recent meta-analysis showed the normal coiling index to be 0.17 (SD 0.009) complete spirals per centimeter (De Laat et al., 2005). Rana et al. (1995), also showed it to be 0.19 (SD 0.1), which is similar to what was observed in the present study. The coiling density is not similar in all segments of the umbilical cord, with increased coiling at the foetal end compared with the placental and middle segments (Blickstein, 2001). This could have an effect on the observed UCI in the present study. This is because the umbilical cord stump left on the fetus was not available for determination of any additional number of coils.

It has been demonstrated that clamped umbilical cords tend to have huge visible vessels relative to the connective tissue, Wharton's jelly and amnion making the coils easier to count. In contrast, vessels in collapsed umbilical cords are almost unrecognizable making the vascular coiling unclear (Blickstein, 2001; Gupta et al., 2006).

In the present study, 88.9% of the cords were of normal coiling (UCI 0.08-0.19) with 5.3% and 5.8% hypo-coiled (UCI <0.08) and hyper-coiled (UCI >0.19) respectively. This shows that a large majority of the cords in this study were of normal coiling. Abnormal coiling (hypo-coiling and hyper-coiling) is known to have chronic (growth retardation) and acute (foetal intolerance to labour and foetal demise) effects on foetal well-being (Gupta et al., 2006). The vessels of the umbilical cord are like a hollow cylinder and are prone to torsion, compression, tension, and subsequent interruption of the blood flow. This risk is minimized by their helical disposition. It is possible that the coiled umbilical cord has elastic properties that

enable it to resist external forces that might compromise the umbilical vascular flow. It may be that, the coiled umbilical cord acts like a semi-erectile organ that is more resistant to snarling torsion, stretch, and compression than the non-coiled one. Hyper-coiled cords often have more thrombi in placental surface veins because the flow is more sluggish, and when coiling becomes excessive, the foetus can strangle circulation in the cord vessels (Benirschke, 2005). Thus antenatal detection of an abnormal coiling index by ultrasound can lead to identification of foetuses at risk. None of the cords in the present study was without a coil. In a recent study by Gupta et al. (2006) it was reported that 5.6% of the umbilical cords used in their study were without coils. In another study by Rana et al. (1995), 4.9 % of the umbilical cords lacked coils.

Among the perinatal outcomes studied in association with UCI, only the PI had a negative but significant correlation with it ($r = -0.172$, $p < 0.05$) (Table 13). This means that as the UCI increases, PI decreases whereas hyper-coiled cords have lower PI than normal coiled and hypo-coiled cords. Furthermore, infants with a PI < 2.5 had a higher UCI than those with PI ≥ 2.5. (T 2.5, $p < 0.05$ (Table 14). Other factors such as gestational age and birth weight did not correlate significantly with the UCI. However Gupta et al. (2006) reported that there was no association between PI and UCI.

5.8. WEIGHT OF THE PLACENTA

The weight of the placenta is used in the determination of the foeto-placental ratio. The weight of the placenta gives an idea of the amount of substance that is exchanged between the mother and the foetus. The mean placenta weight was 563.47g (SD = 132) with a range of 315-933g. The weight of the placenta was found to have a significant positive correlation with the weight of the baby ($r = 0.52$, $p<0.01$), head circumference ($r = 0.38$, $p<0.01$), length of baby ($r= 0.24$, $p<0.01$) and gestational age ($r = 0.32$, $p<0.01$).

Luz (2001), in a similar experiment found the mean placental weight to be 537g (SD=96g). Lurie et al., (1999) also found the mean placental weight to be 613.0±123.8g with a range of 319- 1266g whilst Lo et al., (2002) had the mean placental weight to be 646.2±0.3g. However, (Borton, 2006) put the weight of the term placenta between 400- 600g, whilst (Yetter, 1998), put the term placenta to be about 470g. Comparing the mean placental weight obtained in this experiment to those obtained above, it was realised that the mean placental weight obtained by Yetter, (1998) was too low to be taken as the mean while that of Luz was quite close to the mean obtained in the present study. In contrast, Lurie et al (1999) mean placental weight was found to be higher than the one obtained here. Since Borton gave a range for the term placental weight, the mean placental weight obtained fell within this range even though the range here was 315- 933g. This indicates that the mean placenta weight differs from place to place and may be due to so many factors such as nutrition, genetics, gestational age, maternal size, etc.

It was found that the placental weight correlates significantly with the weight of the baby and for every 1g increase in the placental weight, the foetal weight increases by 2g and this corresponds to (Luz, 2001) who found that for every 1g increase in placental weight, the foetal weight increases by 1.98g. Since the weight of the placenta correlated positively with the weight and the gestational age of the baby, it then implies that, factors which directly affect the weight of the baby will indirectly affect the weight of the placenta. Such factors could include nutrition, maternal size, maternal haemoglobin gain, altitude, paternal factors, maternal and paternal genetics, gestational age, maternal diabetes mellitus, etc. According to (Van den Broek et al., 2005), unfixed placentae that weigh more than 600g are pathologic, but more important may be the placenta/foetal ratio. Chronic low uteroplacental blood flow is the most frequent cause of small placentae, but often the foetal weight is affected, so the ratio may be

normal. The cause of enlargement may be unknown, but it is often revealed if the following are considered: overt or latent maternal diabetes, maternal anaemia, maternal–foetal blood group incompatibility, maternal–foetal transfusion, chronic intrauterine infection (syphilis), foetal malformations (especially of the lung), the twin transfusion syndrome, congenital neoplasms (e.g., neuroblastoma, teratoma, and chorangiomas) and alpha- thalassaemia. Some of these factors may be responsible for the differences between the placental weight obtained in the present study and those obtained by Salafia and Vintziloes (1999**)**.

5.9. DIAMETER OF THE PLACENTA

The diameter of the placenta may give an idea about the size of the placenta which may intend give indirect information about the foetal-placental ratio. The diameter of the placenta will affect the amount of nutrients, oxygen and carbon dioxide that will pass from the mother to the child and vice versa. The mean placental diameter was 18.69 cm (SD=2.05) with a range of 14.0 to 25.0 cm. In the present study 33.92% of the individual placental diameter fell outside the mean diameter range of 18.69±2.05 cm. This indicates an uneven distribution of the results within and beyond the mean diameter.

The diameter of the placenta was found to correlate positively with the weight of the baby ($r = 0.34$, $p<0.01$), the head circumference of the baby ($r = 0.25$, $p<0.01$) and the length of the baby ($r = 0.23$, $p<0.01$). However, the diameter of the placenta did not correlate significantly with the gestational age. Borton (2006), reported a term placental diameter range of 15 cm to 22 cm whilst (Yetter, 1998) reported a mean of about 22 cm. Comparing the mean placenta diameter obtained in the present study with that of Yetter (1998) and Borton (2006), suggests that the mean placenta diameter is in contrast to that of Yetter (1998) but fell within the range of Borton (2006). Although even the lower limit value of the present study is lower than that obtained by Borton (2006). However the upper limit was higher in the present study.

The lower mean diameter may be due to racial or medical conditions. Also this difference could be genetic since the study by Yetter, 1998 involved Caucasian women while the present study and that of Borton (2006) were on blacks. The individual placentae with larger diameter have a large surface area for the exchange of substances from the mother to the foetus and vice versa which is most likely to increase the weight of the baby.

The positive correlation between the placental diameter and the weight of the baby, the head circumference of the baby and the length of the baby indicate that the factors which directly affect the weight of the placenta will indirectly affect the diameter of the placenta. The difference in placental diameter may be due to nutrition, maternal size, maternal and paternal genetic constitution and altitude.

The diameter of the placenta did not correlate significantly with the gestational age. This means that the age of the foetus does not affect the diameter significantly and therefore the mother's size may be the ultimate determinant of placental diameter.

5.10. THICKNESS OF THE PLACENTA

The thickness of the placenta may give indirect information on the foetal-placental ratio. It may give an indication of the amount of substances (nutrients, gases) that is exchanged between the foetus and the mother. In this study, the mean placental thickness was 2.65 cm (SD=0.55) with a range of 1.3cm to 6.0 cm. About 25.15% of the individual placentae fell outside the mean range of 2.65± 0.55 cm. Thickness of the placenta correlated significantly with the weight of the foetus. However, there is no significant correlation between the placental thickness and the head circumference of the baby ($r = 0.046$, $p>0.05$), the length of the baby ($r = 0.16$, $p>0.05$) and the gestational age ($r = 0.09$, $p>0.05$). Borton (2006) reported a range for the term placenta to be 2 cm to 4 cm whilst (Yetter, 1998) gave the term placenta a thickness range of 2.0 cm to 2.5 cm. Results of the present study are in the agreement with the

reports of Yetter, (1998) and Borton (2006). However, the minimum placental thickness is lower than the minimum value of Yetter (1998) and Borton (2006), Borton (2006), while the maximum thickness value is also above those of Yetter (1998) and Borton (2006).

The positive correlation between the placental thickness and the weight of the baby indicate that the factors which directly affect the weight of the baby will indirectly affect the placental thickness. These factors include nutrition, maternal genetics, maternal haemoglobin concentration gain, altitude, etc. Since there was no significant correlation between the placental thickness and the head circumference, the length of the baby and the gestational age, an increase in any of these factors does not influence the thickness of the placenta significantly.

5.11. PERINATAL OUTCOME

The mean birth weight observed in this study was 3.1 kg (SD 0.51). This is similar to the 3.1 kg (SD 0.8) observed in Nigeria (Mutihir and Pam, 2006). The low birth weight rate in this study was 7.81 % while 3.51% were large for gestational age (>400g). Low birth weight has been defined as birth weight less than 2.5 kg (Valsamakis et al., 2006). Nkyerkyer 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 rate of 7.81% observed in this study is lower than in these previous studies. Both low birth weight (<2500 g) and high birth weight (>4000 g) are foetal conditions associated with increased risks of peripartum morbidity and mortality. Low birth weight contributes to a range of poor health outcomes (Valsamakis et al., 2006). Babies born with low birth weight face a greatly increased risk of dying during their early months and years. Those who survive have impaired immune function and increased risk of diseases. They are likely to remain undernourished, with reduced muscle strength, throughout their lives, and to suffer a higher incidence of diabetes and heart diseases (Gupta et al., 2006).

Birth weight greater than 4000g (4.00kg) is considered to be macrosomia. It affects 2- 15% of all pregnant women, depending on the racial, ethnic and socioeconomic composition of the population under study (Sornes, 2000). Foetal macrosomia could be due to;

A) Maternal obesity since the more the mother weighs, the larger her foetus is likely to be.

B) Maternal pregnancy weight gain,

C) Maternal haemoglobin concentration. The relationship between birth weight and circulating maternal haemoglobin concentration is inversely related.

D) Gestational diabetes mellitus.

Uncontrolled maternal diabetes mellitus is commonly associated with excessive foetal weight. 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 3.51% foetal macrosomia identified in the study could be due to any of the above conditions or a combination of factors. Luz (2001) put the mean newborn weight to be 3382.1± 486.7g (3.38±0.486kg) with a range of 2180- 4810g (2.18- 4.81kg). Comparing this with the results obtained in the present study, the mean baby weight is lower than that of Luz, however, the minimum foetal weight is lower than Luz's and our maximum value is higher than his. This may be due to differences in race and genetic make up.

According to Valsamakis et al. (2006), the optimal birth weight range to minimize the risk of foetal and maternal morbidity and mortality is 3.0- 4.0kg (3000-4000g). Valsamakis et al. (2006) and Hershkovitz et al. (2001) compared the mean birth weight of singleton babies in the United States, Great Britain and Singapore. He found out that the mean baby weight in the United States, Great Britain and Singapore from 1975- 1992 was 3060- 3520g (3.06- 3.52kg), 3201- 3753g (3.20- 3.75kg) and 2880- 3290g (2.88- 3.29kg) respectively. The mean foetal weight of the present study fell within the range for the United States and the Singapore. It is

however lower than that of the Great Britain. Many factors, both endogenous and extrinsic can influence the weight of the newborn. These encompass maternal factors (e.g. race, stature and genetics), paternal factors (paternal height, genetics), environmental influences (e.g. altitude, availability of adequate nutrition), physiologic factors (e.g. altered glucose metabolism, haemoglobin concentration, micro vascular integrity), pathologic factors (e.g. hypertension, uterine malformation) and complications of pregnancy (e.g. gestational diabetes mellitus, preeclampsia) (Van den Broek et al., 2005).

Of all these factors, Gestational age at delivery is the most significant determinant of foetal weight (Van Dijk et al., 2002; Van den Broek et al., 2005). On the contrary, the most significant determinant of foetal weight from the present study is the placental weight as the correlation between the foetal weight and the placental weight had a higher correlation coefficient of 0.052 as compared to that of 0.47 between the foetal weight and the gestational age. Preterm delivery is the leading cause of low birth weight of newborns. Other potential causes are collectively termed intrauterine growth retardation (IUGR). Causes of IUGR include intrauterine infections, congenital syndrome, genetic abnormalities, and chronic uteroplacental insufficiency. Since all the babies studied were born within 32- 42 weeks of gestation, the few low birth weight may not be due to preterm delivery but may be due to intrauterine growth retardation (Van Dijk et al., 2002; Van den Broek et al., 2005).

The weight of the baby correlated significantly with the diameter of the placenta, the thickness of the placenta, the gestational age and the age of the mother. It was found that for every one gram increase in the weight of the placenta, the weight of the baby increases by 2.0g which is very close to that obtained by (Luz, 2001) who found that for every one gram increase in the placenta weight, the baby weight increases by 1.98g. For every one centimeter increase in the thickness of the placenta and the diameter of the placenta, the weight of the

baby increases by 18.0g) and 17g respectively. For every one year increase in the mother's age, the weight also increases by 20g suggesting older mother tend to have bigger babies.

5.12. HEAD CIRCUMFERENCE OF BABY

The mean head circumference was 34.27 cm (SD 2.1) with a range of 28.00 cm to 42.00 cm. The head circumference of the baby gives an indirect assessment of the weight of the baby in that the bigger the head circumference, the heavier the baby is expected to weigh and vice versa. The mean head circumference is similar to the 34.2 cm (SD 2.6) observed in Benin-City, Nigeria (Eregie, 1993) and 34.49 cm (SD 1.59) in a study in Jos (Pam, 1999). These similarities may be racial since these studies are all limited to West Africa. In a study conducted in India, the mean head circumference was 32.20 cm (Salafia and Vintziloes, 1999).

There was a significant positive correlation between the head circumference and weight of the placenta ($r = 0.38$, $p<0.01$) and the diameter of the placenta ($r = 0.25$, $p<0.01$) and the age of mother ($r =0.13$, $p <0.05$) and for every unit increase in the weight of the placenta and the diameter of the placenta, the head circumference increased by 0.07mm and 0.04mm respectively. However, there was no significant correlation between the head circumference and the thickness of the placenta

Head circumference appears to be best indicator for the weight of the placenta as the correlation coefficient between the head circumference and the placenta weight was 0.38 ($p< 0.01$). However, head circumference can be influenced by other factors such as anorexia nervosa and bulimia nervosa (Ward, 2008). Ward (2008) found that women with a history of an eating disorder had a higher rate of miscarriage, small for gestational age babies, low birth weight babies, babies with microcephaly, intrauterine growth restriction, and premature labour. The weight and diameter of the placenta may give an idea of the amount of substances (nutrients, oxygen, etc.) that goes to the foetus which can positively influence the development

of the baby, hence the head circumference. The positive correlation between the placenta weight and the diameter, indicate that the factors that affect the development of the weight and the diameter of the placenta indirectly influence the head circumference of the baby.

5.13. LENGTH OF BABY

The mean length of the babies was 48.79 cm (SD= 2.70) with a range of 40.00- 55.00 cm. The length of the baby correlated positively with the weight of the placenta ($r = 0.23$, $p< 0.01$), the diameter of the placenta ($r = 0.23$, $p<0.01$), and the gestational age ($r= 0.32$, $p< 0.01$). However, there was no correlation between the length of the baby and the thickness of the placenta ($r = 0.16$, $p> 0.05$) and the age of the mother ($r = 0.03$, $p> 0.05$). For every unit increase in the weight of the placenta (i.e. 1g), the diameter of the placenta (1cm), and the thickness of the placenta (i.e. 1cm), the length of the baby increases by 1.00 (0.001 cm), 285 mm (0.285 cm), and 785 mm (0.785 cm) respectively.

The mean foetal length of (48.79 cm) and the positive significant correlation between the foetal length and the placental weight in the present study is similar to that obtained by Lo et al (2002) whose mean foetal length was 48.8cm and the correlation between the foetal length and the placental weight was ($r = 0.305$, $p<0.01$).

The positive correlation between the baby length and the placenta weight, placental diameter and the gestational age means that as one of the independent variables increases, the length of the baby also increases. This implies that the heavier the placenta, the wider the diameter of the placenta and the longer the gestational age, the more the foetus receives nutrients from the mother and this could significantly affect the length of the foetus since the rate of exchange of nutrients is due to the surface area of the placenta in contact with the substances.

The length of the baby did not correlate with the age of the mother and the thickness of the placenta because age has no effect on the height of an individual. In fact, age is an independent variable so far as length of the baby is concerned.

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 represents uterine capacity and the potential for growth, is a major determinant of foetal size (Murphy et al., 2006). From the present study, gestational age is the best indicator of baby length since the correlation coefficient between the length of the baby and the gestational age is ($r= 0.32$, $p< 0.01$). However, the length of an individual may be significantly influenced by the genetic make-up of the parents of the baby in that when both parents are tall, the baby will inherit tallness from both parents and if one is short and the other tall, based on their genetic make- up, the baby can be tall or short. This implies that the few individual babies that fell above the mean range may have parents who are tall or one short and the other tall and those short ones have short parents (Borton, 2006; Valsamakis et al., 2006).

5.14. GESTATIONAL AGE

The mean gestational age was 37 weeks (SD 2) at birth with a range of 32- 42 weeks. The preterm delivery rate defined as gestational period less than 37 weeks was 42.65 % although a recent study by Nkyekyer et al. (2006) had reported 9.3%. It is obvious that the 42.65% observed in the present study is very high compared to previous studies. Singleton preterm birth rates differ from one part of the world to the other. Reported rates include 15.2% in Zimbabwe (Feresu et al., 2004) 3 % in USA (Reagan and Salsberry, 2005), 20.3% in rural Malawi (van den Broek, et al., 2005).

There was a significant positive correlation between the gestational age and the baby weight, the baby length, the foetal head circumference and the weight of the placenta. However, the gestational age did not correlate with the diameter of the placenta, the thickness of the placenta and the maternal age. This suggests that as the gestational age increases, the baby weight, baby length, the foetal head circumference and the weight of the placenta increase. However, an increase in the gestational age did not affect the diameter and thickness of the placenta and the maternal age significantly. In contrast to the present study, (Lurie et al., 1999), put the mean gestational age at delivery to be 39.7 weeks with a range of 33- 42 weeks. This means that the mean gestational age for that study is higher than that of the present study. This could be responsible for the high mean newborn weight of 3.38kg as compared to that of the present study of 3.10 kg.

5.15. CONCLUSION

In the present study the higher incidence of normal cord length, in the range of 40-70 cm, suggests that 'normal' cord length should be between 40 cm and 70 cm in length. The combined incidence of central/eccentric insertions of 81.89% shows that umbilical cord is commonly and best positioned central or eccentric. In addition a normal cord must have a UCI in the range of 0.08 to 0.19 coils/cm. Furthermore the observation of 93.6% of cords in the diameter range of 1-2 cm suggests that a normal cord must not exceed 2 cm in diameter.

The present study also shows that cord length and diameter correlate positively with birth weight and head circumference. Correlation of cord parameters with perinatal outcomes suggests that antenatal detection of umbilical cord abnormalities may be useful in the detection of foetuses at risk of cord related complications.

There was a strong relationship between the placenta and the foetus suggesting that the well being of the foetus is highly dependent on the placenta since it serves as a link between

the mother and the developing foetus for nutritional support, excretory functions as well as immunological and hormonal support. Large placentae provide a large surface area for the exchange of substances from the mother to the foetus resulting in high foetal weight, length and head circumference. The best indicator of foetal weight is placental weight and that of foetal length and head circumference is gestational age. Critical examination of the placenta and umbilical cord immediately after delivery should be used to determine the well being of the baby.

There was a significant difference between the intrauterine ultrasonographic measurements and the gross anatomical measurements therefore intrauterine ultrasonography may be used as a preliminary guide for the determination of foetal well-being.

REFERENCES

Abaidoo, C. S., **Boateng, K. A. and Warren, M. A. (2008)** Morphological variations of the "baby's supply line". *Journal of Science and Technology*, **28:** (2) 1-9.

Addai, F. K., Quarshie, F. J. K. and Ockleford, C. D. (1994) The mode of insertion of umbilical cord and vessels: associating with maternal haemoglobin genotype, neonatal factors and placental component volumes. *Anatomy and Embryology*, **189**:107-114.

Akiyama, S. K. and Yamada, K. M. (1987) Fibronectin. *Advance Enzymology*, **59**: 1-57.

Aplin, J. D. (1991) Implantation, Trophoblast Differentiation and Haemochorial Placentation - Mechanistic Evidence in vivo and in vitro. *Journal of Cell Science*, **99** (Pt4): 681-692.

Anath. C.V., Misra, D. P., Desmissie, K. and Smulian, C. J. (2001) Rates of preterm delivery among black women and white women in the United States over two decades: An age period cohort analysis. *American Journal of Epidemiology*, **154** (7): 657-665.

Artis A. A., Bowie J. D. and Rosenberg, E. R. (1985) The fallacy of placenta migration, effect of sonographic techniques *American Journal of Roentgenology*, **144**:799.

Baergen, R. N., Malicki, D., Behling C. and Benirschke, K. (2001) Morbidity, mortality and placental pathology in excessively long umbilical cords: retrospective study. *Pediatric Developmental Pathology*, **4**(2): 144-153.

Beck, M. (2009) How is your baby? Recalling the Apgar score's namesake. *Health journal*, 1-3.

Berk, M. A., Mimouni, F., Miodovnik, M., Hertzberg, V. and Valuck, J. (1989) Macrosomia in infants of insulin-dependent diabetic mothers. *Pediatrics*, 83 (6):1029-1034.

Ben-Arie, A., Wessman, A., Steinberg, Y., Levy, R. and Hagay, Z. (1995) Oligohydramnios, intrauterine growth retardation and foetal death due to umbilical cord torsion. *Archaeology of Gynecology and Obstetrics*, **256**:159-161.

Benirschke, K. (2005) Abnormalities of the Human Placenta. American Academy of Pediatrics. *NeoReviews*, **6(**9):414.

Benirschke, K. and Kauffman P. (1995) Anatomy and pathology of the umbilical cord and major foetal vessels. In: Bernishke, K., Kauffman, P., eds. Pathology of the human placenta. *New York: Springer-Verlag*, pp 319-377.

Benirschke, K. (2004) The Umbilical Cord. *NeoReviews*, **5**(4):34.

Berg, T. G. and Rayburn, W. F. (1995) Umbilical Cord Length and Acid-Base Balance at Delivery. *Journal of Reproductive Medicine*, **40**:9-12.

Blazer, S., Sujov, P., Escholi, Z., Itai, B. H. and Bronshtein, M. (1997) Single umbilical artery-right or left? Does it matter? *Prenatal Diagnostics,* **1**:5-8.

Blickstein, I., Varon, Y. and Varon, E. (2001) Implications of the differences in coiling indices at different segments of the umbilical cord. *Gynecology Obstetric Investigation,* **52:** 203-206.

Borton, C. (2006) Placenta and Placental problems. *Patient Plus*, **20**:159.

Bovicelli, L., Orsin, L. F. and Rizzo, N. (1981) Estimation of gestational age during the first trimester by real time measurement of crown-rump length and biparietal diameter. *Journal of Clinical Ultrasound*, **9**:71-75.

Cohen, H. L., Shapiro, M. L., Haller, J. O. and Schwartz, D. (1992) The Multivessel Umbilical Cord: An Antenatal Indicator of Possible Conjoined Twinning. *Journal of Clinical Ultrasound*, **20**:278-282.

Cho, J. Y., Lee, Y. H., Moon, M. H. and Lee, J. H. (2008) Differences in migration of placenta according to location and type of placenta previa. *Journal of Clinical Ultrasound,* **36** (2):79-84

Collins, J. H., Collins, C. L. and Collins, C. C. (2002) Silent Risk: Issues about the Human Umbilical cord. *The Pregnancy Institute,* pp 1-13.

Davies, B. R., Casanueva, E. and Arroyo, P. (1984) Placentas of small-for date's infants: a small controlled series from Mexico City, Mexico. *American Journal of Obstetrics and Gynaecology,* **149**: 731-736.

De Laat, M. W., Franx, A. and van Alderen, E. D. (2005) The umbilical coiling index, a review of the literature. *Journal of Maternal, Foetal and Neonatal Medicine,* **17**:93-100.

Desoye, G. and Hauguel-de Mouzon, S. (2007) The Human Placenta in Gestational Diabetes Mellitus. *Diabetes Care,* **30**:S120-S126.

Di Salvo, D. N., Benson, C. B., Laing, F. C., Brown, D. L., Frates, C. M. and Doubilet, M. P. (1998) Sonographic evaluation of the placental cord insertion site. *American Journal of Radiology*, **170**: 1295-1298.

Ercal, T., Lacin, S., Altunyurt, S., Saysili, U., Cinar, O. and Mumcu, A. (1996) Umbilical coiling index: is it a marker for the foetus at risk? *British Journal of Clinical Practice*, **50**(5): 254-256.

Eregie, C. O. (1993) Arm and head measurements in the newborn. *East African Medical Journal,* **70***:* 46-47.

Fleischer, A. C. (1991) Transabdominal and transvaginal sonography of ovarian masses. *Clinical Obstetrics*, **34**(2): 433-42.

Feresu, S. A., Harlow, S. D., Welch, K. and Gillespie, B. W. (2004) Incidence of and socio-demographic risk factors for still birth, preterm birth and low birth weight among Zimbabwean women. *Paediatric Perinatal Epidemiology*, **18**: 154-163.

Foidart, J. M., Hustin, J., Dubois, M. and Schaaps T. J. P. (1992) The human placenta becomes haemo-chorial at the 13th week of pregnancy. *International Journal of Developmental Biology*, **36**: 451-453.

Fox, H. (1986) Pathology of the placenta**.** *Clinical Obstetrics and Gynaecology* **13**:501.

Furtuny, A. (1995) Biochemical and Doppler predictors of poor perinatal outcome in a foetus with four umbilical vessels. *European Journal of Obstetrical and Gynecological Reproductive Biology*, **62**:145-147.

Genbacex O., McMaster M. T., Lazic J., Nedeljkovic S., Cvetkovic M. and Fisher S. J. (2000) Concordant in situ and in vitro data show that maternal cigarette smoking negatively regulates placental cytotrophoblast passage through the cell cycle. *Reproductive Toxicology*, **14:** 495-506.

Gudmundsson S., Korszun P., Olofsson P. and Dubiel M. (2003) New score indicating placental vascular resistance. *Acta Obstetrics et Gynecology Scandinavica*, **82**(9):807-12.

Gupta, S., Faridi, M. M. A. and Krishnan, J. (2006) Umbilical Coiling Index. *Journal of Gynecology, India*, **56** (4): 315-319.

Guy, G. P., Reisner, D. B. and Tinor–Tritseh, I. E. (1990) Ultrasonographic evaluation of uteroplacental blood flow patterns of abnormality located and adherent place. *Journal Obstetrics and Gynecology*, **163**:723.

Habib, F. A. (2002) Prediction of low birth weight infants from ultrasound measurement of placental diameter and thickness. *Annals of Saudi Medicine*, **22**(5-6):312-314.

Haddad, B., Mercer, B. M., Livingston, J. C., Talati, A. and Sibai, B. M. (2000) Outcome after successful resuscitation of babies born with Apgar score 0 at both 1 and 5 minutes. *American Journal of Obstetrics and Gynecology*, **182**: 1210-1214.

Hadlock, F. B., Deter, R. and Harris, R. B. (1982) Foetal biparietal diameter, a critical re-evaluation of the relation to menstrual age by means of real time ultrasound. *Journal of Ultrasound Medicine*, **1**:97.

Hadlock, F. B., Deter, R. and Harris, R. B. (1983) Computer assisted analysis of foetal age in the third trimester using multiple foetal growth parameters. *Journal of Clinical Ultrasound*, **11**:313-320.

Hanley, M. L., Anath, C. V., Shen-Schwrz, S., Smulian, J. C., Yuling, L. and Veintzileos, A. M. (2002) Placental cord insertion and birth weight discordancy in twin gestation. *Obstetrics and Gynecology,* **99**:477-482.

Hasegawa, J., Matsuoka, R., Ichizuka, K., Sekizawa, A. and Okai, T. (2006) Velamentous cord insertion: significance of prenatal detection to predict perinatal complications. *Taiwan Journal of Obstetrics and Gyncecology, **45:***21-25.

Hefetz, S. A. (1996) The umbilical cord, obstetrically important lesions. *Clinical Obstetrics and Gyncecology,* **39:** 87.

Hershkovitz, R., Sisberstein, T., Sheiner, E., Shoham-Vardi, I., Holcberg, G. A. and Katz, M. (2001) Risk factors associated with true knots of the umbilical cord. *European Journal of Obstetrical and Gynecological Reproductive Biology,* **98**:36-39.

Hertzberg, B. S., Bowie, J. D., Carroll, B. A., Kliewer, M. A. and Weber, T. M. (1992) Diagnosis of placenta previa during the third trimester: role of transperineal sonography. *American Journal of Roentgenology*, **159**: 83-87.

Hill, D. J., Crace, C J., Starin A. J. and Milner, R. D. G. (1986) Regulation of amino acid uptake and DNA Synthesis in Isolated human foetal fibroblast and myoblasts: effect of human placenta lactogen somatomedin C multiplication stimulating activity and insulin. *Journal of Clinical Endocrinology and Metabolism,* **62**:753-760.

Hoffman–Tretin, J. C., Koenugsberg, M. and Rabin, A. (1992) Placenta Acreta: Additional Sonographic observations. *Journal of Ultrasound Medicine*, **11**:29.

Ismail, S. R., (2007) The relationship Between Location and Foetal Gender (Ranzi's Method): Can Placental/Chorionic villi location be used as foetal gender indicator at six weeks of gestation using 2D and color flow sonography? *OBGYN.net: The universe of women's health.18:00GMT, December 2008.*

Isemura, M., Yamaguchi, Y., Munakata, H., Aikawa, j., Kan M., Yamana, I. and Yosizawa Z. (1984) Isolation and characterization of human placenta fibronectin. *Journal of Biochemistry,* **96**:163-9.

Itskovitz, J., LaGamma, E. F. and Rudolph, A. M. (1987) Effects of cord compression of foetal blood flow distribution and delivery. *American Journal of Physiology,* **252**:H100-H109.

Iyasu, S., Saftlas, A. K. and Rowley, D. L. (1993) The epidemiology of placenta previa in the United States. *American Journal of Obstetrics and Gynecology,* **168**:1424.

Jones, A. (1998) Truly knotted cords. *Australian and New Zealand Journal of Obstetrics and Gynecology,* **381**:98-99.

Kamitomo, M., Sueyoshi, K., Matsukita, S., Matsuda, Y., Hatae, M. and Ikenoue, T. (1999) Hemangioma of the umbilical cord: stenotic change of the umbilical vessels. *Foetal Diagnostic Therapy,* **14**:328-31.

Kaplan, C.G. **(1995)** Forensic aspect of the placenta. *Prospect of Pediatric Pathology*, **19**:20-42.

Kapto, M. M., May, R. R. and Crane, J. P. (1983) A comparison of the reliability of estimated date of confinement predicted by crown-rump and biparietal diameter. *American Journal of Obstetrics and Gynecology,* **145:**562-565.

Kashanian, M., Akbarian, A. and Kouhpayehzadeh, J. (2006) The umbilical coiling index and adverse perinatal outcome. *International Journal of Gynecology and Obstetrics, **95** (1): 8-13.*

Kingdom, J. P. C., Huppertz, B., Burton G. and Cross J. C. (2006) Placenta, from molecule to mother –a dedication to Peter Kaufman. *Journal of Placenta (a review),* **27**(20): S5.

Kliman, J. H. (1997) Behind every healthy baby is a healthy placenta. *Reproductive and Placenta Reseach Unit,* pp 1.

Krakowiak, P., Smith, E. N., de Bruyn, G . and Lydon-Rochelle, M. T. (2004) Risk factors and outcomes associated with a short umbilical cord. *Obstetrics and Gynecology,* **103**:1119-11127.

Kremkau, F. (1983) Ultrasound instrumentation: physical principles *Ultrasonography in Obstetrics and Gynecology,* pp 313-324.

Kulkarni, M.L., Matadh, S.P., Ashok, C., Pradeep N., Avinash T. and Kulkarni A.M. (2007) Absence of Wharton's jelly around the umbilical arteries. *Indian Journal of Pediatrics,* **74** (8): 787-789.

Kurtz, A. B. and Wapner, R. J. (1980) Analysis of biparietal diameter as an accurate indicator of gestational age. *Journal of Clinical Ultrasound*, **8**: 319-326.

Lacro, R. V., Jones, K. L. and Bennirschke, K. (1987) The umbilical cord twist: Origin, direction and relevance. *American Journal of Obstetrics and Gynecology,* **157**: 833-838.

Lanari M., Lazzarotto T., Papa I., Venturi V. and Bronzetti G. (2001) Neonatal aortic arch thrombosis as a result of congenital cytomegalovirus infection. *Pediatrics,* **108**:E114.

Leibschang J., Marcickiewicz J., Chazan B. and Troszyński M. (1983) Clinical value of the foeto-placental ratio. *Problemy Medycymy Wieku Rozwojowego,* **12**:174-180.

Leonadis, J. G., Beathy, E. C. and Hall, R. T. (1975) Choriongiomas of the placenta. *Radiology*, **123**:703.

Leung, A. K. and Robson, W. L. (1989) Single umbilical artery, report of 159 cases. *American Journal of Child Diseases,* **143**: 108-111.

Liu, C. C., Pretorius, D. H., Scioscia, A. L. and Hull, A. D. (2002) Sonographic prenatal diagnosis of marginal placental cord insertion. *Journal of Ultrasound in Medicine,* **21:** 627-632.

Lo, Y. F., Jeng, M. J., Lee, Y. S., Soong, W. J. and Hwang, B. (2002) Placental weight and birth characteristics of healthy singleton newborns. *Journal of Practical Obstetrics and Gynecology,* **43**:21-25.

Loke, Y. W. (1990) Experimenting With Human Extravillous Trophoblast - a Personal View. *American Journal of Reproductive Immunology,* **24** (1): 22-28.

Lurie, S., Feinstein, M. and Mamet, Y. (1999) Human Foetal-Placental Weight Ratio in Normal Singleton Near-Term Pregnancies, *Gynecologic and Obstetric Investigation,* **48**:155-157.

Luz, H. S., López, S. R., Olivares, E. T., Terrazas, M. C., Silva, M. A. R. and Carrillo M. L. (2001) Relation between Birth Weight and Placenta Weight. *Neonatology, Biology of the Neonate,* **80**:113-117.

Machin, G. A. (1997) Velamentous cord insertion in monochorionic twin gestation: An added risk factor. *Journal of Reproduction in Medicine*, **42**:785-789.

Machin, G. A., Ackerman, J. and Gilbert-Barness, E. (2000) Abnormal umbilical cord coiling is associated with adverse perinatal outcomes. *Pediatric and Developmental Pathology,* **3**: 465-471.

Martin J. A., Hamilton B. E. and Sutton P. D. (2008) Births: Final data for 2006. *National Vital Statistics Reports,* **vol 57**, **no 7.** *Hyattsville, MD: National Center for Health Statistics.*

Martinez-Frias, M. L., Bermejo-Sanchez, E., Rodriguez-Pinilla, E. and Prieto-Merino, D. (2006) Characteristics of neonates with and without a single umbilical artery. Analysis of two consecutive series of neonates with and without congenital defects. *Annals of Pediatrics (Barch),* **65:** 541-550.

Martinez, J. M., Comas, C., Antolin, E., Borrell, A., Puerto, B., Casals, E., Mallofre, M. C., Muppala, H., Bedoya-Ronga, A. and Martindale, E. (2007) Abnormally Long Umbilical Cord with Marked Spiraling and True Knots: A Case Report. *The Internet Journal of Gyencology and Obstetrics,* **vol 7**, **no 2.** 18:00GMT December 2008.

Mital, P., Hooja, N. and Mehndiratta, K. (2002) Placental thickness: a sonographic parameter for estimating gestational age of the foetus. *Indian Journal of Radiology and Imaging,* **12**:553-554.

Mollogy, C. E., McDowell, R. and Armour, R. (1983) Ultrasonographic diagnosis of Placenta membranacea in utero. *Journal of Ultrasound Medicine*, **2**:377.

Murphy, V. E., Smith, R., Giles, W. B. and Clifton, V. L. (2006) Endocrine Regulation of Human Foetal Growth: The Role of the Mother. *Placenta and Foetus*, **27** (2): 141-169.

Moster, D., Lie, R. T., Irgens, L. M., Bjerkedal, T. and Markestad, T. (2001) The association of Apgar score with subsequent death and cerebral palsy, a population based study in term infants. *Journal of Pediatrics*, **138**: 789-809.

Mutihir, J. T. and Pam, S. D. (2006) Anthropometric and other Assessment indices of the Newborn of Jos, Nigeria. *Annals of African Medicine*, **5** (4):192-196.

Naeye, R. L. (1985). Umbilical cord, clinical significance. *Journal of Pediatrics*, **107**:278-81.

Nahum G. G. and Huffaker B. J. (1993) Racial differences in oral glucose screening test results: establishing race-specific criteria for abnormality in pregnancy. *Obstetrics Gynecology*, **81**(4):517-22.

Nahum G. G., Pham K. Q and Stanislaw H. (2004) Prediction of term birth weight in Hispanic women using an equation based on maternal characteristics. *European Journal of Obstetrics Gynecological Reproductive Biology*, **112**(2):145-50

Neaumoff, P., Zulman, A. E. and Weinstein, B. (1981) Ultrasonography of partial hydatidiform mole. *Radiology*, **140**:467.

Nelson, K. B. and Ellenberg, J. H. (1981) Apgar score as a predictor of chronic neurological disability. *Pediatrics*, **68**:36-84.

Nkyekyer, K., Enweronu-Laryea, C. and Boafor, T. (2006) Singleton Preterm Births in Korle Bu Hospital, Accra, Ghana-origin and outcomes. *Ghana Medical Journal*, **40***(3):93-98.*

Oyelese, Y., Catanzarite, V. and Prefumo, F. (2004) Vasa previa: the impact of prenatal diagnosis on outcomes. *Obstetrics and Gynecology*, **103**: 937-942.

Paria, B. C., Lim, H., Das, S. K., Reese, J. and Dey, S. K. **(2000)** Molecular Signaling in Uterine Receptivity for Implantation. *Cell & Developmental Biology*, **11**:67-76.

Pam, S. D. (1999) Assessment of the use of birth weight surrogates for the detection of low birth weight infants in Jos. *Seminar of West African College of Physicians*, Lagos.

Papile, L. A. (2001) The Apgar scores in the 21st century. *New England Journal of Medicine*, **344**:519-520.

Petraglia F. (1996) Endocrine role of the placenta and related membranes. *European Journal Endocrinology*, **135**: 166-167

Pierce, B. T., Dance, V. D., Wagner, R. K., Apodaca, C. C., Nielsen, P. E. and Calhoun, B. C. (2001) Perinatal outcome following foetal single umbilical artery diagnosis. *Journal of Maternal and Foetal Medicine,* **10**:59-63.

Pijnenborg, R., Dixon, G., Robertson, W. B. and Brosens, I. (1980) Trophoblastic invasion of decidua from 8-18 weeks of pregnancy. *Placenta,* **1**: 3-19.

Pijnenborg, R., Bland, J. M., Robertson, W. B. and Brosens, I. (1983) Uteroplacental arterial changes related to interstitial trophoblast migration in early human pregnancy. *Placenta,* **4:**387-414.

Predanic, M., Perni, C. S., Chasen, S. T., Baergen, N. R. and Chervenak, A. F. (2005) Assessment of Umbilical cord Coiling during the Routine Foetal Sonographic Anatomic Survey in the Second Trimester. *Journal of Ultrasound in Medicine,* **24**:185-191.

Quin, Y., Lau, T. K., and Rogers, M. S. (2002) Second-trimester ultrasonographic assessment of the umbilical coiling index. *Ultrasound in Obstetrics and Gynecology,* **20:**458-463.

Rana, J., Ebert, G. A. and Kappy, K. A (1995) Adverse perinatal outcome in patients with an abnormal umbilical coiling index. *Obstetrics and Gynecology,* **85**:573-577.

Randall, G. C. B. (1989) Form and development of the umbilical cord in pigs and their association with the delivery of viable pigs. *American Journal of Veterinary Research,* **50**:1512-1515.

Reagan, P. B. and Salsberry, P. J. (2005) Race and ethnic differences in determinants of preterm birth in the USA: broadening the social context. *Social Sience and Medicine,* **60**:2217-2228.

Roit, I. M. (1991) Essential Immunology. *Blackwell Scientific Publications,* 296.

Roh, C. R., Budhraja, V., Kim, H. S., Nelson, D. M. and Sadovsky, Y. (2005) Microarray-based identification of differently expressed genes in hypoxic human term trophoblast and in placental villi of pregnancies with growth restricted foetuses. *Placenta* **26**:319-328

Salafia, C. and Vintziloes, A. M. (1999) Why all placentae should be examined by a pathologist. *American Journal of Obstetrics and Gynaecology,* **163** (4pt 1):1282-1293.

Schimmel, M. S. E. and Idelman, A. I. (1988) Supernumery umbilical vein resulting in four-vessel umbilical cord. *American Journal of Perinatology,* **15**:299-301.

Seeds, J. W. and Cafelo, R. C. (1982) Relationship of foetal limb to both biparietal and gestational age. *Obstetrics and Gynecology,* **60**: 680-684.

Sepulveda, W. (2006) Velamentous insertion of the umbilical cord: a first-trimester sonographic screening study. *Journal of Ultrasound in Medicine,* **25**:963-968.

Sepulveda, W., Rojas, I., Robert, J. A., Schnapp, C. and Alcalde, J. L. (2003) Prenatal detection of velamentous insertion of the umbilical cord: a prospective color Doppler ultrasound study. *Ultrasound in Obstetrics and Gynecology,* **21**:564-569.

Shi-wen, X., Stanton, L. A., Kennedy, L., Pala, D., Chen, Y., Howat, S. L., Renzoni, E. A., Carter, D. E., Bou-Gharios, G., Stratton, R. J., Pearson, J. D., Beier, F., Lyons, K. M., Black C. M., Abraham, D. J. and Leask, A. (2006) CCN2 is necessary for adhesive responses to transforming growth factor- in embryonic fibroblasts. *Journal of Biological Chemistry,* **281**: 10715-10726.

Singh, V., Khanum, S. and Singh, M. (2003) The placenta, Placenta disk and shape. *Archives of Pathology and Laboratory Medicine,* **127**(7):850-853.

Sornes T., (2000) Umbilical Cord Knots. *Acta Obstetricia et Gynecologica Scandinavia,* **79**:157-159.

Sornes, T., Bakke, T. (1989) Uterine size, Parity and Umbilical Cord length. *Acta Obstetrics and Gynecology of Scandinavia,* **68**:439-41.

Spirit, B. A., Kagan, E. H. and Rozanski, R. M. (1984) Sonoluccent areas in the placenta. Sonographic and pathologic correlation. *American Journal of Radiology,* **131**: 1-10.

Spirit, B. A. and Gordon, L. P. (1984) The placenta as an indicator of foetal maturity– fact and fancy. *Seminar on Ultrasound,* **5**:290.

Stephenson, T. J., Stammers, J. P. and Hith, D. (1990) Maternal to foetal transfer of free fatty acids in the in perfused rabbit placenta. *Journal of Developmental Physiology,* **13**:117-123.

Strong, T. H., Elliot, J. P. and Radin, T. (1993) Non-coiled umbilical blood vessels: a new marker for the foetus at risk. *Obstetrics and Gynecology,* **81**:409-11.

Strong, T.H., Jarles, D.L. and Vega, J. S. (1994) The umbilical coiling index. *American Journal of Obstetrics and Gynecology,* **170**: 29-32.

Tabibzadeh, S. and Babaknia, A. (1995). The signals and molecular pathways Involved in implantation, a symbiotic interaction between blastocyst and endometrium involving adhesion and tissue invasion. *Human Reproduction,* **10** (6): 1579-1602.

Thummala, M. R., Raju, T. N. and Langenberg, P. (1998) Isolated single umbilical artery anomaly and the risk for congenital malformations: a metaanalysis. *Journal of Pediatric Surgery,* **33**:580-585.

Usher, R. H., Boyd, M. E. and McLean, F. H. (1988) Assessment of foetal risk in postdated pregnancies. *American Journal of Obstetrics and Gynecology,* **158**:259.

Valsamakis, G., Kanaka-Gantenbein, C., Malamitsi-Puchner, A. and Mastorakos, G. (2006) Causes of intrauterine growth restriction and postnatal development of the metabolic syndrome. *Annals of the New York Academy of Sciences,* **1092**: 138-147.

Van den Broek, N., Ntonya, C., Kayira, E., White, S. and Neilson, J. P. (2005) Preterm birth in rural Malawi: high incidence in ultrasound-dated population. *Human Reproduction,* **20**: 3235-3237.

Van Dijk, C. C., Franx, A. and De Latt, M. W. M. (2002) The umbilical coiling index in normal pregnancy. *Journal of Maternal, Fetal and Neonatal Medicine,* **11**:280-283.

Vicovac, L., Jones, C. J. and Aplin, J. D. (1995) Trophoblast differentiation during formation of anchoring villi in a model of the early human placenta *In Vitro Placenta,* **16** (1): 41-56.

Vicovac, L. and Aplin, J. D. (1996) Epithelial-mesenchymal transition during trophoblast differentiation. *Acta Anatomical,* **156** (3): 202-216.

Wang, Y., Lewis, D. F., Gu, Y., Zhang, Y., Alexander, J. S. and Granger, D. N. (2004) Placental Trophoblast-Derived Factors Diminish Endothelial Barrier Function. *Journal of Clinical Endocrinology and Metabolism,* **89**: 2421-2428.

Ward, V. B. (2008) Eating Disorders in Pregnancy, *Journal of Nutrition,* **336**: 93- 96.

Wehlan, M. A. (2006) The Apgar score, letter to the editor. *Pediatrics,* **188**(3):1313-1314.

Woo, J. S. K. (2006) A Comprehensive guide to ultrasound scans in pregnancy; *Seminar on Ultrasound,* **15**:290.

Wright, J. W. R. and Ridgway, L. E. (1990). Sources of variability in the umbilical artery systolic/diastolic ratios: Implications of the Poiseuille equation. *American Journal of Obstetrics and Gynecology,* **163**:1788-1791.

Wu, J. F., Chang, S. Y., Hsu, T. Y., Kung, F. T., Chan, T.C. and Hsieh, C. H. (1996) Multivariate analyses of the relationship between umbilical cord length and obstetric outcome. *Changgeng Yi Xue Za Zhi,* **19(**3):247-252.

Yetter, J. F. (1998) Examination of the Placenta, *American Academy of Family Physicians,* **57**(5):1045-1054.

Zhou, C. J. (1990) Foetal distress caused by umbilical cord anomalies; analysis of 456 cases. *Journal of Practical Obstetrics and Gynecology,* **6**:316-17.