Assessment of the fetal umbilical and middle-cerebral arteries in Intrauterine Growth Restriction Using Doppler Ultrasound

تقييم شريان الحبل السري و الشريان الدماغي الأوسط في حالة ضعف نمو الجنين باستخدام الموجات الصوتية (نظام دوبلر)

A Thesis Submitted for the Fulfillment for the Requirement of the Award of Ph.D degree in Medical Diagnostic Ultrasound

By: Saadia Ibrahim Khalid Nour Eldaim

Supervisor: Prof. Dr. Bushra Hussein Ahmed Abdelmalik

June 2016
بسم الله الرحمن الرحيم

قال تعالى:

(ويسألونك عن الروح فقل الروح من أمر ربي وما أوتينا من العلم إلا قليلا)
الإسراء (85)

صدق الله العظيم
DEDICATION

This research is dedicated to my great Parents whom have never failed to give me all supports, for giving all our need during the time and for teaching us that even the largest task can be accomplished if it is done one step at a time.

This thesis also dedicated to my husband, my lovely kids, sister, and brothers.
Acknowledgement

First of all I would like to say thanks of Allah, for giving us the gift of mind, and for give me the strength and health to do this thesis until it done completely.

My gratitude to my supervisor prof. Dr. Bushra Hussein whose excellent supervising and guidance have always inspired me.

I would like to thanks Dr. Ahmed Abukonna for moral support and also great thanks to Dr Sedieg Adam and my colleagues in Soba hospital for help. My thanks extend to the patients of the fetal medicine to co-operation.
ABSTRACT

Intrauterine Growth Restriction (IUGR) or fetal growth restriction is defined as less than 10th percent of predicted fetal weight for gestational age. It is a serious condition in which the fetus is not growing adequately and is smaller than expected for its dates.

The purpose of this study was to use Doppler indices to measure umbilical (UA) and middle cerebral (MCA) arteries in women with high risk pregnancy at 3rd trimester. Peak systolic velocity (PSV), end diastolic velocity (EDV), resistive index (RI) and pulsatility index (PI) for each artery were measured in 100 subjects and compared with control group of 50 normal pregnant women.

The result of the study showed that the mean (UA) indices were (PI 1.299, RI 0.749, S/D 5.137) and the mean indices for (MCA) were (PI 1.347, RI 0.732, S/D 3.833). The end diastolic flow (EDF) in (UA) was decreased in 39.3% cases, absent in 17.6%, positive in 37.2% and reversed in 5.9% cases but the (EDF) in (MCA) was increased in 75% and positive in 25% . The study showed (37.3%) of cases have oligohydrominus, (15%) decreased liquor, (3.9%) polyhyrominus and (43.11%) were normal. Symmetric (IUGR) (76%) and asymmetric (IUGR) (23.5%) was also observed. The study concluded that (RI) of (UA) was a good predictive tool for neonatal outcome in pregnant women.
ملخص البحث

تم عمل هذه الدراسة بمستشفى سوبا الجامعي بالخرطوم. الهدف الرئيسي من هذه الدراسة هو تقييم وتسجيل التغيرات التي تحدث في قراءت شرائى الحبل السري والشريان الدماغى الأوسط في حالات ضعف نمو الجنين في الثلث الأخير من الحمل باستخدام الموجات الصوتية (نظام دوبلر).

ضعف نمو الجنين يعبر على أنه هو تأخر نمو الجنين داخل الرحم وأن الجنين أصغر من عمره وأن وزن الجنين أقل من 10% لعمره الجنين وهي حالة حرجة حيث نجد ان اكتساب الوزن بالنسبة للجنين لا يتم بصورة طبيعية.

الهدف من الدراسة هو استخدام الموجات فوق الصوتية باستخدام مؤشر دوبلر لقياس المتغيرات في شرائى الحبل السري والشريان الدماغى الأوسط في حالة ضعف نمو الجنين في الثلث الأخير من الحمل وهذه المؤشرات هي الممانعه، وميؤشر النبضات ومعدل الانقباض والانبساط.

وجدت الدراسة أن متوسط قراءات الدوبلر لشرائى الحبل السري في الحالات الطبيعية (مؤشر النبضات 0.862، مؤشر الممانعه 0.582، معدل الانقباض والانبساط 2.51).

أما متوسط قراءات الدوبلر لشرائى الدماغى الأوسط في الحالات الطبيعية (مؤشر النبضات 1.782، مؤشر الممانعه 0.82، معدل الانقباض والانبساط 5.53).

وضحت الدراسة أن متوسط المؤشرات في شرائى الحبل السري في حالة ضعف نمو الجنين (مؤشر النبضات 2.99، مؤشر الممانعه 0.749، معدل الانقباض والانبساط 5.137) وأن قراءات حالات الدراسة الطبيعية متوافقة مع القيمة المرجعية.

وأن متوسط المؤشرات في الشريان الدماغى الأوسط في حالة ضعف نمو الجنين (مؤشر النبضات 1.347، مؤشر الممانعه 0.732، معدل الانقباض والانبساط 3.833) وأيضاً متوسط وزن الجنين 1.866.

تتفاقم الدم عند الانقباض يقل لدى 40% من الحالات ويتوقف لدى 17% ويعكس لدى 6% بينما يزداد تدفق الدم عند الانبساط في الشريان الدماغي لدى 75% من الحالات ويكون إيجابيا لدى 25% منهم.

نكس ماء الجنين الحاد وجد في 38% من الحالات، ويتراوح الحاد في السائل الأليمني ووجدت لدى 4% بينما 43% من الحالات لديهم كمية طبيعية منه. نجد في الدراسة أن معظم حالات ضعف نمو الجنين هي من نوعية الممتئلة 75% والاقليه هي من النوعية غير الممتئلة 25%. معظم الحوامل الذين لديهم تاريخ مرضي هم ذوو الضغط المرتفع 30%، أمراض القلب 4%، الصرع 6%، التهاب الحمراء 2% بينما 58% ليس لديهم تاريخ مرضي.

وجدت الدراسة أن هناك علاقة عكسية بين مؤشر الممانعه في شرائى الحبل السري ووزن الجنين (معامل الارتباط = 0.345) ووايضاً يوجد اختلاف معنوي بين عمر الجنين بواسطة الموجات وعمر الجنين الفعلي يقدر بالثاني اسابيع.

خلصت الدراسة بتوصية الدوبلر ومؤشر الميمنه في شرائى الحبل السري في تشخيص وضع فضف نمو الجنين وبالتالي تحسين فرصة ولادة الطفل وتأمين أفضل الأوضاع.
List of figures

Figure 2.1: General structure of blood vessel.................................................................1

Figure 2.2: the capillaries................................................................................................11

Figure 2.3: Development of umbilical artery (UA) and Umbilical cord of a three-minute-old child...12

Figure 2.4: The connection of umbilical artery (UA) with placenta.................................14

Figure 2.5: the fetal circulation........................................................................................16

Figure 2.6: The umbilical artery in ultrasound image.......................................................18

Figure 2.7: Anatomy of the middle cerebral artery (MCA)...............................................20

Figure 2.8: The cardiac cycle. .........................................................................................26

Figure 2.9: diagram shows the cardiac cycle time............................................................31

Figure 2.10: the cardiac cycle curve..................................................................................32

Figure 2.11: Changes in the cardiac function curve..........................................................34

Figure 2.12: Graph demonstrating autoregulation.............................................................35

Figure 2.13: Autonomic Control of the Heart and Blood Vessels.....................................40

Figure 2.14: demonstrate cortical vascular territorie.........................................................46

Figure 2.15: shows the cerebral venous drainage...............................................................48
Figure 2.16: Velamentous insertion

Figure 2.17: the vasa previa

Figure 2.18: varies insertions of umbilical cord

Figure 2.19: Nuchal cord

Figure 2.20: ultrasound image showed the Umbilical cord knot

Figure 2.21: ultrasound image showed Two-vessel umbilical cord

Figure 2.22: ultrasound image showed umbilical cord cyst

Figure 2.23: ultrasound images demonstrate the Placenta previa

Figure 2.24: ultrasound images demonstrate the Placental abruption

Figure 2.25: fetal growth chart percentile

Figure 2.26: demonstrate the Distribution of small for gestational age (SGA) in the world

Figure 2.27: Intrauterine growth restriction (IUGR)

Figure 2.28: shows case of Intrauterine Growth Restriction (IUGR)

Figure 2.29: shows the mortality and morbidity of IUGR

Figure 2.30: the management of IUGR

Figure 2.31: Effect of Reflector Motion on the Frequency of the Returning Wave

Figure 2.32: show the detected Doppler shift frequency with angle insonation
Figure 2.33: Effect of changing the angle of insonation .............................................103

Figure 2.34: shows simple diagram of continuous wave (CW) Doppler ..................105

Figure 2.35: pulsed doppler instrument .................................................................108

Figure 2.36: sample volume length ........................................................................110

Figure 2.37: shows Doppler signal processing .........................................................111

Figure 2.38: shows characteristic of blood flow .......................................................114

Figure 2.39: shows the sample volume .................................................................116

Figure 2.40: showed spectral window .......................................................................117

Figure 2.41: diagram demonstrate the Acceleration time .........................................121

Figure 2.42: Image demonstrating aliasing ...............................................................123

Figure 2.43: demonstrate the aliasing ......................................................................124

Figure 2.44: images of Aliasing ..............................................................................126

Figure 3.1: General Electric (GE) medical system ..................................................131

Figure 3.2: convex probe with a frequency of 3.5MHZ ..........................................132

Figure 3.3: Higeen ultrasound transmission gel made by households and Toiletries Company.133

Figure 3.4: illustrates digital graphic Sony printer with addition to high quality printing ....134

Figure 3.5: illustrates high quality thermal papers type I .......................................135
Figure 3.6: shows the patient and transducer position...........................................137

Figure 3.7: determine accurate and normal Umbilical Artery (UA) Doppler measurement…138

Figure 3.8: determine accurate Middle Cerebral Artery (MCA) Doppler ......................139

Figure 4.1: demonstrate the relationship between fetal weight and RI of UA.................144

Figure 4.2: demonstrate the difference between fetal GA and GA by LMP....................147

Figure 4.2: demonstrate UA Doppler indices in IUGR and control group....................148

Figure 4.2: demonstrate MCA Doppler indices in IUGR and control group....................148
List of tables

Table 2.1: Classification of arteries ................................................................. 8

Table 2.2: Cardiac cycle diastole phase .......................................................... 30

Table 2.3: Theories of Auto-regulation .......................................................... 36

Table 2.4: Ions that dilate or constrict local blood vessels .......................... 38

Table 2.5: Sections of the vasomotor centre .................................................. 41

Table 2.6: Regression formulas used to obtain estimated fetal weight .......... 72

Table 2.7: Causes of IUGR ............................................................................ 85

Table 2.8: Classification of IUGR ................................................................. 88

Table 4.1: The fetal gender frequency and percentage ................................. 141

Table 4.2: The Descriptive Statistics of UA and MCA indices ...................... 141

Table 4.3: The Umbilical Artery EDF frequency and percentage ................. 142

Table 4.4: The Middle Cerebral Artery EDF frequency and percentage ......... 142

Table 4.5: The liquor volume in IUGR ............................................................ 143

Table 4.6: The IUGR Classification ............................................................... 143

Table 4.7: The maternal clinical history ......................................................... 144

Table 4.8: The Correlation between RI Umbilical Artery and Fetal Weight .... 145
Table 4.9: the Correlation between the Fetal Weight and RI Middle Cerebral Artery……145

Table 4.10: The EDF Umbilical Artery vs.Liquor Volume Cross tabulation………………146

Table 4.11: GA estimation Paired Sample T- Test…………………………………………146

Table 4.12: the descriptive statistics of UA and MCA indices for control group…………147
1. Chapter one

1.1 Introduction ................................................................. 1
1.2 Problem of the study....................................................... 4
1.3 General objective.......................................................... 4
1.4 Specific objectives......................................................... 4
1.5 Hypothesis........................................................................ 5

2. Chapter two

2.1 Anatomy......................................................................... 7
2.1.1 Arteries......................................................................... 7
2.1.1.1 General structure of blood vessels.......................... 7
2.1.1.2 Classification of arteries........................................ 8
2.1.2 Umbilical cord............................................................ 13
2.1.2.1 Umbilical cord development.................................. 13
2.1.2.2 Connection of umbilical cord to fetal circulatory system........... 16
2.1.3 Anatomy of middle cerebral artery (MCA).......................... 20
2.2.19 Control of Blood Flow to Specific Organs and Dysfunction ........................................44
2.2.20 Physiology of umbilical arteries ..................................................................................44
2.2.21 Cerebral Blood Flow ..................................................................................................45
2.2.22 Cerebral circulation ...................................................................................................46
2.2.23 Physiology of placenta ...............................................................................................50
2.2.24 Secretion of estrogens by the placenta ......................................................................51
2.2.26 Function of estrogen in pregnancy ............................................................................51
2.2.26 Secretion of progesterone by the placenta ..................................................................52
2.2.27 Human Chorionic Somatomammotropin .................................................................53

2.3 Pathology .........................................................................................................................54

2.3.1 Cerebral artery disorders ..............................................................................................54
   2.3.1.2 Atherosclerosis ......................................................................................................54
   2.3.1.3 Aneurysms ...........................................................................................................54
2.3.2 Hemorrhagic cerebrovascular disease .........................................................................56
2.3.3 Ischemia .........................................................................................................................56
2.3.4 Cerebral embolism .........................................................................................................57
2.3.5 Middle cerebral artery syndrome ..................................................................................57
2.3.6 Pathology of umbilical cord ..........................................................................................58
   2.3.6.1 Insertion abnormalities ..........................................................................................58
   2.3.6.2 Abnormal coiling ..................................................................................................60
   2.3.6.3 Nuchal cord ..........................................................................................................60
   2.3.6.4 Umbilical cord knot ..............................................................................................61
   2.3.6.5 Single umbilical artery ........................................................................................63
   2.3.6.6 Umbilical cord cyst ..............................................................................................65
2.3.7 Placental abnormalities ................................................................................................65

XV
2.4.11 Approaches to IUGR

2.4.12 Outcomes and clinical significance

2.5 Theoretical Studies of Doppler ultrasound

2.5.1 Doppler shift for audible sounds

2.5.2 Doppler Shift Applied to vascular ultrasound

2.5.3. The Doppler equation

2.5.4 The Doppler angle

2.5.5 Effect of angle of insonation on the color flow image

2.5.6 Diagnostic Doppler Instruments

2.5.7 Continuous wave Doppler instrumentation

2.5.7.1 The CW Doppler Transducer

2.5.7.2 The Oscillator

2.5.7.3 The Receiver

2.5.8 Pulsed Doppler

2.5.8.1 Pulsed wave Doppler instrumentation

2.5.8.2 Size of the pulsed Doppler Sample Volume

2.5.9 Extracting the Doppler Signal

2.5.10 Duplex ultrasound

2.5.11 Doppler spectral analysis

2.5.11.1 Spectral analysis

2.5.11.2 Spectral Display

2.5.11.3 Diagnostic Spectral Display Features and Measurements
2.5.12 Flow Velocity

2.5.13 Acceleration Time (AT)

2.5.14 Acceleration Index (AI)

2.5.15 Nyquist Limit and Aliasing

2.5.16 Eliminating aliasing

2.5.17 Poiseuille’s Law and Equation

2.6 Previous studies

3. Chapter three

3.1 Material of Study

3.1.1 Tools and equipment

3.1.2 Ultrasound system

3.1.3 Patient preparation

3.2 Method of the study

3.2.1 Examination protocol

3.2.2 Sample selection

3.2.3 Patient position

3.2.4 Transducer position

3.3 Data analysis

3.3.1 Data storage

4. Chapter four

4.1 The results
5. Chapter five

5.1 Discussion .................................................................................................................. 155

5.2 Conclusion .................................................................................................................. 158

5.3 Recommendation ...................................................................................................... 160

Reference ........................................................................................................................ 161
1. Chapter one

1.1 Introduction

Intrauterine Growth Restriction (IUGR) or fetal growth restriction is defined as less than 10th percent of predicted fetal weight for gestational age (Alan, H.D. and N. Lauren, 2003). It is a serious condition in which the fetus is not growing adequately and is smaller than expected for its dates. IUGR is present in almost half of all stillbirths. Surviving infants with severe IUGR are at risk for long-term developmental delay, neuromotor disabilities such as cerebral palsy and neurobehavioral disorders including impaired school performance, social skills, and fine motor control. Epidemiologic studies have linked IUGR with significant metabolic conditions (obesity, type 2 diabetes mellitus) and cardiovascular disorders (ischemic heart disease, hypertension). The fetal origins hypothesis of adult morbidities may be due to insulin resistance, which may be evident in early childhood. (Alan, H.D. and N. Lauren, 2003)

IUGR has many possible causes. A common cause is a problem with the placenta (placental insufficiency), umbilical arteries Doppler provide an estimate of downstream placental vascular resistance and placental blood flow, abnormal blood flow increase risk of fetal acidosis (Asim, Frank, 2006). Less common factors include genetic anomalies, congenital infections, maternal disorders and drugs (John .C, H., 2008).

IUGR may be symmetrical or asymmetrical, symmetrical growth restriction is generally characterized by early-onset (beginning of the 2nd trimester) and a proportional reduction in fetal parameters. This form of IUGR is typically seen in fetuses with chromosome anomalies or infections. Even if recognized in utero, very little can be done to improve fetal outcome. But in the asymmetrical IUGR generally about two-thirds of cases and is generally characterized by late onset
(end of the 2nd or early 3rd trimester) and relative “brainsparing” at the expense of abdominal and soft tissue growth, with varying degrees of compromise in fetal length (Asim Kuorjak, 2006).

Delayed growth puts the Fetus at risk of certain health problems during pregnancy, delivery and after birth. They include low birth weight, decreased oxygen levels, low resistance of infection, low Apgar scores, and other complications. In the most severe cases, IUGR can lead to stillbirth. It can also cause long-term growth problems (Vandenbosche, R.C. and J.T. Kirchner, 1998).

IUGR needs special care to reduce its complications, continuous assessment is a key factor that eliminates these complications and the understanding of assessing parameters should be established. In successive pregnancies, there is a tendency to repeat IUGR/SGA deliveries. To reduce this risk, any potentially treatable causes should be addressed. (e.g. smoking cessation, appropriate nutrition).

Doppler ultrasound can measure blood flow through major fetal arteries or veins and it is used in the evaluation of pregnancies complicated by intrauterine growth restriction. Previously, invasive techniques such as amniocentesis or direct fetal blood sampling had to be performed every few weeks in pregnancies with IUGR for severe fetal anemia that could result in stillbirth (e.g., Rh disease or parvovirus infection). In the late 1990s, maternal-fetal medicine specialists found that Doppler ultrasonography could accurately diagnose moderate to severe fetal anemia by measuring blood flow in the baby’s brain. This novel and noninvasive approach has revolutionized monitoring of pregnancies with IUGR and has made invasive fetal testing for this indication generally unnecessary. (Jane. A Bates, 2004)

Umbilical artery, can be evaluated anywhere along the length of the free-floating
Umbilical cord, angle independent indices (pulsatility index or systolic/diastolic (S/D) ratio) decrease with advancing gestation because of a decreased placental vascular resistance and increase in end-diastolic velocity, which physiologically occurs with advancing gestation. In pathologic conditions, intrauterine-growth-restricted (IUGR) fetuses, the EDF decreased due to blood shunting to vital organs (brain, heart), the umbilical artery wave-forms change and the angle-independent indices become abnormal (values above their reference ranges). These changes reflect an increased placental vascular resistance. (Jane. A Bates, 2004)

Angle-independent indices differ among the different cerebral arteries. The middle cerebral artery is the most studied cerebral artery because (a) it is easy to sample; (b) it provides information on the cerebral blood flow in normal and IUGR fetuses; and (c) it can be sampled at an angle of 0° between the ultrasound beam and the direction of the blood flow (because we can visualize it in an axial view of the fetal head just caudal to the plane of the BPD). Therefore, for the middle cerebral artery we are able to determine angle-independent indices (the most used is the pulsatility index) and also the real velocity of blood flow. In normal fetuses the MCA have a high PI (reduced with advancing GA) and decreased EDF. In IUGR fetuses there is an increase in MCA diastolic flow velocities, and a corresponding decrease in MCA PI reflecting to the redistribution of the blood flow from the fetal periphery to the brain; this phenomenon is called the “brain-sparing effect in response to chronic hypoxemia. In this study we focus our measurements on fetal umbilical and middle-cerebral arteries because of their importance for detection of any abnormalities underlying IUGR.
1.2 Problem of the study:

The intrauterine growth restriction (IUGR) is a global problem, it has high morbidity and high mortality, more than 10% of pregnant women have IUGR. It puts the fetus and maternal at risk of certain health problems during pregnancy, delivery and after birth, poor prenatal outcome will increase mortality rate. In addition there is lack of knowledge about experimental information related to Doppler u/s findings regarding IUGR in Sudan.

1.3 General objective:

1. Ultrasound can assess the fetal well-being and estimated fetal weight (EFW) by using fetometrics values like (BPD, AC, HC, FL) and Doppler ultrasound. This study intended to identify the Doppler ultrasound wave forms velocimetry of fetal umbilical and MC arteries in IUGR in the third trimester.

2. Generally is used in ANC for fetal and neonatal wellbeing and determine the suitable expected delivery date (EDD) according to fetal and maternal situation.

1.4 Specific objectives:

1. To create a reliable reference for the wave forms velocimetry of umbilical and MC arteries in intrauterine growth restriction in the 3rd trimester.

2. To identify the difference and changes between indices in intrauterine growth restriction and normal pregnancy.

3. To detect IUGR and assess fetal well-being in intrauterine growth restriction.

4. To predict early and late onset of IUGR.

5. To differentiate between types of Intrauterine Growth restriction.
Chapter two

(Literature review)
Chapter two

(Literature review)

2.1 Anatomy

2.1.1 Arteries

2.1.1.1 General structure of blood vessels:

Blood vessels differ in structure and function. Blood leaves the heart through the arteries, which conduct the oxygenated blood (except in the case of the pulmonary artery) to the various tissues and organs. Deoxygenated blood returns from the tissues and organs to the heart via a set of vessels, called veins (except the pulmonary vein). The actual exchange of oxygen, carbon dioxide, foodstuffs and waste matter between the blood and the tissue fluid occurs in microscopically small vessels, called capillaries. (Carol M, 2005)

The blood vessels consist of three layers: tunica intima: delimits the vessel wall towards the lumen of the vessel and comprises its endothelial lining (typically simple, squamous) and associated connective tissue. Beneath the connective tissue, we find the internal elastic lamina, which delimits the tunica intima from. The tunica media: is formed by a layer of circumferential smooth muscle and variable amounts of connective tissue. A second layer of elastic fibers, the external elastic lamina, is located beneath the smooth muscle. It delimits the tunica media from. the tunica adventitia: which consist mainly of connective tissue fibres. The tunica adventitia blends with the connective tissue surrounding the vessel. The definition of the outer limit of the tunica adventitia is therefore somewhat arbitrary. (Gailani, 2003)
2.1.1.2 Classification of arteries

Arteries carry blood away from the heart. Pulmonary arteries transport blood that has low oxygen content from the right ventricle to the lungs. Systemic arteries transport oxygenated blood from the left ventricle to the body tissues. Blood is pumped from the ventricles into large elastic arteries that branch repeatedly into smaller and smaller arteries until the branching results in microscopic arteries called arterioles. The arterioles play a key role in regulating blood flow into the tissue capillaries. About 10 percent of the total blood volume is in the systemic arterial system at any given time. (Gartner and Hiatt, 2001).
Table 2-1: Classification of arteries

<table>
<thead>
<tr>
<th>Intima (Internal layer)</th>
<th>Media (Middle layer)</th>
<th>Adventitia (External layer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monolayer of endothelial cells</td>
<td>Smooth muscle cells (SMC) and extracellular matrix (collagen, elastin and proteoglycans)</td>
<td>Connective tissue</td>
</tr>
</tbody>
</table>

The Arteries are further subdivided according to their microscopic structure into the following vessels; large/elastic/conducting arteries are the thick-walled arteries near the heart, i.e. the aorta and its major branches. These arteries are the largest in diameter, ranging from 2.5 cm to 1 cm, and the most elastic. Because their large lumen make them low-resistance pathways that conduct blood from the heart to medium-sized arteries, they are sometimes referred to as conducting arteries. They contain more elastin than any other vessel type. The elastic arteries expand and recoil passively to accommodate changes in blood volume. Consequently, blood flows fairly continuously rather than starting and stopping with the pulsating rhythm of the heartbeat. Aorta, Brachiocephalic, common carotid, Subclavian, Vertebral, Pulmonary, and Common iliac arteries are the elastic arteries. (Carol M, 2005)

Medium-sized/ muscular/distributing arteries lie distal to the elastic arteries. Constituting most of the named arteries seen in the anatomy lab, muscular arteries supply groups of organs, individual organs, and parts of organs, (hence the name distributing). Their internal diameter ranges from that of a little finger (1cm) to that of a pencil lead (about 0.3 mm). They are called muscular because they have very high amount of smooth muscle fibers in the tunica media of their walls. By actively
altering the diameter of the artery, this muscular layer regulates the amount of blood flowing to the organ supplied according to the specific needs of that organ. (Carol M, 2005)

Arterioles are the smallest form of arteries (almost microscopic arteries). Arterioles have a lumen diameter ranging from 0.3 mm down to 10 µm. Larger arterioles have all three tunics, but their tunica media is chiefly smooth muscle with a few scattered elastic fibers. Smaller arterioles which lead to the capillary beds are little more than a single layer of smooth muscle cells spiraling around the endothelial lining. Under the influence of autonomic nervous system (sympathetic and parasympathetic) they play a key role in regulating peripheral blood pressure.

Capillaries are the microscopic vessels connecting the arterioles to the venules. Their diameter is 8 to 10 micron, just large enough for erythrocytes to pass through in single file. The structure of capillaries is well suited to this function. Capillary walls are composed of only a single layer of endothelial cells and a thin basement membrane. They form extensive branching networks called capillary beds that run throughout almost all body tissues, but their number varies with the metabolic activities of the tissue they serve. Capillaries are known as the “exchange vessels" because their prime function is the exchange of nutrients and wastes between the blood and tissue cells through the interstitial fluid Therefore, they are the most important vessels in the circulatory system. (Carol M, 2005)

The body contains three different types of capillaries:

1. Continuous capillaries, are the most common type, they are abundant in skin, skeletal and smooth muscles, connective tissues and lungs. They are continuous in the sense that their endothelial cells provide an uninterrupted lining.
2. Fenestrated capillaries, this variety of capillaries has much greater permeability to fluids and small molecules. They are found where active capillary absorption or filtrate formation occurs like in the kidneys, villi of the small intestine, choroid plexuses of the ventricles in the brain, and some endocrine glands.

3. Sinusoids are wider and more winding than other capillaries, they are highly modified, leaky capillaries found only in certain organs like liver, red bone marrow, lymphoid tissues and some endocrine glands. Their endothelial lining is modified - it exhibits fewer tight junctions and larger intercellular clefts than other capillaries. These structural adaptations allow large molecules (such as proteins) and even blood cells to pass between the blood and the surrounding tissues.

Microcirculation and its Components Capillaries do not function independently. Instead, they tend to form interweaving networks called "capillary beds". The flow of blood from an arteriole to a venule - that is, through a capillary bed - is called the microcirculation. A capillary bed consists of two types of vessels: (1) a vascular shunt (met arteriole - thoroughfare channel), a short vessel that directly connects the arteriole and venule at opposite ends of the bed, and, (2) true capillaries, the actual exchange vessels. The terminal arteriole feeding the bed leads into a metarteriole (a vessel structurally intermediate between an arteriole and a capillary, forming the proximal end of the shunt), which is directly continuous with the thoroughfare channel (intermediate between a capillary and a venule, forming the distal end of the shunt)). The thoroughfare channel joins the postcapillary venule that drains the bed. (Gailani, 2003)

Venules are formed when capillaries unite. The smallest venules, the 'postcapillary venules', consist entirely of endothelium. They are extremely porous and fluid and white blood cells move easily from the bloodstream through their walls. The venules drain blood into the small veins.
Figure 2: shows the capillaries (Gray H, et al 2011)
2.1.2 Umbilical cord

2.1.2.1 Umbilical cord development

The umbilical cord develops when the embryonic disc bulges into the amniotic cavity with the result that the junction between the embryonic disc and the amnion (the amnion-ectodermal junction) is carried into the ventral aspect of the embryo and its line of reflection becomes oval shaped and is called the primitive umbilical ring. By the 5th weeks, the primitive umbilical ring constricts changing the primitive umbilical ringing to a tubular sheath of amnion called the primitive umbilical cord. Rapid enlargement of the amniotic cavity soon occurs and results into excessive lengthening of the umbilical cord flexing movements of the embryo and coils in the amniotic cavity. (Jane. A Bates, 2004)

Figure 3: shows diagram of development of umbilical artery (UA) and Umbilical cord of a three-minute-old child (Chudleigh et al 2004)

When the membranes of the amniotic cavity come into contact with those of the chorionic cavity and the two extra-embryonic mesoderm layers that cover both membranes, fuse. With the flexing movements of the embryo, the amnion encircles the body stalk, the ductus omphalo-entericus and the umbilical vessels, thus circumscribing the elements of the umbilical cord. In the early stage (at around the 8th week) the umbilical cord is in the form of a very thick and short section with the following structures: The ductus
omphalo-entericus which connects the primitive intestines with the umbilical vesicle and two vitelline vessels (vasa omphalomesenterica, 2 arteries and 2 veins). (Asim et al, 2004)

The umbilical vesicle is located in the chorionic cavity (exocoelom = extra-embryonic coelom). The body stalks with the allantoises, the umbilical vessels (2 arteries and 1 vein). During the development it gets shifted ventrally in order to finally fuse with the stem of the umbilical vesicle. The umbilical coelom that connects the extra-embryonic coelom with the intra-embryonic coelom (Jane. A Bates, 2004)

The umbilical cord connects the placenta with the ventral aspect of the embryo. It is a soft tortuous cord which measures 50-60 cm long and about 1 cm in diameter. It contains three umbilical vessels (one vein and two arteries) embedded in agelatinous material called Wharton’s Jelly. The umbilical vein has a wider lumen and a thinner wall than the umbilical arteries. (Jane. A Bates, 2004).
Figure 4: The connection of umbilical artery (UA) with placenta (Chudleigh et al 2004)
2.1.2.2 Connection of umbilical cord to fetal circulatory system:

The umbilical cord enters the fetus via the abdomen, at the point which (after separation) will become the umbilicus (or navel). Within the fetus, the umbilical vein continuous towards the transverse fissure of the liver, where it splits into two. One of these branches joins with the hepatic portal vein (conneting to its left branch), which carries blood into the liver. The second branch (known as the ductus venosus) allows the majority of the incoming blood (approximately 80%) to bypass the liver and flow via the left hepatic vein into the inferior vena cava, which carries blood towards the heart. The two umbilical arteries branch from the internal iliac arteries, and pass on either side of the urinary bladder before term ones. (Jane. A Bates, 2004)
Figure 5: shows the fetal circulation (http://www.developmentalAnatomy.sa.org).
Within the child, the umbilical vein and ductus venosus close up, and degenerate into fibrous remnants known as the round ligament of the liver and the ligamentum venosum respectively. Part of each umbilical artery close up (degenerating into what are known as the medial umbilical ligaments), while the remaining sections are retained as part of the circulatory system. After birth, the umbilical cord is clamped or tied and is then cut. The stump of the cord that remains attached to the baby withers and falls off after a few days, leaving the circular depression in the abdomen known as the navel. (Jane A Bates, 2004).
Figure 6: showed the umbilical artery in ultrasound image (www.u/s images.com)
2.1.3 Anatomy of middle cerebral artery (MCA):

The brain is supplied by four vessels—the right and left internal carotid and vertebral arteries and receives 15% of the cardiac output. The term extracranial cerebral arteries refer to all the arteries that carry blood from the heart up to the base of the skull. The left and right sides of the extracranial circulation are not symmetrical. On the left side, the common carotid (CCA) and subclavian arteries arise directly from the aortic arch, whereas on the right side the brachiocephalic artery, also known as the innominate artery, arises from the aorta and divides into the subclavian artery and CCA. The CCA, which has no branches, divides into the internal and external carotid arteries, but the level of the carotid bifurcation in the neck is highly variable. (Edoardo et al, 2007).

In approximately 90% of cases, the internal carotid artery (ICA) lies posterolateral or lateral to the external carotid artery (ECA) and, unlike the ECA, has no branches below the skull. The proximal branches of the ECA are the superior thyroid, lingual, facial and maxillary arteries. The carotid artery widens, at the level of the bifurcation, to form the carotid bulb. In some cases, the carotid bulb may only involve the proximal ICA, and not the distal CCA, and the degree of widening of the carotid bulb is quite variable. Within the skull, the distal segment of the ICA follows a curved path, known as the carotid siphon. The most important branch of the ICA is the ophthalmic artery, which supplies the eye. The terminal branches of the ophthalmic artery, the supratrochlear and supraorbital arteries, unite with the terminal branches of the ECA. (Edoardo et al, 2007).
Figure 7: anatomy of the middle cerebral artery (MCA) (Gray H, et al 2011)

The ICA finally divides into the middle cerebral artery (MCA) and the anterior cerebral artery (ACA). The posterior circulation of the brain is mainly supplied by the left and right vertebral arteries, via the basilar artery. The vertebral artery is the first branch of the subclavian artery,
arising from the highest point of the subclavian arch. At the sixth cervical vertebra, the vertebral artery runs posteriorly to travel upward through the transverse foramen of the cervical vertebrae. It is common for one vertebral artery to be larger than the other, with the left often being larger than the right. The two vertebral arteries join, at the base of the skull, to form the basilar artery, which then divides to form the posterior cerebral arteries. Show how the circle of Willis, (Drake et al, 2007)

situated at the base of the brain, joins the cerebral branches of the ICAs and basilar artery via the anterior and posterior communicating arteries. Blood flow to the brain is regulated by changes in cerebrovascular resistance, with carbon dioxide playing a major role in vasodilation. (Drake et al, 2007)

2.1.4 Placenta:

Placenta is essentially a fetal organ and represents the link between the developing fetus and the mother. In the human placenta trophoblast erodes into the deciduas so that endothelium of the maternal blood vessels is destroyed and maternal blood is indirect contact with the chorion. Because of that placenta enables the fetus to take oxygen and nutrients from the maternal blood and serves as the excretory organ for carbon dioxide and other waste products of fetal metabolites. As well as that the placenta forms a barrier against the transfer of infection to the fetus and secretes a large amount of hormones in maternal circulation. (Asim K& Frank A.2006)

Many clinical problems are attributed to the placenta despite the fact that they cannot always be explained on pathologic explanation. As placenta has attained its final thickness and shape at the end of the fourth gestational month, this is an ideal time to perform initial ultrasound examination (Asim kurjak & Frank AChervenak-2006).
2.1.4.1 Developmental and anatomy of placenta:

While the trophoblastic cords from the blastocyst are attaching to the uterus, blood capillaries grow into the cords from the vascular system of the newly forming embryo. By the 16th day after fertilization, blood also beings to be pumped by the heart of the embryo itself. Simultaneously, blood sinuses supplied with blood from the mother develop around the outsides of the trophoblastic cords. The trophoblast cells send out more and more projections, which become placental villi into which fetal capillaries grow. Thus, the villi carrying fetal blood are surrounded by sinuses that contain maternal blood. (Asim K& Frank A.2006)

The final structure of the placenta that the fetus’s blood flows throw two umbilical arteries, then into the capillaries of the villi, and the finally back throw a single umbilical vein into the fetus. At the same time the mother’s blood flows from her uterine arteries into large maternal sinuses that surround the villi and then back into the uterine veins of the mother. The total surface area of the villi of mature placenta is only a few square meters—many times less than the area of the pulmonary membrane in the lungs. Nevertheless, nutrients and other substances pass throw this placental membrane mainly by diffusion in much the same manner that diffusion occurs throw the alveolar membranes of the lungs and the capillary membranes elsewhere in the body. (Asim K& Frank A.2006)

2.2 Physiology:

2.2.1 Blood vessels function:
The blood vessels are the part of the circulatory system that transports blood throughout the body. There are three major types of blood vessels: the arteries, which carry the blood away from the heart; the capillaries, which enable the actual exchange of water and chemicals between the blood and the tissues; and the veins, which carry blood from the capillaries back toward the hear. Blood vessels do not actively engage in the transport of blood (they have no appreciable peristalsis), but arteries and veins to a degree can regulate their inner diameter by contraction of the muscular layer. This changes the blood flow to downstream organs, and is determined by the autonomic nervous system. Vasodilatation and vasoconstriction are also used antagonistically as methods of thermoregulation. (Ganong, 1997)

As part of the circulatory system, the blood vessels aid in gas exchange. Oxygen (bound to hemoglobin in red blood cells) is the most critical nutrient carried by the blood. In all arteries, apart from the pulmonary artery, hemoglobin is highly saturated (95-100%) with oxygen. In all veins, apart from the pulmonary vein, the hemoglobin is desiderated at about 75%, but veins carry carbon dioxide, which will eventually be expelled from the lungs. (The values are reversed in the pulmonary circulation.) While blood vessels have no appreciable peristalsis, arteries (and veins, to a degree) can regulate their inner diameter by contraction of the muscular layer. This changes the blood flow to downstream organs, which is determined by the autonomic nervous system. Vasodilatation and vasoconstriction are also used antagonistically as methods of thermoregulation. The endothelium is permeable so that nutrients carried in the blood can be released to the tissues. (Ganong, 1997)

2.2.2 Circulatory system:
The circulatory system also called the cardiovascular system, is an organ system that permits blood to circulate and transport nutrients (such as amino acids and electrolytes), oxygen, carbon dioxide, hormones, and blood cells to and from cells in the body to nourish it and help to fight diseases, stabilize body temperature and pH, and to maintain homeostasis. (Brengelmann, 2003)

The circulatory system is often seen to be composed of both the cardiovascular system, which distributes blood, and the lymphatic system, which circulates lymph. These are two separate systems. The passage of lymph for example takes a lot longer than that of blood. Blood is a fluid consisting of plasma, red blood cells, white blood cells, and platelets that is circulated by the heart through the vertebrate vascular system, carrying oxygen and nutrients to and waste materials away from all body tissues. Lymph is essentially recycled excess blood plasma after it has been filtered from the interstitial fluid (between cells) and returned to the lymphatic system. The cardiovascular (from Latin words meaning 'heart vessel') system comprises the blood, heart, and blood vessels. The lymph, lymph nodes, and lymph vessels form the lymphatic system, which returns filtered blood plasma from the interstitial fluid (between cells) as lymph. (Brengelmann, 2003)

While humans, as well as other vertebrates, have a closed cardiovascular system (meaning that the blood never leaves the network of arteries, veins and capillaries), some invertebrate groups have an open cardiovascular system. The lymphatic system, on the other hand, is an open system providing an accessory route for excess interstitial fluid to get returned to the blood. The more primitive, diploblastic animal phyla lack circulatory systems. (Brengelmann, 2003)

2.2.3 Mechanical events of the cardiac cycle
Cardiac cycle is a term that describes the sequence of events occurring during the cardiac activity in one heart beat. In each cycle the atria and ventricles contract (systole) and relax (diastole) alternately, pumping the blood from areas of high pressure to those of low pressure. The blood is ejected from the atria to the ventricles through the atriovenricular (AV) valves and from the ventricles to the aorta and pulmonary trunk through the semilunar valves (aortic and pulmonary valves). (Emslie-smith rt al, 1998).
Figure 8: the cardiac cycle. (Brengelmann, 2003)

2.2.4 Events in late diastole:
Begins with atrial contraction and occurs just before the first heart sound. Active filling from atrial systole contributes about 20% of the blood volume to the ventricles during diastole (in contrast with the 80% from rapid, passive filling in mid diastole). Normally, active filling is silent, but when blood impacts a stiff, non-compliant ventricle, the result is a fourth heart sound (S4). The presystolic murmur of mitral stenosis also occurs in this phase. (Emslie-smith rt al, 1998)

2.2.5 Arterial systole:

Atrial systole represents the contraction of myocardium of the left and right atria. Atrial systole occurs late in ventricular diastole. One force driving blood from the atria to the ventricles is the decrease in ventricular pressure that occurs during ventricular diastole. The drop in ventricular pressure that occurs during ventricular diastole allows the atrioventricular valves to open, emptying the contents of the atria into the ventricles. Contraction of the atrium confers a relatively minor, additive effect toward ventricular filling; atrial contraction becomes significant in left ventricular hypertrophy, in which the ventricle does not fully relax during ventricular diastole. Loss of normal electrical conduction in the heart, as seen during atrial fibrillation, atrial flutter, and complete heart block, may abolish atrial systole. The aortic valve and pulmonary valve remain closed, while the atrioventricular mitral and tricuspid valves remain open because the pressure gradient between the atrium and ventricle is preserved during late ventricular diastole. (Emslie-smith rt al, 1998)

Atrial fibrillation represents a common electrical malady apparent during the time interval of atrial systole. Theory suggests that an ectopic focus, usually within the pulmonary trunks, competes with
the sinoatrial node for electrical control of the atrial chambers to the detriment of atrial myocardial performance. Ordered sinoatrial control of atrial electrical activity is lost, as a result coordinated pressure generation does not occur in the upper cardiac chambers. Atrial fibrillation represents an electrically disordered but well blood perfused atrial mass working in an uncoordinated fashion with an electrically (comparatively) healthy ventricle. (Emslie-smith rt al, 1998)

Right atrial systole coincides with right ventricular diastole, driving the blood through the tricuspid valve (TV), into the right ventricle. The time variable of right atrial systole, is (TV) open to (TV) close corrected and the Left atrial systole coincides with left ventricular diastole, driving blood through the mitral valve (MV) (also known as the bicuspid valve), into the left ventricle. The time variable of left atrial systole is (MV) open to (MV) close. The atria contain two valves, the mitral (bicuspid) and the tricuspid valves which open during the late stages of diastole. (Emslie-smith rt al, 1998)

2.2.6 Ventricular systole:

Ventricular systole is a written description of the contraction of the myocardium of the left and right ventricles. Ventricular systole induces increased pressure in the left and right ventricles. Pressure in the ventricles rises to a level above that of the atria, thus closing the tricuspid and mitral valves, which are prevented from inverting by chordae tendineae and associated papillary muscles. Ventricular pressure continues to rise in isovolumetric contraction with maximal pressure generation (max dP/dt) occurring during this phase, until the pulmonary and aortic valves open in the ejection phase. In the ejection phase, blood flows down its pressure gradient through the aorta and pulmonary artery from left and right ventricles respectively. It is important to note that cardiac
muscle perfusion through coronary vessels does not occur during ventricular systole, but occurs during ventricular diastole. Ventricular systole is the origin of the pulse. (Brengelmann, 2003)

Right ventricular systole drives blood through the pulmonary valve (PV) into the lungs. Right ventricular systole is volumetrically defined as right ventricular ejection fraction (RVEF). The time variable of right ventricular systole is PV open to PV close. Increased RVEF is indicative of pulmonary hypertension. Left ventricular systole drives blood through the aortic valve (AV) to the body and organs excluding the lungs. Left ventricular systole is volumetrically defined as left ventricular ejection fraction (LVEF). The time variable of left ventricular systole is AV open to (AV) close (Ganong, 1997)

2.2.7 Early diastole:

Begins with the second heart sound (S2). Early diastolic murmurs run right out of S2 and are decrescendo in shape. They are the result of backflow from pulmonic regurgitation or aortic regurgitation. (Brengelmann, 2003)

2.2.8 Mid diastole:

Begins when the tricuspid and mitral valves open, also known as the rapid filling phase, because about 80% of ventricular filling occurs passively in this period (in contrast with the 20% filling that occurs during active atrial contraction). Usually the rapid filling phase is silent, but when blood emptied from the atrium encounters an already full or distended ventricle, the impact of blood results in a third heart sound (S3). Diastases is a period of minimal filling between the rapid filling phases of mid diastole and presystole . (Brengelmann, 2003)
Table 2.2 cardiac cycle diastole phase

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early Diastole</strong></td>
<td>Ventrices relax.</td>
</tr>
<tr>
<td></td>
<td>Semilunar valves close.</td>
</tr>
<tr>
<td></td>
<td>Atrioventricular valves open.</td>
</tr>
<tr>
<td></td>
<td>Ventrices fill with blood.</td>
</tr>
<tr>
<td><strong>Mid Diastole</strong></td>
<td>Atria and Ventricles are relaxed.</td>
</tr>
<tr>
<td></td>
<td>Semilunar valves are closed.</td>
</tr>
<tr>
<td></td>
<td>Atrioventricular valves are open.</td>
</tr>
<tr>
<td></td>
<td>Ventricles continue to fill with blood.</td>
</tr>
<tr>
<td><strong>Late Diastole</strong></td>
<td>SA node contracts.</td>
</tr>
<tr>
<td></td>
<td>Atria contract.</td>
</tr>
<tr>
<td></td>
<td>Ventricles fill with more blood.</td>
</tr>
<tr>
<td></td>
<td>Contraction reaches AV node.</td>
</tr>
</tbody>
</table>

2.2.9 Duration of cardiac cycle:
The duration of the cardiac cycle is inversely proportional to the heart rate. The cardiac cycle duration increases with a decrease in the heart rate and on the other hand it shortens with increasing heart rate. At a normal heart rate of 75 beats per minute, one cardiac cycle lasts 0.8 second. Under resting conditions, systole occupies $\frac{1}{3}$ and diastole $\frac{2}{3}$ of the cardiac cycle duration. At an increasing heart rate (e.g. during an intensive muscle work), the duration of diastole decreases much more than the duration of systole (Systole: 0.27 sec, Diastole: 0.53 sec). (Brengelmann, 2003).

**Figure 9**: diagram shows the cardiac cycle time (Guyton A.et al 2006)

2.2.10 Cardiac function curve:
A cardiac function curve is a graph showing the relationship between right atrial pressure (x-axis) and cardiac output (y-axis). Superimposition of the cardiac function curve and venous return curve is used in one hemodynamic model. (Brengelmann, 2003)

Figure 10: shows the cardiac cycle curve (Guyton A. et al. 2006)

2.2.10.1 Shape of curve:
It shows a steep relationship at relatively low filling pressures and a plateau, where further stretch is not possible and so increases in pressure have little effect on output. The pressures where there is a steep relationship lie within the normal range of right atrial pressure (RAP) found in the healthy human during life. This range is about -1 to +2 mmHg. The higher pressures normally occur only in disease, in conditions such as heart failure, where the heart is unable to pump forward all the blood returning to it and so the pressure builds up in the right atrium and the great veins. Swollen neck veins are often an indicator of this type of heart failure.

At low right atrial pressures this graph serves as a graphic demonstration of the Frank–Starling mechanism, that is as more blood is returned to the heart, more blood is pumped from it without extrinsic signals. (Brengelmann, 2003)

2.2.10.2 Changes in the cardiac function curve:
Extrinsic factors such as an increase in activity of the sympathetic nerves, and a decrease in vagal tone cause the heart to beat more frequently and more forcefully. This alters the cardiac function curve, shifting it upwards. This allows the heart to cope with the required cardiac output at a relatively low right atrial pressure. We get what is known as a family of cardiac function curves, as the heart rate increases before the plateau is reached, and without the RAP having to rise dramatically to stretch the heart more and get the Starling effect. In vivo sympathetic outflow within the myocardium is probably best described by the time honored description of the sinoatrial tree branching out to Purkinges fibers. Parasympathetic inflow within the myocardium is probably best described by influence of the vagus nerve and spinal accessory ganglia. (Brengelmann, 2003)

Figure 11: Changes in the cardiac function curve (Guyton A.et al 2006)

2.2.11 Blood flow control:
The physiological mechanisms controlling organ blood flow encompass local, hormonal, neural and long term actions. Regulating blood flow is important to maintain the varying needs of different organs and tissues while the body is in various states of rest or exertion. Dysfunction with this control can have major consequences. (Emslie-smith rt al, 1988)

2.2.11.1 Local Control:

Autoregulation refers to the ability of each tissue to maintain normal blood flow during changes in arterial pressure between ~70-175 mmHg by changing vascular resistance. (Emslie-smith rt al, 1998)

![Graph demonstrating autoregulation](Guyton A.et al 2006)

During auto regulation, the increase in pressure initiates increases in vascular resistance via local control mechanisms. The resultant decrease in arterial pressure reduces the blood flow. The converse is also true. This active and entirely local process allows blood flow to be maintained at
a fairly constant rate. Two theories have been suggested to explain the phenomenon: (a) metabolic theory and (b) myogenic theory. (Emslie-smith et al., 1998)

### Table 2-3. Theories of Auto-regulation

<table>
<thead>
<tr>
<th></th>
<th>What happens when arterial pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drops</td>
</tr>
<tr>
<td><strong>(a) Metabolic theory</strong></td>
<td></td>
</tr>
<tr>
<td>Nutrients:</td>
<td>↓</td>
</tr>
<tr>
<td>Metabolic products:</td>
<td>↑ (especially effect of O2)</td>
</tr>
<tr>
<td></td>
<td>Rises</td>
</tr>
<tr>
<td><strong>(b) Myogenic theory</strong></td>
<td></td>
</tr>
<tr>
<td>Degree of stretch:</td>
<td>↓</td>
</tr>
<tr>
<td>Causing smooth muscle:</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Contraction</td>
</tr>
<tr>
<td>Resulting in:</td>
<td>Arteriolar dilation, vascular resistance decreases and blood flow increases to normal</td>
</tr>
<tr>
<td></td>
<td>Arteriolar constriction, vascular resistance increases and blood flow decreases to normal</td>
</tr>
</tbody>
</table>

#### 2.2.12 Metabolic Theory of Autoregulation:

When arterial pressure increases, the increased flow provides excessive nutrients to the tissue and removes vasodilators released by the tissues. This causes the blood vessels to constrict and the flow returns to normal. The same applies for the converse. (Emslie-smith et al., 1998)

The myogenic mechanisms are especially evident in arterioles and this is important because it prevents excessive stretch of blood vessels in response to increases in blood pressure. However, the role of myogenic mechanism in blood flow regulation is unclear because only changes in pressure are detected directly. This can be observed in vigorous exercise when the metabolic needs
of muscle tissue increase rapidly and override myogenic mechanisms allowing blood flow to increase significantly meeting the increased requirements. (Emslie-smith rt al, 1998)

2.2.13 Active Metabolic Hyperemia:

Two mechanisms have been suggested pertaining to a higher metabolic function of tissues: Vasodilator theory: The rate of accumulation of vasodilatory metabolic byproducts is a function of both tissue perfusion and metabolic rate. Higher metabolism or decreased tissue perfusion leads to an accumulation of vasodilator substances. These diffuse through the tissue, causing the vessels to dilate and so increase blood flow. Vasodilatory products may include: adenosine, adenosine phosphate compounds, carbon dioxide. Oxygen Lack theory: Vascular muscle contraction requires adequate availability of nutrients and oxygen. If concentrations of these substances decrease contractility will eventually be compromised, leading to vasodilatation.

After a period of vascular occlusion, blood flow to the tissue increases relative to the period of the blockage. That is, the extra blood flow makes up for the tissue blood flow deficit during the time the tissue was obstructed. This transient rise in blood flow is achieved by the activation of vasodilatory factors (Emslie-smith rt al, 1998)

2.2.14 Endothelium Derived Local Factors:

The endothelial cells lining the blood vessels synthesize several substances that can affect the degree of relaxation and contraction of the arterial wall. Nitric Oxide (NO): One of the most important endothelial-derived relaxing factors, nitric oxide is synthesized from arginine and oxygen via nitric oxide syntheses, by the reduction of inorganic nitrate. This occurs in response to a variety of chemical and physical stimuli. The wall shear stress caused by blood flow contorts the
endothelial cells in the direction of flow causing increased release of NO. Its plasma half-life is only ~6 seconds and thus it acts mainly locally causing dilation. However the diameters of the larger vessels are still increased due to the shear stress and increased flow from the smaller vessels. Endothelin-A Endothelin causes powerful vasoconstriction. It increases in the endothelial cells when vessels are injured and prevents extensive bleeding. It is believed to contribute to vasoconstriction when the endothelium is damaged by hypertension or during trauma. (Emslie-smith rt al, 1998)

2.2.15 Ions and Chemicals:

Several ions and chemicals in the body can dilate or constrict local blood vessels (Table 4). Most however have little function in the overall regulation of circulation (Emslie-smith rt al, 1998)

<table>
<thead>
<tr>
<th>Ion / Chemical Factor</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in Ca$^{2+}$</td>
<td>Vasoconstriction — form the general effect of calcium to stimulate smooth muscle contraction</td>
</tr>
<tr>
<td>Increase in K$^+$</td>
<td>Vasodilation — from the ability of potassium ions to inhibit smooth muscle contraction</td>
</tr>
<tr>
<td>Increase in Mg$^{2+}$</td>
<td>Powerful vasodilation — inhibit smooth muscle contraction</td>
</tr>
<tr>
<td>Increase in H$^+$ (decrease in pH)</td>
<td>Dilation of arterioles (increase in pH would cause the opposite effect)</td>
</tr>
<tr>
<td>Acetate and citrate anions</td>
<td>Mild vasodilation</td>
</tr>
<tr>
<td>Increase in CO$_2$</td>
<td>Moderate vasodilation, marked vasodilation in the brain.</td>
</tr>
</tbody>
</table>

Table 4: Ions that dilate or constrict local blood vessels

38
2.2.16 Neural Control:

Neural control of organ blood flow is achieved through autonomic input to cardiovascular tissues. The parasympathetic system acts while a person is at rest while the sympathetic system is activated upon mild exertion or stimulation. The heart and a small number of blood vessels are innervated by the parasympathetic nervous systems. Parasympathetic innervation is largely limited to cardiac function. (Emslie-smith rt al, 1998)

On the other hand, the sympathetic nervous system innervates the heart and many blood vessels, consequently having a wider range of control. This system generates a response via noradrenalin released from nerve terminals or adrenaline released from the adrenal medullae. The type of response is dependent on the predominant type of adrenoceptor in the tissue. (Emslie-smith rt al, 1998)

- Alpha-1 adrenoceptor stimulation causes constriction of blood vessels, thus reducing blood flow. It predominantly effects arteries and arterioles except the coronary arteries, hepatic artery and skeletal muscle arteries/arterioles

- Beta-2 adrenoceptor stimulation causes vasodilatation and thus increased blood flow. These are predominant in arteries and arterioles of the coronary and skeletal muscle vasculature as well as the hepatic artery

In vessels with multiple layers of smooth muscle only the outer layer is innervated by the sympathetic system. The contractility of the inner layer is dependent upon noradrenalin diffusion and the intercellular transmission of depolarizing potentials via gap junctions.
Figure 13: Autonomic Control of the Heart and Blood Vessels (Guyton A.et al 2006)
2.2.16.1 Vasomotor Centre:

The vasomotor centre (cardiovascular control centre) lies in the medulla and pons. Here, parasympathetic impulses are transmitted to the heart via the vagus nerve. Sympathetic impulses are conducted via the spinal cord and peripheral sympathetic nerves to practically all the veins, arterioles and arteries. The vasomotor centre itself can be controlled by the hypothalamus and cerebral cortex.

Table: Sections of the vasomotor centre

<table>
<thead>
<tr>
<th>Section</th>
<th>Location</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasoconstrictor</td>
<td>Bilaterally in the anterolateral parts of the</td>
<td>Neurones distribute their fibres to the spinal cord.</td>
</tr>
<tr>
<td>area</td>
<td>upper medulla</td>
<td>Excite preganglionic vasoconstrictor nerves [sympathetic stimulation]</td>
</tr>
<tr>
<td>Vasodilator area</td>
<td>Bilaterally in the anterolateral section of the</td>
<td>Neuron fibres project to the vasoconstrictor area and inhibit activity here thus causing vasodilation</td>
</tr>
<tr>
<td></td>
<td>lower half of the medulla</td>
<td></td>
</tr>
<tr>
<td>Sensory area</td>
<td>Bilaterally in the tractus solitaries within the</td>
<td>Neurones get sensory nerve signals from the circulatory system- primarily through glossopharyngeal and vagus nerves. Output signals help controlling activities in the other two areas. This provides the “reflex control” of many circulatory functions.</td>
</tr>
<tr>
<td></td>
<td>posterolateral part of medulla and pons</td>
<td></td>
</tr>
</tbody>
</table>

Table5: Sections of the vasomotor centre.

The lateral parts of the vasomotor centre (shown in Table 3) transmit excitatory impulses to increase heart rate and contractility via the sympathetic system. The medial parts signal the dorsal
motor nuclei of the vagus nerve, transmitting parasympathetic impulses to the heart via the vagus nerve. Consequently heart rate and contractility decreases. Sympathetic nerve fibers stimulate the adrenal medullae to release noradrenalin and adrenaline into the blood circulation. Here they act directly in blood vessels usually stimulating vasoconstriction and occasionally stimulating vasodilatation via beta-adrenoceptors. (Brengelmann, 2003)

2.2.17 Hormonal Control:

Histamine is released in essentially every tissue of the body in response to damage or inflammation. It is a powerful vasodilator and increases capillary porosity to allow leakage of fluid and plasma protein into the tissues occasionally leading to oedema. Bradykinin causes both arteriolar dilation and increased capillary permeability. Once formed it only persists for a few minutes, as it is inactivated by the enzymes carboxypeptidase N or angiotensin converting enzyme. It acts via B2 kinin receptors to stimulate the release of endothelium-derived nitric oxide, prostacyclin, and hyperpolarizing factor. These hormones, secreted from the adrenal gland and from nerve endings in tissues, are powerful vasoconstrictors. When the sympathetic nervous system is stimulated, nerve endings release noradrenalin, contracting the vessels via alpha-adrenoceptors. Additionally, the sympathetic nerves cause the adrenal medullae to secrete noradrenalin and adrenaline which act systemically. (Brengelmann, 2003)

Angiotensin II powerfully constricts small arterioles. The blood flow can be severely decreased if this occurs in an isolated tissue area. Vasopressin is an even more powerful vasoconstrictor than angiotensin II. It is formed in the hypothalamus of the brain and transported to the posterior pituitary where it is secreted in the blood. (Brengelmann, 2003)
2.2.18 Long Term Control of Blood Flow:

Long-term control is primarily the domain of:

- angiogenesis
- vascular remodeling

These are in response to changes in tissue requirements.

These processes alter both the size and number of blood vessels supplying the tissue, thus regulating perfusion. Oxygen availability in the tissue is an important mediator of long-term control with sustained or repeated transient decreases in availability stimulating angiogenesis and vascular remodelling. This is achieved by the release of growth factors such as vascular endothelial growth factor and angiogenin by the tissue in response to decreased oxygen availability. (Brengelmann, 2003)

2.2.19 Control of Blood Flow to Specific Organs and Dysfunction

Organs have differing metabolic needs in various situations and require blood flow for various reasons (e.g. thermoregulation at the skin). Thus the control of blood flow to various organs differs greatly and a variety of problems can disrupt and alter the blood supply to individual organs. (Brengelmann, 2003)

2.2.20 Physiology of umbilical arteries:

The umbilical arteries transport wastes, such as carbon dioxide, from the fetus to the placenta. Fetuses have two arteries that travel through the umbilical cord and one vein. The vein transports
fresh blood, containing oxygen and nutrients, from the placenta to the baby’s body. (Guyton Arther C. and Hall John E- 2004)

The deoxygenated blood is supplied from the fetus to the placenta (in the umbilical cord) of the mother by the Umbilical arteries. Usually 2 umbilical arteries together with one umbilical vein are present in the umbilical cord. The umbilical arteries supply the blood and nutrients to the hind limbs in the fetus. These are located surrounding the urinary bladder. They carry all the deoxygenated blood out through the umbilical cord of the fetus. Other than the Pulmonary arteries, only the umbilical arteries carry deoxygenated blood in the humans. (Guyton Arther C. and Hall John E- 2004)

2.2.21 Cerebral Blood Flow:

Control of cerebral blood flow relies heavily upon intrinsic mechanisms. Local chemical factors are important role in directing and controlling blood flow to specific areas of the brain. These are; CO2, H+ ions, O2 and Substances released from astrocytes. (Brengelmann, 2003)

Cerebral blood flow is tightly regulated by autoregulation, with a steady blood flow being maintained between pressures of 60 and 140mmHg. ANS input is less important and does not greatly affect the constriction of cerebral arterioles. However, sympathetic activity serves as a protective mechanism in rare circumstances when exceedingly high pressures are reached. Sympathetic innervation constricts cerebral arterioles at these high pressures minimizing chance of heamorrhage, thus preventing stroke. The organisation of the vessels also minimises this risk. Two carotids and two vertebral arteries feed into a ring of vessels supplying the brain known as the Circle of Willis. This provides many collaterals and thus if one branch becomes stenosed or
occluded blood generally still reaches the part of the brain supplied by that vessel. (Brengelmann, 2003)

Cerebral blood flow is needed to be tightly regulated. When there is hyperemia, intracranial pressure can increase, leading to compression and damage of cerebral tissue. Cerebral damage can also result from ischemia as a result of such factors as stroke or shock. (Brengelmann, 2003)

2.2.22 Cerebral circulation:

Is the movement of blood through the network of blood vessels supplying the brain. The arteries deliver oxygenated blood, glucose and other nutrients to the brain and the veins carry deoxygenated blood back to the heart, removing carbon dioxide, lactic acid, and other metabolic products. Since the brain is very vulnerable to compromises in its blood supply, the cerebral circulatory system has many safeguards. Failure of these safeguards results in cerebrovascular accidents, commonly known as strokes. The amount of blood that the cerebral circulation carries is known as cerebral blood flow. The presence of gravitational fields or accelerations also determine variations in the movement and distribution of blood in the brain, such as when suspended upside-down (Brengelmann, 2003)

The arterial cerebral circulation is normally divided into anterior cerebral circulation and posterior cerebral circulation. There are two main pairs of arteries that supply the cerebral arteries and the cerebrum: Internal carotid arteries and vertebral arteries. The anterior and posterior cerebral circulations are interconnected via bilateral posterior communicating arteries. They are part of the Circle of Willis, which provides backup circulation to the brain. In case one of the supply arteries is occluded, the Circle of Willis provides interconnections between the anterior and the posterior
cerebral circulation along the floor of the cerebral vault, providing blood to tissues that would otherwise become ischemic. (Brengelmann, 2003)

Figure 14: demonstrate cortical vascular territorie (Guyton A.et al 2006)

The anterior cerebral circulation is the blood supply to the anterior portion of the brain. It is supplied by: Internal carotid arteries These large arteries are the left and right branches of the common carotid arteries in the neck which enter the skull, as opposed to the external carotid branches which supply the facial tissues. The internal carotid artery branches into the anterior
cerebral artery and continues to form the middle cerebral artery, anterior cerebral artery (ACA), Anterior communicating artery connects both anterior cerebral arteries, within and along the floor of the cerebral vault and Middle cerebral artery (MCA)

The posterior cerebral circulation is the blood supply to the posterior portion of the brain, including the occipital lobes, cerebellum and brainstem. It is supplied by the; vertebral arteries: These smaller arteries branch from the subclavian arteries which primarily supply the shoulders, lateral chest and arms. Within the cranium the two vertebral arteries fuse into the basilar artery, Posterior inferior cerebellar artery (PICA), Basilar artery Supply the midbrain, cerebellum, and usually branches into the posterior cerebral artery, Anterior inferior cerebellar artery (AICA).Pontine branches, Superior cerebellar artery (SCA), Posterior cerebral artery (PCA)and finally the Posterior communicating artery.

The venous drainage of the cerebrum can be separated into two subdivisions: superficial and deep. The superficial system is composed of dural venous sinuses, which have wall composed of dura mater as opposed to a traditional vein. The dural sinuses are, therefore located on the surface of the cerebrum. The most prominent of these sinuses is the superior sagittal sinus which flows in the sagittal plane under the midline of the cerebral vault, posteriorly and inferiorly to the torcula, forming the confluence of sinuses, where the superficial drainage joins with the sinus that primarily drains the deep venous system. From here, two transverse sinuses bifurcate and travel laterally and inferiorly in an S-shaped curve that forms the sigmoid sinuses which go on to form the two jugular veins. In the neck, the jugular veins parallel the upward course of the carotid arteries and drain blood into the superior vena cava.
The deep venous drainage is primarily composed of traditional veins inside the deep structures of the brain, which join behind the midbrain to form the vein of Galen. This vein merges with the inferior sagittal sinus to form the straight sinus which then joins the superficial venous system mentioned above at the confluence of sinuses.

Figure 15: shows the cerebral venous drainage (Guyton A. et al. 2006)

### 2.2.23 Physiology of placenta:

The perfusion of the intervillous spaces of the placenta with maternal blood allows the transfer of nutrients and oxygen from the mother to the fetus and the transfer of waste products and carbon
dioxide back from the fetus to the maternal blood supply. Nutrient transfer to the fetus occurs via both active and passive transport. Active transport systems allow significantly different plasma concentrations of various large molecules to be maintained on the maternal and fetal sides of the placental barrier. Adverse pregnancy situations, such as those involving maternal diabetes or obesity, can increase or decrease levels of nutrient transporters in the placenta resulting in overgrowth or restricted growth of the fetus. Waste products excreted from the fetus such as urea, uric acid, and creatinine are transferred to the maternal blood by diffusion across the placenta. IgG antibodies can pass through the human placenta, thereby providing protection to the fetus in utero. This transfer of antibodies begins as early as the 20th week of gestational age, and certainly by the 24th week. This passive immunity lingers for several months after birth, thus providing the newborn with a carbon copy of the mother's long-term humoral immunity to see the infant through the crucial first months of extrauterine life. IgM, however, cannot cross the placenta, which is why some infections acquired during pregnancy can be hazardous for the fetus. (Guyton Arther C. and Hall John E- 2004)

Furthermore, the placenta functions as a selective maternal-fetal barrier against transmission of microbes. However, insufficiency in this function may still cause mother-to-child transmission of infectious diseases. Also in humans, aside from serving as the conduit for oxygen and nutrients for fetus, the placenta secretes, from the syncytial layer of chorionic villi, hormones that are important during pregnancy. (Guyton Arther C. and Hall John E- 2004)

2.2.24  Secretion of estrogens by the placenta:

The placenta like the corpus luteum secretes both estrogens and progesterone. Histochemical and physiological studies show that these two hormones like most other placental hormones, are
secreted by the syncytial trophoblast cells of the placenta. Toward the end of pregnancy, the daily production of placental estrogens increases to about 30 times the mother’s normal level of production. However the secretion of the estrogens by the placenta is quite different from secretion by the ovaries. Most important the estrogens secreted by the placenta are not synthesizes from basic substrates in the placenta. Instead they are form almost entirely from androgenic steroid compounds, dehydroepiandrosterone and 16 hydroxydehydroepiandrosterone which are formed both in the mother’s adrenal glands and in the adrenal of the fetus. This weak androgens are transported by the blood to the placenta and converted by the trophoblact cells into estradiol, estrone, and estrion. (the cortices of the fetal adrenal glands are extremely large, and about 80 per cent consist of a so-called fetal zone, the primary function of which seems to be to secret dehydroepiandrosterone during pregnancy.) Guyton Arther C. and Hall John E- 2004)

2.2.25 Function of estrogen in pregnancy:

These hormones exert mainly a proliferative on most reproductive and associated organs of the mother. During pregnancy, the extreme quantities of estrogens cause (1) enlargement of the mother’s uterus, (2) enlargement of the mother’s breasts and growth of the breast ductal structure, and (3) enlargement of mother’s female external genitalia. The estrogens also relax the pelvic ligaments of the mother, so that the sacroiliac joints become relatively limber and the symphysis pubis becomes elastic. These changes allow easier passage of the fetus throw the birth canal. There is much reason to believe that estrogens also affect many general aspects of fetal development during pregnancy, for example, by affecting the rate of reproduction in the early embryo. (Guyton Arther C. and Hall John E- 2004)

2.2.26 Secretion of progesterone by the placenta:
Progesterone is also essential for successful pregnancy—in fact, it is just as important estrogen. In addition to being secreted in moderate quantities by the corpus luteum at the beginning of pregnancy, it is secreted later in tremendous quantities by the placenta, averaging about a 10-fold increase during the course of pregnancy. The special effects of progesterone that are essential for the normal progression of pregnancy are as follows:

Progesterone causes decidual cells to develop in uterine endometrium, and these cells play an important role in the nutrition of the early embryo, decreases the causing of contractility of the pregnant uterus, thus preventing uterine contraction from causing spontaneous abortion, contributes it specifically increase the secretion of the mother’s fallopian tubes and uterus to provide appropriate nutritive matter for the developing morula uand blastocyst. There is also reason to believe that progesterone affects cell cleavage in the early developing embryo. The progesterone secreted during pregnancy helps the estrogen prepare the mother’s breasts for lactation. (Guyton Arther C. and Hall John E- 2004)

### 2.2.27 Human Chorionic Somatomammotropin:

A more recently discovered placenta hormone is called human chorionic somatomamotropin. It is a protein with a molecular weight of about 38,000, and it begins to be secreted by the placenta at about the fifth week of pregnancy. Secretion of this hormone increases progressively throughout the remainder of pregnancy in direct proportion to the weight of the placenta. Although the functions of the chorinic Somatomamomotropin are uncertain, it is secreted in quantities several times greater than all the other pregnancy hormones combined. it has several possible important effects. First, when administered to several types of lower animals, human chorionic Somatomamomotropin causes at least partial development of the animals breasts and in some
instances causes lactation. Because this was the first function of the hormone discovered, it was first named human placental lactogen and was believed to have functions similar to those of prolactin. (Guyton Arthur C. and Hall John E- 2004)

however, attempts to promote lactation in humans with its use have not been successful. Second, this hormone has weak actions similar to those of growth hormone does. It also has a chemical structure similar to that of growth hormone, but 100 times as human chorionic Somatomammotropin as growth hormone is required to promote growth. Third, human chorionic Somatomammotropin causes decreased insulin sensitivity and decreased utilization of glucose in the mother, thereby making larger quantities of glucose available to the fetus. Because glucose is the major substrate used by the fetus to energize its growth, the possible importance of such a hormonal effect is obvious. Further, the hormone promotes the release of free fatty acids from the fat stores of the mother, thus providing this alternative source of energy for the mother’s metabolism during pregnancy. Therefore, it appears that human chorionic Somatomammotropin is a general metabolichormone that has specific nutritional implications for both the mother and the fetus (Guyton Arthur C. and Hall John E-2004)

### 2.3 Pathology

#### 2.3.1 Cerebral artery disorders:

Cerebrovascular disease refers to a group of conditions that affect the circulation of blood to the brain, causing limited or no blood flow to affected areas of the brain.

##### 2.3.1.1 Strokes:
Strokes are a heterogeneous group of disorders involving sudden, focal interruption of cerebral blood flow that causes neurologic deficit. Strokes can be ischemic (80%), typically resulting from thrombosis or embolism, or hemorrhagic (20%), resulting from vascular rupture (eg, subarachnoid or intracerebral hemorrhage). Transient stroke symptoms (typically lasting < 1 h) without evidence of acute cerebral infarction (based on diffusion-weighted MRI) are termed a transient ischemic attack (TIA). In the US, stroke is the 4th most common cause of death and the most common cause of neurologic disability in adults. Strokes involve the arteries of the brain either the anterior circulation (branches of the internal carotid artery) or the posterior circulation (branches of the vertebral and basilar arteries). (Kumar et al, 1997).

2.3.1.2 Atherosclerosis
Is one of the conditions that can cause cerebrovascular disease. During this process, high cholesterol levels coupled with inflammation in areas of the arteries in the brain can cause the cholesterol to build up in the vessel in the form of a thick, waxy plaque. This plaque can limit, or completely obstruct, blood flow to the brain, causing a stroke, transient ischemic attacks, or dementia, which may lead to a variety of other health complications. (Kumar et al, 1997).

2.3.1.3 Aneurysms:
A cerebral (or cranial) aneurysm is an area where a blood vessel in the brain weakens, resulting in a bulging or ballooning out of part of the vessel wall. Usually, aneurysms develop at the point where a blood vessel branches, because the "fork" is structurally more vulnerable. The disorder may result from congenital defects or from other conditions such as high blood pressure, atherosclerosis (the buildup of fatty deposits in the arteries), or head trauma. (Kumar et al, 1997).

Aneurysms occur in all age groups, but the incidence increases steadily for individuals age 25 and older, is most prevalent in people ages 50 to 60, and about three times more prevalent in women.
The outcome for patients treated before a ruptured aneurysm is much better than for those treated after, so the need for adequate evaluation of patients suspected of having a cerebral aneurysm is very important. (Kumar et al, 1997).

Unruptured cerebral aneurysms can be detected by noninvasive measures, including MRA and a carotid angiogram. A rupture can be detected by a CT scan or lumbar puncture. If these tests suggest the presence of an aneurysm, formal cerebral angiography may be performed.

People who suffer a ruptured brain aneurysm may have some or all of these warning signs: localized headache, nausea and vomiting, stiff neck, blurred or double vision, sensitivity to light (photophobia), or loss of sensation. Many people with unruptured brain aneurysms have no symptoms. Others might experience some or all of the following symptoms, which may be possible signs of an aneurysm: cranial nerve palsy, dilated pupils, double vision, pain above and behind eye, and localized headache. (Kumar et al, 1997).

When cerebral aneurysms rupture, they usually cause bleeding in the brain, resulting in a subarachnoid hemorrhage. Blood can also leak into the cerebrospinal fluid (CSF) or areas surrounding the brain and cause an intracranial hematoma (a blood clot). Blood can irritate, damage, or destroy nearby brain cells. This may cause problems with bodily functions or mental skills. In more serious cases, the bleeding may cause brain damage, paralysis or coma. Ruptured brain aneurysms are fatal in about 50 percent of cases. (Kumar et al, 1997).

2.3.2 Hemorrhagic cerebrovascular disease:

Intracranial hemorrhage falls into two major categories: (1) spontaneous hemorrhage (associated with hypertension and with congenital or other arterial aneurysms and arteriovenous
malformations); and (2) traumatic hemorrhages into the epidural, subdural, and subarachnoid spaces or parenchyma of the central nervous system. Spontaneous intracranial hemorrhage accounts for approximately 20% of all strokes. The primary hemorrhage may be into the parenchyma of the central nervous system or into the subarachnoid space. Parenchymal hemorrhages often rupture into the ventricular system or into the subarachnoid space; whereas primary subarachnoid hemorrhages frequently dissect into the cerebral parenchyma.

2.3.3 Ischemia

Cerebral ischemia is a condition in which there is insufficient blood flow to the brain to meet metabolic demand. This leads to poor oxygen supply or cerebral hypoxia and thus to the death of brain tissue or cerebral infarction / ischemic stroke. It is a sub-type of stroke along with subarachnoid hemorrhage and intracerebral hemorrhage. Ischemia leads to alterations in brain metabolism, reduction in metabolic rates, and energy crisis. There are two types of ischemia: focal ischemia, which is confined to a specific region of the brain; and global ischemia, which encompasses wide areas of brain tissue. The main symptoms involve impairments in vision, body movement, and speaking. The causes of brain ischemia vary from sickle cell anemia to congenital heart defects. Symptoms of brain ischemia can include unconsciousness, blindness, problems with coordination, and weakness in the body. Other effects that may result from brain ischemia are stroke, cardiorespiratory arrest, and irreversible brain damage.

An interruption of blood flow to the brain for more than 10 seconds causes unconsciousness, and an interruption in flow for more than a few minutes generally results in irreversible brain damage. In 1974, Hossmann and Zimmerman demonstrated that ischemia induced in mammalian brains for
up to an hour can be at least partially recovered. Accordingly, this discovery raised the possibility of intervening after brain ischemia before the damage becomes irreversible.

2.3.4 Cerebral embolism:

A condition in which an embolus blocks blood flow through the vessels of the cerebrum, resulting in tissue ischemia distal to the occlusion, sudden blocking of an artery by a clot of foreign material (EMBOLUS) that has been brought to its site of lodgment by the blood current. The obstructing material is most often a blood clot, but it may be a fat globule, air bubble, piece of tissue, or clump of bacteria.

2.3.5 Middle cerebral artery syndrome:

Is a condition whereby the blood supply from the middle cerebral artery (MCA) is restricted, leading to a reduction of the function of the portions of the brain supplied by that vessel: the lateral aspects of frontal, temporal and parietal lobes, the corona radiata, globus pallidus, caudate and putamen. The MCA is the most common site for the occurrence of ischemic stroke depending upon the location and severity of the occlusion, signs and symptoms may vary within the population affected with MCA syndrome. More distal blockages tend to produce milder deficits due to more extensive branching of the artery and less ischemic response.

In contrast, the most proximal occlusions result in widespread effects that can lead to significant cerebral edema, increased intracranial pressure, loss of consciousness and could even be fatal. In such occasions, mannitol (osmotic diuretic) or hypertonic saline are given to draw fluid out of the oedematus cerebrum to minimise secondary injury. Hypertonic saline is better than mannitol, as mannitol being a diuretic will decrease the mean arterial pressure and since cerebral perfusion is
mean arterial pressure minus intracranial pressure, mannitol will also cause a decrease in cerebral perfusion.

Contralateral hemiparesis and hemisensory loss of the face, upper and lower extremities is the most common presentation of MCA syndrome. Lower extremity function is more spared than that of the faciobrachial region. The majority of the primary motor and somatosensory cortices are supplied by the MCA and the cortical homunculus can, therefore, be used to localize the defects more precisely.

2.3.6 Pathology of umbilical Cord:

2.3.6.1 Insertion abnormalities:

Occurs in 1% of singletons and in almost 15% of twins. The cord inserts into the membranes far away from the placental margin. Umbilical vessels run unprotected by Whartons jelly and are vulnerable to injury. Velamentous vessels run over the internal os are called vasa previa. These vessels are at risk of rupture during delivery. (Chudleigh T., Thilaganathan B.2004)

Figure 16: shows the Velamentous insertion (www.u/s image.com)
The mortality of vasa previa hemorrhage is very high, the fetus exsanguinates within minutes. Velamentous insertion can be detected before the delivery using color Doppler ultrasound. The fetus is delivered by elective cesarean section. (Chudleigh T., Thilaganathan B.2004)

Figure 17: shows the vasa previa(www.u/s image.com)

Marginal insertion: Insertion at the placental margin (battledore placenta) occurs in 5 – 7% pregnancies.
Figure 18: varies insertions of umbilical cord (http/www.developmental Anatomy/.sa.org)

2.3.6.2 Abnormal coiling

Hypocoiled umbilical cord, achirality (absence of coiling) has adverse fetal outcome (intrauterine distress, intrauterine demise).

Hypercoiled cord, torsion Umbilical cord torsion (hypercoiling) is a frequent cause of abortion in the 2nd trimester. Characteristic findings include long hypercoiled cord, stricture of the cord usually at the fetal end (focal depletion of Whartons jelly) or multiple strictures. The fetus is macerated. (Chudleigh T., Thilaganathan B.2004)

2.3.6.3 Nuchal cord:

A nuchal cord occurs when the umbilical cord becomes wrapped around the fetal neck 360 degrees. Nuchal cords are very common, with prevalence rates of 6% to 37%. Up to half of nuchal cords resolve before delivery. "Type A" nuchal cord is wrapped around the neck 360 degrees. Type B" pattern is described as a hitch which cannot be undone and ends up as a true knot. (Chudleigh T., Thilaganathan B.2004)
2.3.6.4 Umbilical cord knot:

Knot in the baby’s umbilical cord. Some knots form during pregnancy as the baby flips and turns in his or her amniotic sac; other knots form during delivery. Umbilical cord knots occur in about one in every hundred pregnancies, but only one in 2,000 deliveries will have a true tight knot that could present problems for the baby. (More common than knots are nuchal loops, the technical term for when the cord wraps around a baby’s neck. Nuchal loops also known as nuchal cords occur in as many as a quarter of all pregnancies but rarely pose risks to the baby). Babies with long cords and those who are large-for-gestational age are at greater risk for developing true knots. Researchers also speculate that nutritional deficiencies that affect the structure and protective barrier of the cord, or other risk factors such as smoking or drug use, carrying multiples, or having
Hydramnios may make a woman more prone to having a pregnancy with a cord knot. (Chudleigh T., Thilaganathan B. 2004)

The most common sign of a cord knot is decreased fetal activity after week 37. If the knot occurs during labor, a fetal monitor will detect an abnormal heart rate. A substance called Wharton's jelly provides cushioning around the important blood vessels of the cord and protects them even if the cord gets knotted. This means that the odds are in your favor (and your baby's) that a true tight knot won't occur. As long as the knot remains loose, it won't cause harm to your baby. But if the knot becomes tight, it could interfere with the circulation of blood from the placenta to the baby and cause oxygen deprivation. Such a complication is most likely to occur during your baby's descent through the birth canal, but these cases are rare. (Chudleigh T., Thilaganathan B. 2004)

Figure 20: ultrasound image showed the Umbilical cord knot (www.u/s image.com)
2.3.6.5 Single umbilical artery

Occasionally, there is only the one single umbilical artery (SUA) present in the umbilical cord. Approximately this affects between 1 in 100 and 1 in 500 pregnancies, making it the most common umbilical abnormality. It is more common in multiple births. Its cause is not known. (Chudleigh T., Thilaganathan B.2004)

Most cords have one vein and two arteries. The vein carries oxygenated blood from the placenta to the baby and the arteries carry deoxygenated blood from the baby to the placenta. In approximately 1% of pregnancies there are only two vessels — usually a single vein and single artery. In about 75% of those cases, the baby is entirely normal and healthy and the missing artery isn't missed at all. One artery can support a pregnancy and does not necessarily indicate problems. For the other 25%, a 2-vessel cord is a sign that the baby has other abnormalities — sometimes life-threatening and sometimes not. SUA does increase the risk of the baby having cardiac, skeletal, intestinal or renal problems. Babies with SUA may have a higher likelihood of having other congenital abnormalities, especially of the heart. However, additional testing (high level ultrasound scans) can rule out many of these abnormalities prior to birth and alleviate parental anxiety. Echocardiograms of the fetus may be advised to ensure the heart is functioning properly. Genetic counseling may be useful, too, especially when weighing the pros and cons of more invasive procedures such as chorionic villus sampling and amniocentesis. (Chudleigh T., Thilaganathan B.2004)

Although the presence of an SUA is a risk factor for additional complications, most fetuses with the condition will not experience other problems, either in utero or after birth. Especially encouraging are cases in which no other soft markers for congenital abnormalities are visible via
ultrasound. Prior to ultrasound technology, the only method for determining the presence of a SUA was at birth, following an examination of the placenta. Given that the vast majority of expectant mothers do not receive the kind of advanced ultrasound scanning required to confirm SUA in utero, most cases may never be detected antenatally even today. (Chudleigh T., Thilaganathan B.2004)

Doctors and midwives often suggest parents take the added precaution of having regular growth scans near term to rule out intrauterine growth restriction, which can happen on occasion and warrant intervention. Yet the majority of growth restricted infants with the abnormality also have other defects. Finally, neonates with the finding may also have a higher occurrence of renal problems, therefore close examination of the infant may be warranted shortly after birth. Among SUA infants, there is a slightly elevated risk for post-natal urinary infections. (Chudleigh T., Thilaganathan B.2004)

Figure 21: ultrasound image showed Two-vessel umbilical cord (www.u/s image.com)
2.3.6.6 Umbilical cord cyst

Can refer to any cystic lesion associated with the umbilical cord. They can be single (commoner) or multiple. There are increased associations (especially when there are additional sonographic abnormalities and if there is persistence in the 2nd or 3rd trimester) with certain chromosomal/structural anomalies (reported in the up to 20% in one study 8). Such include aneuploidic conditions such as trisomy 18, trisomy 13. (Chudleigh T., Thilaganathan B.2004)

Figure 22: ultrasound image showed umbilical cord cyst (www.ultrasound image.com).

2.3.7 Placental abnormalities

2.3.7.1 Placenta previa

With the exception of women undergoing chorionic villus sampling, accurate assessment of placental position is not necessary when examining the first trimester uterus. Because of positional changes of the body of the uterus in early pregnancy. The placental site can change relative to the internal os. (Chudleigh T., Thilaganathan B.2004)
Approximately 95% of women will have an obviously fundal placenta at the 20 to 22 week gestational and, therefore, will not have placenta at 20-22 weeks and should therefore be rescanned in the third trimester. One in five of these women will have a true placenta previa.

If the woman has had no bleeding it is probably only necessary to request a rescan in the third trimester. If the woman has bled or if she has lost several previous pregnancies she might be admitted to hospital or advised to refrain from sexual intercourse. Placenta previa classified as: I - encroaches the lower segment but does not reach the cervical os. II - reaches the internal cervical os but does not cover it. III - covers part of the cervical os. IV - completely covers the os, even when the cervix is dilated. (Chudleigh T., Thilaganathan B. 2004)

Figure 23: ultrasound images demonstrate the Placenta previa (www.ultrasoundimage.com)
2.3.7.2 Placental Abruption:

Placental abruption (also known as abruptio placentae) is a complication of pregnancy, wherein the placental lining has separated from the uterus of the mother prior to delivery. It is the most common pathological cause of late pregnancy bleeding. In humans, it refers to the abnormal separation after 20 weeks of gestation and prior to birth. It occurs on average of 0.5% or 1 in 200 deliveries. Placental abruption is a significant contributor to maternal mortality worldwide; early and skilled medical intervention is needed to ensure a good outcome, and this is not available in many parts of the world. Treatment depends on how serious the abruption is and how far along the woman is in her pregnancy. (Chudleigh T., Thilaganathan B. 2004)

Placental abruption has effects on both mother and fetus. The effects on the mother depend primarily on the severity of the abruption, while the effects on the fetus depend on both its severity and the gestational age at which it occurs. The heart rate of the fetus can be associated with the severity. Placental Abruption classified as: Class 0: asymptomatic, Diagnosis is made retrospectively by finding an organized blood clot or a depressed area on a delivered placenta, Class 1: mild and represents approximately 48% of all cases. Characteristics include the following: No vaginal bleeding to mild vaginal bleeding, Slightly tender uterus, Normal maternal BP and heart rate, No coagulopathy, No fetal distress. Class 2: moderate and represents approximately 27% of all cases. Characteristics include the following: No vaginal bleeding to moderate vaginal bleeding, Moderate-to-severe uterine tenderness with possible tetanic contractions, Maternal tachycardia with orthostatic changes in BP and heart rate, Fetal distress, Hypofibrinogenemia (i.e., 50–250 mg/dL). Class 3: severe and represents approximately 24% of all cases. Characteristics include the following: No vaginal bleeding to heavy vaginal bleeding,
Very painful tetanic uterus, Maternal shock, Hypofibrinogenemia (i.e., <150 mg/dL), Coagulopathy, Fetal death (Chudleigh T., Thilaganathan B.2004)

Figure 24: ultrasound images demonstrate the Placental abruption (www.u/s image.com)

2.3.7.3 Circumvallate placenta

Circumvallate placenta is a placental disease in which the fetal membranes (chorion and amnion) "double back" on the fetal side around the edge of the placenta.\textsuperscript{11} After delivery, a circumvallate placenta has a thick ring of membranes on its fetal surface. (Chudleigh T., Thilaganathan B.2004)

Complete circumvallate placenta occurs in approximately 1% of pregnancies. It is diagnosed prenatally by medical ultrasonography, although one 1997 study of prenatal ultrasounds found that "of the normal placentas, 35% were graded as probably or definitely circumvallate by at least one sonologist," and "all sonologists misgraded the case of complete circumvallation as normal. The condition is associated with perinatal complications such as placental abruption, oligohydramnios, abnormal cardiotocography, preterm birth, and miscarriage. (Chudleigh T., Thilaganathan B.2004)

2.3.7.4 Chorioangioma:
Chorioangioma is the A benign tumor of a blood vessel in the placenta. Large chorioangiomas can cause complications, including excess amniotic fluid (polyhydramnios), maternal and fetal clotting problems (coagulopathies), premature delivery, toxemia, fetal heart failure, and hydrops (excess fluid) affecting the fetus. Chorioangiomas probably act as shunts between arteries and veins (arteriovenous shunts), leading to progressive heart failure of the fetus. (Chudleigh T., Thilaganathan B. 2004)

2.4 Normal intrauterine Growth:

Physical growth begins when the egg and sperm combine. The size and shape of a human result from the original genetic information or program. The ability of a person to reach his/her ultimate potential depends on this as well as numerous other factors. This is also true for growth during the time an individual is in the womb. Factors, other than inheritance, which can influence growth, include the environment in the womb, nutritional factors regarding the placenta and mother, hormones and other unknown factors. (Scott and Usher, 1966)
### TABLE 28.2 Developmental Events of the Fetal Period (continued)

<table>
<thead>
<tr>
<th>Time</th>
<th>Changes and Accomplishments</th>
</tr>
</thead>
<tbody>
<tr>
<td>17–20 weeks (fifth month)</td>
<td>Vernix caseosa (fatty secretions of sebaceous glands) covers body; lanugo (silky hair) covers skin. Fetal position (body flexed anteriorly) assumed because of space restrictions. Limbs reach near-final proportions. Quickening occurs (mother feels spontaneous muscular activity of fetus). Approximate crown-to-rump length at end of interval: 190 mm.</td>
</tr>
<tr>
<td>21–30 weeks (sixth and seventh months)</td>
<td>Period of substantial increase in weight. (May survive if born prematurely at 27–28 weeks, but hypothalamic temperature regulation and lung production of surfactant are still inadequate.) Myelination of cord begins; eyes are open. Distal limb bones are beginning to ossify. Skin is wrinkled and red; fingernails and toenails are present; tooth enamel is forming on deciduous teeth. Body is lean and well proportioned.</td>
</tr>
<tr>
<td>At birth</td>
<td>Bone marrow becomes sole site of blood cell formation. Testes reach scrotum in seventh month (in males). Approximate crown-to-rump length at end of interval: 280 mm.</td>
</tr>
<tr>
<td>30–40 weeks (term) (eighth and ninth months)</td>
<td>Skin whitish pink; fat laid down in subcutaneous tissue (hypodermis). Approximate crown-to-rump length at end of interval: 360–400 mm (14–16 inches); weight: 2.7–4.1 kg (6–10 pounds).</td>
</tr>
</tbody>
</table>

Table: Developmental Events of the fetal period(http://www.developmental Anatomy/.sa.org)
Normal growth in the womb occurs at a very rapid rate. The average time in the womb is forty weeks and is called the gestational period. A normal full-term baby is on the average, 7 1/2 pounds, and is known as appropriate for Average Gestational Age newborns. A premature baby is smaller but is usually AGA because the size is appropriate for the length of time the baby is in the womb. The small for gestational age (SGA) infant is below the 10th percentile on a standard growth chart. Intrauterine Growth Restriction and SGA are often used interchangeably but the distinction is important. The term Intrauterine Growth Restriction should not be used where there is no evidence of abnormal genetic or environmental influences affecting growth. The IUGR infant is really less than the third percentile (1 in 33 children) and not one in ten newborns as is the case for AGA newborns. Thus, all Intra-Uterine Growth Restriction infants are Small for Gestational Age but not all SGA infants are Intra-Uterine Growth Restriction. This is an important issue for the parent to consider when the doctors and nurses use these different terms. (Scott and Usher, 1966).
Figure 25: fetal growth chart percentile, Percentile Example: Out of 100 babies, a reading of forty percent (this is the percentile value) indicates that the baby is smaller than sixty other babies and larger than forty other babies. The mean or average is fifty percent. A value that reads below 50% indicates that the measurement is lower than the average. Thus, a value that is above 50% indicates that the measurement is above average (http/www.growthdevelopmental/.sa.org)
2.4.1 Fetal weight:

Fetal weight (FW) is an important predictive parameter of neonatal outcome. Accurate prenatal estimation of birth weight based on gestational age (GA) and would be extremely useful in the management of labor and delivery. Ultrasonographically estimated fetal weight is obtained from measurements of fetal parts and the use of these measurements in a regression formula to derive a fetal weight. Over the past 30 years there are many published formulas for ultrasonographic estimated fetal weight (EFW). Mostly used formulas in USA are those from Hadlock and colleagues, in Great Britain formulas from Campbell and Wilkin and from Shepard, and in Germany the formula from Merz, Fetal weight was estimated for each fetus using the formulas of Campbell and Wilkin (using fetal AC), Shepard (using fetal BPD and AC), two Hadlock formulas (one using fetal AC and FL; another using fetal HC, AC and FL) and formula of Merz (using fetal BPD and AC). The hadlock formula which was using three fetal biometry parameters (HC, AC and FL) is the most accurate one to estimate fetal weight (Kurmanavicius et al, 2004). The formulas are shown in following Table.

Table 2.6: Regression formulas used to obtain estimated fetal weight.

<table>
<thead>
<tr>
<th>Author</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hadlock et al. (1)</td>
<td>Log10EFW=1.304+0.05281<em>ACq0.1938</em>FL-0.004<em>AC</em>FL</td>
</tr>
<tr>
<td>Hadlock et al. (2)</td>
<td>Log10EFW=1.3260.00326<em>AC</em>FL+0.0107<em>HC+0.0438</em>AC+0.158*FL</td>
</tr>
<tr>
<td>Campbell and Wilkin</td>
<td>Log10EFW=1.2508+0.166<em>BPD+0.046</em>AC-0.002646<em>AC</em>BPD</td>
</tr>
<tr>
<td>Shepard et al. Tokyo</td>
<td>LogEFW=-4.564+0.282<em>AC-0.00331</em>AC2</td>
</tr>
<tr>
<td>Merz et al. Osaka</td>
<td>EFW= - 3200.40479-157.07186<em>AC+15.90391</em>BPD2</td>
</tr>
</tbody>
</table>
The most common determination of fetal growth restriction is based on the estimated fetal weight (EFW). Both low birth weight and excessive fetal weight at delivery are associated with an increased risk of newborn complications during labor and the puerperium. For macrosomic fetuses (see the image below), potential complications associated with delivery include shoulder dystocia, brachial plexus injuries, bony injuries, and intrapartum asphyxia, as well as maternal risks that include birth canal injuries, pelvic floor injuries damage, and postpartum hemorrhage. (Hadlock FP et al 1984)

The accurate estimation of fetal weight is most necessary for fetuses with suspected significant deviations of intrauterine growth. The gestational age of the pregnancy must first be defined because fetal weight increases rapidly after the second trimester of pregnancy, in 38-42 weeks of gestational age during this 4-week interval, the typical fetus gains approximately 12.7 ±1.4 g/day. Fetal weight may be characterized as falling into 1 of 3 categories: (1) reference range (generally defined as the 10th - 90th percentile for gestational age), (2) small for gestational age (< 10th percentile), or (3) large for gestational age (>90th percentile). Many factors affected the fetal weight; maternal factors (e.g., race, stature, genetics), physiologic factors (e.g., altered glucose metabolism, hemoglobin concentration, microvascular integrity), pathologic factors (e.g., hypertension, uterine malformations), and complications of pregnancy (e.g., gestational diabetes mellitus, preeclampsia). (Hadlock FP et al 1984). After birth simple formulas were applied:

- 1 - 12 months \( (0.5 \times \text{age months}) + 4 \)
- 1 - 5 years \( (2 \times \text{age years}) + 8 \)
- 6 - 12 years \( (3 \times \text{age years}) + 7 \)

(Advanced Paediatric Life Support (APLS) weight calculations).
2.4.2 Low Birth Weight (LBW):

Low birth weight (LBW) is a particular risk factor. Children of low (or very low) birth weight have been variously identified as at increased risk from neurosensory, developmental, physical, and psychological problems. Specific problems include increased risk of cerebral palsy, asthma, upper and lower respiratory infections and ear infections. Low birth weight children are also likely to suffer from reduced rates of cognitive development and learning. Low birth weight also provides a powerful predictor of the future health of the child. Problems later in life include increased risks of coronary heart disease, diabetes and high blood pressure. Size at birth, however, reflects two factors: duration of gestation and rate of foetal growth. Thus birth weight should be considered with respect to gestational age. Ideally the preferred indicator should therefore be intrauterine growth retardation (IUGR). Small-for-gestational age or IUGR enables, for example, distinction between infants who are too small because they were born preterm and those who are small but at term. (Hadlock FP et al 1994)

2.4.3 Assessment of gestational Age:

In recent years, ultrasound assessment of gestational age has become an integral part of obstetric practice. (Kalish RB, Chervenoak FA 2002) Precise knowledge of gestational age is also essential in the evaluation of fetal growth and the detection of intrauterine growth restriction. The sonographic estimation is derived from calculations based on fetal measurements and serves as indirect indicator of gestational age. Over the three decades, numerous equations regarding the relationship between fetal biometric parameters and gestational age have been described and proven early antenatal ultrasound to be an objective and accurate means of establishing gestational age. (Hadlock FP et al 1994)
Gestational age (or menstrual age) is a measure of the age of a pregnancy where the origin is the woman's last normal menstrual period (LMP), or the corresponding age as estimated by other methods. Such methods include adding 14 days to a known duration since fertilization (as is possible in vitro fertilization), or by obstetric ultrasonography. The popularity of using such a definition of gestational age is that menstrual periods are essentially always noticed, while there is usually a lack of a convenient way to discern when fertilization occurred.

Determining the first day of the LMP traditionally is the first step in establishing the EDD. By convention, the EDD is 280 days after the first day of the LMP. Because this practice assumes a regular menstrual cycle of 28 days, with ovulation occurring on the 14th day after the beginning of the menstrual cycle, this practice does not account for inaccurate recall of the LMP, irregularities in cycle length, or variability in the timing of ovulation. It has been reported that approximately one half of women accurately recall their LMP. In one study, 40% of the women randomized to receive first-trimester ultrasonography had their EDDs adjusted because of a discrepancy of more than 5 days between ultrasound dating and LMP dating. Estimated due dates were adjusted in only 10% of the women in the control group who had second-trimester ultrasonography, suggesting that first-trimester ultrasound examination can improve the accuracy of the EDD, even when the first day of the LMP is known. (Hadlock FP et al 1994)

First trimester ultrasound is a useful anreliable tool in the assessment of gestational age. In particular, sonographic measurement of the CRL during the first trimester is the best parameter for estimating gestational age and is accurate within five days of the actual conception date. The longitudinal axis of the fetus using the transabdominal method. The calipers demonstrate measurement of the crown-rump length. Although routine ultrasonography at 18-20 weeks gestation essential in evaluation of fetal growth and and the detection of intrauterine growth restriction.
During the third trimester, fundal height assessment may be helpful in determining appropriate fetal growth by comparing the measurement to a known to gestational age. In addition, dating pregnancy is imperative for scheduling invasive diagnostic tests such as chorionic vilus sampling or amnio-centesis, as appropriate timing in interperation of biochemical serum screening test result and may help avoid undue parental anxiety from miscalculation and superfluous invasive procedure, which may increase the risk of pregnancy loss. Assessment of gestational age is also crucial for counseling patients regarding the option of pregnancy termination. (Hadlock FP et.al, 1994).

**2.4.4 Importance of accurate GA Assessments:**

Accurate determination of gestational age can positively affect estimation of fetal weight and pregnancy outcomes. For instance, one study found a reduction in the need for posterm inductions in a group of women randomized to receive routine first-trimester ultrasonography compared with women who received only second-trimester ultrasonography. A Cochrane review concluded that ultrasonography can reduce the need for posterm induction and lead to earlier detection of multiple gestations. Because decisions to change the EDD significantly affect pregnancy management, their implications should be discussed with patients and recorded in the medical record (Hadlock FP et al 1994).

**2.4.5 The Intrauterine Growth Restriction (IUGR):**

Intrauterine growth restriction it is part of a wider group referred to as small for gestational age (SGA) fetuses where the fetus is smaller than expected for the gestational age. The SGA includes fetuses which are constitutionally small and those whose growth has been restricted, which is
most commonly defined as a weight below the 10th percentile for the gestational age. (Williams 1982, WHO 1995)

At the end of pregnancy, it can result in a low birth weight. Intrauterine growth restriction (IUGR) refers to poor growth of a baby while in the mother's womb during pregnancy. At least 60% of the 4 million neonatal deaths that occur worldwide every year are associated with low birth weight (LBW), caused by intrauterine growth restriction (IUGR), preterm delivery, and genetic/chromosomal abnormalities, demonstrating that under-nutrition is already a leading health problem at birth.

After birth Two physical criteria are used to differentiate between a small baby and intrauterine growth restriction (for example, skin texture and thickness, creases on soles of feet, firmness of ears, and appearance of the genitals) and neurological (for example, posture or type of flexion of hands and feet). (Williams 1982, WHO 1995)
Figure 27: Intrauterine growth restriction (IUGR) is defined as a failure of the fetus to attain its pre-determined growth potential. That is, the baby does not grow at the normal, expected rate. The image above shows a normally-grown baby (right) and a growth-restricted baby (left). (http://www.mountsinai.on.ca/care/placenta-)

The potential medical difficulties after birth may be different. Some premature newborns have no problems at all whereas some may have immature lungs causing respiratory distress syndrome, "yellow" jaundice due to immaturity of liver function, and apnea which is an irregular breathing pattern caused by an immature nervous system. On the other hand, some of the medical problems of Intra-Uterine Growth Restriction babies include low blood sugar (hypoglycemia), low blood calcium (hypocalcemia), thick blood (polycythemia), and swallowing of fluid from the amniotic sac at birth (meconium aspiration). Both groups of newborns must be observed closely for signs of lack of oxygen, infection and low temperature (this latter problem in the IUGR infant results from the diminished fat tissue which would help hold the infant's body temperature). (Krebs, C, and R.L. Eisenberg, 1999).
Figure: showed abdominal circumference AC of case of iugr, cross section of

(stomach, liver and umbilical vein, vertebra and 12th rib)
Figure: showed Biparital diameter BPD of case of IUGR (BPD 78.8mm, GA 30w5d)
Figure 28: shows case of Intrauterine Growth Restriction (IUGR), Image 1a,b,c

(Ultrasound, 33 weeks gestation): The fetus is in a cephalic presentation. The placenta is situated on the posterior uterine wall, clear of the cervix. Measurements: Biparietal diameter 78mm, Head circumference 283mm, Abdominal circumference 266mm, Femur length 58mm. Estimated fetal weight 1625g +/- 237g. Amniotic fluid volume is normal (Amniotic Fluid Index = 12cm). On Doppler imaging, there is reverse end diastolic flow in all sections of the umbilical artery evaluated.
2.4.6 General causes of intrauterine growth restriction (IUGR):

If the cause of IUGR is extrinsic to the fetus (maternal or uteroplacental), transfer of oxygen and nutrients to the fetus is decreased. This causes a reduction in the fetus’ stores of glycogen and lipids. This often leads to hypoglycemia at birth. Polycythemia can occur secondary to increased erythropoietin production caused by the chronic hypoxemia. Hypothermia, thrombocytopenia, leucopenia, hypocalcaemia, and pulmonary hemorrhage are often results of IUGR. If the cause of IUGR is intrinsic to the fetus, growth is restricted due to genetic factors or as a sequela of infection. (Krebs, C, and R.L. Eisenberg, 1999)

Hypertension complicates approximately 9% of all pregnancies with preeclampsia, in severe preeclampsia uteroplacental perfusion is usually diminished and this results in increased IUGR incidence, fetal hypoxia and prenatal death.(Coleman, et al., 2004)

After identifying a fetus with IUGR, an accurate and thorough history and physical examination are the most important tools for differentiating fetal from maternal and placental causes to direct antepartum management and optimize fetal outcomes

2.4.6.1 Maternal causes:

- pre-pregnancy weight and nutritional status
- poor weight gain during pregnancy
- poor nutrition
- anemia
- alcohol and/or drug use
- maternal smoking
• recent pregnancy
  • pre-gestational diabetes
  • gestational diabetes
  • pulmonary disease
  • cardiovascular disease
  • renal disease
  • hypertension
  • Celiac disease increases the risk of intrauterine growth restriction by an odds ratio of approximately

2.4.6.2 Uteroplacental causes:

• preeclampsia
• multiple gestation
• uterine malformations
• Placental insufficiency

2.4.6.3 Fetal causes:

• chromosomal abnormalities
• Vertically transmitted infections
### Table 2.7: causes of IUGR

<table>
<thead>
<tr>
<th>Fetal factors</th>
<th>Placental factors</th>
<th>Maternal factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosomal disorders</td>
<td>Utero-placental insufficiency</td>
<td>Chronic illness (e.g. diabetes**, hypertension, renal disease, anemia, pulmonary disease)</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>Abnormal implantation</td>
<td>Pre-eclampsia</td>
</tr>
<tr>
<td>Multiple gestation</td>
<td>Vascular anomalies</td>
<td>Early or advanced age</td>
</tr>
<tr>
<td>Infection (e.g. TORCH*, malaria, varicella)</td>
<td>Abnormal placentation abruption</td>
<td>Malnutrition</td>
</tr>
<tr>
<td>Metabolic disorders</td>
<td>Infarction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Villous placentitis (bacterial, viral, parasitic)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Confined placental mosaicism</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**Note:**
- IUGR: Intrauterine growth restriction
- TORCH*: Toxoplasmosis, other infections, rubella, cytomegalovirus, herpetic infections
- **: Indicates a risk factor
- ***: Indicates a significant risk factor

---

85
Figure 26: demonstrate the Distribution of small for gestational age (SGA) in the world
2.4.7 Classification OF IUGR:

There are 2 major categories of IUGR: symmetrical and asymmetrical: Some conditions are associated with both symmetrical and asymmetrical growth restriction. (Krebs, C, and R.L. Eisenberg, 1999).

Asymmetrical IUGR is more common (70%). In asymmetrical IUGR, there is restriction of weight followed by length. The head continues to grow at normal or near-normal rates (head sparing). A lack of subcutaneous fat leads to a thin and small body out of proportion with the head. This is a protective mechanism that may have evolved to promote brain development. In these cases, the embryo/fetus has grown normally for the first two trimesters but encounters difficulties in the third, sometimes secondary to complications such as pre-eclampsia. Other symptoms than the disproportion include dry, peeling skin and an overly-thin umbilical cord. The baby is at increased risk of hypoxia and hypoglycemia. This type of IUGR is most commonly caused by extrinsic factors that affect the fetus at later gestational ages. Specific causes include: Chronic high blood pressure, Severe malnutrition, Genetic mutations, Ehlers–Danlos syndrome. (Krebs, C, and R.L. Eisenberg, 1999)

Symmetrical IUGR is less common (20-25%). It is commonly known as global growth restriction, and indicates that the fetus has developed slowly throughout the duration of the pregnancy and was thus affected from a very early stage. The head circumference of such a newborn is in proportion to the rest of the body. Since most neurons are developed by the 18th week of gestation, the fetus with symmetrical IUGR is more likely to have permanent neurological sequela. Common causes include: Early intrauterine infections, such as cytomegalovirus, rubella or toxoplasmosis Chromosomal abnormalities, Anemia Maternal
substance abuse (prenatal alcohol use can result in Fetal alcohol syndrome). (Krebs, C, and R.L. Eisenberg, 1999)

**Table 2.8: Classification OF IUGR**

<table>
<thead>
<tr>
<th>Symmetric</th>
<th>Asymmetric</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30% of IUGR</td>
<td>70-80% of IUGR</td>
</tr>
<tr>
<td>Usually occurs early in pregnancy</td>
<td>Usually occurs later in pregnancy (3rd trimester)</td>
</tr>
<tr>
<td>Head circumference, length, and weight are</td>
<td>Head circumference is spared relative to decreased weight,</td>
</tr>
<tr>
<td>decreased proportionally</td>
<td>length, and/or abdominal circumference</td>
</tr>
<tr>
<td>Thought to result from an intrinsic (i.e.</td>
<td>Thought to result from adaptation to a hostile environment</td>
</tr>
<tr>
<td>genetic) or first-trimester insult (e.g.</td>
<td>by redistributing blood flow in favour of vital organs (e.g.</td>
</tr>
<tr>
<td>infection) that interferes with early fetal</td>
<td>brain, heart) at the expense of nonvital fetal organs (e.g.</td>
</tr>
<tr>
<td>cellular hyperplasia, producing uniformly</td>
<td>liver, kidneys)</td>
</tr>
<tr>
<td>reduced growth</td>
<td></td>
</tr>
</tbody>
</table>
2.4.8 Diagnosis of IUGR:

One of the major requirements for an accurate diagnosis of IUGR is an accurate calculation of gestational age (Lugo, 1971). Assuming that dates can be determined from LMP or early first trimester ultrasound, the following are ways to diagnose IUGR. While IUGR can be apparent visually (maternal characteristics), it can also be diagnosed using the ultrasound imaging techniques and Doppler imaging studies available to obstetricians and Maternal-Fetal Medicine specialists. There are Symptoms and Signs of iugr such as, Poor maternal weight gain, Development of hypertension (up to 50% of mothers with IUGR pregnancies develop hypertension due to associated placental insufficiency), Reduced fetal activity, Small-for-dates pregnancy (determined by the symphysis-fundal height, SFH). Normal pregnancies progress at 1cm/week, so 30cm at 30 weeks. Any SFH that is 3cm or more behind dates requires ultrasound investigations. Following tests should be done:

2.4.8.1 Ultrasound scans

Ultrasound scanning techniques are used to monitor fetal growth and record fetal biometry. These are useful for the estimation of fetal weight and measuring of body proportions (ex. abdominal circumference vs. head circumference). Doppler studies of the fetal, placental and uterine vasculature were developed in the 1980's and have since become an integral part of protocols used to assess IUGR. These studies utilize a non-invasive ultrasound method, based on the doppler principle, to evaluate velocities of red blood cells within arteries. In the umbilical artery, rising ratios of the systolic/diastolic frequency in a cardiac cycle reflect an increasing amount of impedance to flow in the placenta. This is due to increased placental circulatory resistance as a result of a reduced number of tertiary villous arteries, mostly resulting from maternal vascular
disease such as hypertension. (Giles, 1985). Decreasing diastolic flow, absent diastolic flow and reversed diastolic flow during a cardiac cycle are signs of worsening IUGR.

2.4.8.2 Estimated fetal weight (EFW)

The EFW is estimated by measuring the bi-parietal diameter (BPD) and head circumference (HC) of the baby's head, abdominal (belly) circumference (AC), and femur (thigh bone) length (FL) on ultrasound. The average sizes are used as a reference to determine if the developing fetus is too small. If the fetus is below the 10th percentile, this is termed small-for-gestational age (SGA) and a proportion of these foetus will be found to have true IUGR.

2.4.8.3 Monitoring of fetal body proportions

Babies with IUGR caused by placental insufficiency often develop asymmetrically, that is, the ratio of the baby's head circumference (HC) to the baby's abdominal circumference (AC) is elevated (the head remains the normal size while the abdomen becomes smaller because the body organs, like the liver, grow slower). Asymmetrical growth also includes short femur length (FL). Small babies in healthy mothers with a normal HC/AC ratio and normal FL may simply be smaller than normal due to their mother's size and ethnicity. For example, a baby predicted to be 6lb near birth might be normal for a slim 5’ tall South Asian woman, but would likely be true IUGR if born to a 5’ 10” tall Caucasian woman. (Scott and Usher, Lubo)
2.4.8.4 Doppler studies

Doppler studies are used to study blood flow to the fetuses. Early-onset IUGR pregnancies (typically found <32 weeks’ gestation) have high resistance to flow in the umbilical arteries. They may also have:

- Brain redistribution: abnormal flow in the baby's brain characterized by increased flow in the middle cerebral artery or MCA;
- Abnormal flow in the ductus venosus (a channel within the liver that sends oxygenated blood from the umbilical vein/placenta at high speed across the heart to go up to the fetus's brain);
- Uteroplacental vascular insufficiency: a small and/or damaged placenta characterized by abnormal blood supply to the placenta via the maternal uterine arteries;

By contrast, in the more common late-onset IUGR (found after 36 weeks), the uterine and umbilical artery Doppler studies are mostly normal. However, late onset-IUGR babies may have abnormal middle cerebral artery (MCA) Doppler and/or very mature (Grannum grade 3) placentas. (Scott and Usher, Lubo)

2.4.9 Morbidity and mortality of IUGR:

The degree of risk depends on what caused the growth problem in the first place, how severe the growth restriction is, how early in pregnancy it starts, and the baby's gestational age at birth. The 10th percentile has been used to define "small for gestational age" at all gestational ages. This approach assumes that the risk of perinatal mortality is the same at all gestational age. The risk of neonatal death at the 10th percentile has a bimodal distribution with peaks at 26 and 34 weeks' gestation. Hence, the 10th percentile is associated with an increased, but variable, risk of
subsequent neonatal mortality. There is an acceleration in mortality and neonatal complications as the fetal weight falls below the 5th percentile. It is a serious condition in which the fetus is not growing adequately and is smaller than expected for its age. IUGR is present in almost half of all stillbirths. And the risk of both short-term and long-term complications is higher for growth-restricted babies who are also born prematurely. Growth-restricted babies may have lower levels of oxygen and nutrients in the womb and at birth, and are at higher risk of being stillborn. They may have a more difficult time tolerating labor, so c-sections are more common. And at birth they're also more likely to have low blood sugar, lower resistance to infection, trouble maintaining their body temperature, and an abnormally high red blood cell count. They're also more prone to jaundice and to meconium aspiration. (Lugo, 1991)

Surviving infants with severe IUGR are at risk for long-term developmental delay and neuromotor disabilities such as cerebral palsy. Epidemiologic studies have linked low birth weight with the development of adult chronic diseases including hypertension, diabetes, and heart disease. (Lugo, 1991)
Figure 29: shows the mortality and morbidity of IUGR(http://www.mountsinai.on.ca/care/iugr-)

2.4.10 Management of Intrauterine Growth Restriction (IUGR):

the optimal management of the IUGR affected fetus aims to achieve the delivery of the newborn in the best possible condition, balancing the risks of prematurity against those of continued intrauterine existence(Lugo, 1991)

The first step in the appropriate management of small-for-gestational age fetuses is to delineate those fetuses who are truly at risk. An individual fetus' growth potential may be compromised, resulting in any or all of the neonatal complications of intrauterine growth restriction (IUGR)
above the arbitrary 10th percentile cut-off. Customized standards for fetal growth are better able to distinguish between "physiologically small" and "pathologically small" fetuses\(^3\). (Lugo, 1991)

Serial abdominal circumference or fetal weight estimates are the best screening tests for IUGR\(^4\). Doppler studies are the mainstay for diagnosis and management. Complicated cases of early onset IUGR (< 30 weeks' gestation) may require a multi-vessel Doppler approach to evaluate pre-load, as well as after-load, affects of severe intrauterine growth restriction. Many steps may be taken: Confirm that the pregnancy dating is correct, If the developing baby is genuinely smaller than average, Review of maternal and pregnancy risk factors for abnormal placental function, Investigate non-placental causes of IUGR, If there is no evidence of non-placental causes of IUGR, placental function testing is performed, A plan of serial monitoring is then developed and Pediatric consultation before delivery (Lin, 1991)
Figure 30: the intrauterine management of IUGR

(http://www.mountsinai.on.ca/care/iugr-)

Note: Recommendations on timing of fetal surveillance intervals and delivery vary.

Surveillance and delivery times are adapted from the Royal College of Obstetricians and Gynaecologists Guidelines (2013).
2.4.11 Approach to IUGR:

Accurate dating of the pregnancy is essential! Dating is estimated based on the last menstrual period using Nägele’s rule (estimated due date = LMP – 3 months + 7 days). If the dating of the pregnancy is in question, the gestational age can also be assessed by first trimester ultrasound measurement of the crown-rump length. If these estimates differ by more than 7 days, ongoing ultrasound measurements are done every 2-4 weeks to assist with dating and estimating fetal growth.

In general, screening for IUGR relies on symphysis-fundal height measurements as part of routine prenatal care. Ultrasound is used to confirm IUGR based on estimated fetal weight and measurements of head & abdominal circumference. (Lin, 1991)

2.4.12 Outcomes and clinical significance:

IUGR affects 3-10% of pregnancies. 20% of stillborn infants have IUGR. Prenatal mortality rates are 4-8 times higher for infants with IUGR, and morbidity is present in 50% of surviving infants. The newborn period the doctors will want to do diagnostic studies to determine the cause of IUGR if at all possible. They will also try to determine the gestational age of the newborn. Ultimately, the most important aspects of IUGR are the intellectual or other neurological developmental outcomes, including learning disabilities. This, to a major degree, reflects the underlying cause. These issues point out the importance of attempting to find out the underlying cause so the appropriate plan of therapy is developed for the specific child. (P. Cox and T. Marton, 2009)

There are some investigations used to direct antepartum management and optimize fetal outcomes such as, Serial measurements of blood flow velocity in fetal vessels using Doppler ultrasound,
Absent or reversed end diastolic flow in the umbilical artery suggests the fetus is in poor condition. Non-stress test, Biophysical profile (a composite score based on fetal breathing movements, gross body movements, fetal tone, fetal heart rate, and qualitative amniotic fluid volume), Serial fetal weight assessments, Amniotic fluid volume. A detailed fetal anatomic survey by ultrasound (as major congenital anomalies are frequently associated with fetal growth restriction): Omphalocele, congenital diaphragmatic hernia, skeletal dysplasia and congenital heart defects are among the congenital anomalies associated with failure to maintain normal fetal growth. Other studies, such as testing for congenital infections or karyotype (chromosomal analysis), are considered on an individual basis depending on risk factors and other clinical features. A course of antepartum steroids is recommended for preterm fetuses to promote lung maturation. (P. Cox and T. Marton, 2009)

IUGR infants who are also premature are at greater risk for medical problems than full-term IUGR infants. In terms of growth some IUGR babies do catch up and become average-sized children and adults. The pattern for this catch-up growth is likely first and best seen during the first year of life. The growth patterns or growth charts of children with various disorders (for example: Turner, Russell-Silver, and Down Syndromes) are available for parents (D. G. Jang, Lee, N. Kim, 2010)

2.5 Theoretical Studies of Doppler ultrasound
Doppler is a major component of ultrasound imaging especially in the investigation of cardiac and peripheral vascular diseases. Modern Doppler systems are sophisticated and can provide accurate information about the effects of disease on blood flow. Our knowledge of blood flow is helpful in understanding the effects of certain diseases on organ function, and can help the physician in the management and treatment of patients. (Corbett et al, 2005).

2.5.1 Doppler shift for audible sounds:

The Doppler Effect is the change in the observed frequency due to the relative motion of the source and the observer. The frequency heard by the listener differs from that produced by the source, depending on whether the source and the listener are moving toward or away from one other. This change in the perceived frequency relative to the transmitted frequency is called Doppler shift. In general, a Doppler shift can occur for a moving source and stationary listener, a moving listener and stationary source, or a moving source and moving listener (Zagzebski, 1996).

2.5.2 Doppler Shift Applied to vascular ultrasound:

In the case of vascular ultrasound, the Doppler Effect is used to study blood flow. The simplest Doppler ultrasound instruments use transducers consisting of two piezoelectric elements, one to transmit ultrasound beams and the other to receive the returning echoes back-scattered from the moving blood cells. In this situation, the Doppler Effect occurs twice. First, the transducer is a stationary source while the blood cells are moving receivers of the ultrasound waves. The ultrasound is then back-scattered from the blood cells, which now act as a moving source, with the transducer acting as a stationary observer. (Corbett et al, 2005)

The Doppler shift observed depends on the frequency of the ultrasound originally transmitted by the transducer and the velocity of the blood cells from which the ultrasound is backscattered.
2.5.3 The Doppler equation:

The Doppler equation relates the change in frequency or Doppler shift to variables which affect the size of the Doppler shift.

\[
\Delta f = \frac{2f_o \nu \cos \theta}{c} \tag{1}
\]

\( \Delta f \) - Change in frequency

\( f_o \) - frequency of the transmitted sound

\( \nu \) - velocity of red blood cells

\( c \) - speed of ultrasound in blood

\( V \) - Velocity of the reflecting surface (RBCs)
Theta - beam-flow direction angle

The emitted or transmitted frequency of a Doppler transducer \( f_o \) is determined by the transducer. Note that \( f_o \) is above the line in the Doppler equation. This means the Doppler shift is directly related to the emitted or transmitted frequency. Thus, the higher the transmitted frequency, the greater the Doppler shift, and vice versa. The choice of transducer frequency for a Doppler examination is important especially when there is high velocity blood flow which must be measured accurately. The "2" in the equation is basically a mathematical constant. The speed of sound \( c \) in the medium is essentially a constant and is not a significant factor in Doppler shift analysis. As the equation indicates, the magnitude of the Doppler shift is directly related to the velocity of RBCs. The greater the velocity of RBCs, the greater the Doppler shift, and vice versa. This relationship is very important in clinical practice. It means that Doppler instruments with the proper circuits and controls have the capability or the potential of measuring the velocity of blood which can lead to specific conclusions about the functional status of valves, heart chambers, and vessels. Keep in mind this very important fact about blood velocity measured by the Doppler shift. (Corbett et al, 2005)

2.5.4 The Doppler angle:

The magnitude of the Doppler shift depends on Doppler angle. Cosine Versus Angle This angle must be known and must be accurate in order to estimate true blood velocity from the Doppler shift. The only variable left to consider in the Doppler equation is cosine angle \( \cos(\theta) \) value. This is the angle between the axis of the Doppler beam and the direction of blood flow. The Doppler equation shows that the relationship between Doppler shift and RBC velocity is dependent on this cosine value. (Corbett et al, 2005)
The Doppler equation shows that the detected Doppler shift depends on the angle of insonation \( \Theta \), through the term \((\cos \Theta)\), the \((\cos \Theta)\) term varies between 0 and 1 as the angle changes from 0° to 90°. When the angle of insonation is 90°, the \(\cos \Theta\) is 0, so virtually no Doppler shift is detected. When the angle of insonation is 0° (i.e., the Doppler beam is parallel to the direction of flow), the costerm is 1, giving the maximum detectable Doppler shift frequency for a given velocity of blood and transmitted frequency. Figure 3.3 shows how the detected Doppler shift frequencies change as the Doppler angle changes. When the transducer is pointing toward the flow, a positive frequency shift is seen, but once the transducer is pointing away from the direction of flow, a negative frequency shift is seen. The smaller the angle of insonation, the larger the frequency shift detected, but as the angle of insonation approaches a right angle, very small frequency shifts are detected. (Corbett et al., 2005)
2.5.5 Effect of angle of insonation on the color flow image:

As the colors used to display the flow depend on the Doppler frequencies detected, which in turn depend on the angle of insonation between the blood flow and the color Doppler beam, the appearance of the color image is very much dependent on the angle of insonation. Many of the peripheral vessels run parallel to the skin, perpendicular to the imaging beam. However, the color Doppler beam should ideally be less than 70° in order to obtain a Doppler signal. If the angle of insonation is near 90°, only a small Doppler shift will be detected; this will be removed by the high-pass filter, known as the clutter filter, and no signal will be displayed on the image. (Corbett et al., 2005)

The linear array transducer is used to create the color image, from left or right. The direction of the color Doppler beam runs parallel to the sides of the color box displayed on the image. When
imaging tortuous vessels, it is useful to obtain images with the color box steered in different directions to visualize the blood flow along the entire vessel. If the direction of the blood flow changes in relation to the Doppler beam, a different Doppler frequency will be detected even though the blood velocity is the same. The color image will demonstrate a change of color within the vessel as the path of the vessel alters direction, there will be a change in the angle of insonation along the vessel, unless the vessel is parallel to the Doppler beam. This will lead to a change in the Doppler frequencies detected and therefore will affect the color displayed on the image. (Corbett et al, 2005)

Figure 33: Effect of changing the angle of insonation (shown on the image), by steering the color box, on the image produced. A: A small angle gives a good image. B: A moderate angle displays flow but is not optimal. C: A large angle gives an unusable image (www.u/simage.cm)

2.5.6 Diagnostic Doppler Instruments:
There are currently four types of Doppler instruments commercially available for clinical studies:

- Continuous wave
- Pulsed wave
- Color flow imaging
- Color power imaging

All these instruments are inherently capable of presenting the processed Doppler data as an audible sound (loudspeakers) and visual display (spectral analysis and waveform display). Basic continuous and pulsed wave instruments may present only audible signals.

**2.5.7 Continuous wave Doppler instrumentation:**

Continuous wave (CW) Doppler continuously emits a single frequency while the receiving element continuously detects any echoes from the sensitive region of the beam (i.e., where transmitted and received beams overlap). This region usually covers a depth of a few centimeters, and any flow within this area will be detected. This means that CW Doppler is unable to provide information about the depth from which the Doppler signal is returning. CW Doppler is therefore said to have poor range resolution. Veins often lie adjacent to arteries and so, in many cases, the CW Doppler will simultaneously detect arterial and venous flow. (zagzebski, 1996).

The three primary components are the CW transducer, oscillator and receiver. The audio output from the receiver goes to the loudspeaker, and the visual output goes to the spectral analyzer,
memory and display for visual presentation. Of interest, hand held obstetrical CW-Doppler devices are simple and inexpensive, and only have an audio output.

Figure 34: shows simple diagram of continuous wave (CW) Doppler (Dubiel, M., et al 2000)

2.5.7.1 The CW Doppler Transducer:

CW Doppler instruments utilize transducers that contain two separate piezoelectric crystals mounted at the end of a cylindrical probe. These transducers are offset by a few degrees in order to cause some overlap of the transmitted and the received ultrasound waves. This region of sensitivity (also called the region of overlap), is the site from which Doppler signals are received.
The first piezoelectric crystal serves as a transmitter, and the second as a receiver. The transmitting crystal is made to oscillate at approximately 2-10 MHz, emitting sound waves of the same frequency. (zagzebski, 1996).

The second crystal (the receiving crystal) detects the reflected ultrasound waves for processing by the Doppler instrument. We know from our earlier discussion of Doppler that if the reflecting object is stationary, the detected frequency will be identical to the transmitted frequency. If the reflector (typically an RBC) is moving, the reflected frequency will be greater or less than the transmitted frequency depending on whether the motion is toward or away from the ultrasound source. The magnitude of the frequency shift is proportional to the velocity of the red blood cells in respect to the sound beam. The size of the region or zone of sensitivity varies with the frequency of the transducer. Low frequency CW transducers have a larger zone than high frequency CW transducers. Any flow within the region of sensitivity will result in a Doppler shift being detected by the instrument. (zagzebski, 1996).

2.5.7.2 The Oscillator:

The oscillator or CW voltage generator supplies a continuous voltage to the transmitting or source transducer in the CW probe. The voltage applied to the transducer varies from 2-10 MHz in frequency and is continuous (sound is constantly produced while the system is on). The ultrasound frequency is equal to the oscillator voltage frequency, which is generally set to equal the resonance frequency of the transducer crystal. (zagzebski, 1996).

2.5.7.3 The Receiver:

The CW Doppler receiver is a multitasking component which amplifies, mixes, filters (mixing and filtering are part of demodulation). As the block diagram illustrates, receiver components include
the RF amplifier, demodulator, and AF amplifier. The demodulator consists of mixer and filter circuits which extract the Doppler shift frequency. The receiver gets its voltage input from the receiving transducer in the CW probe and first performs RF amplification on the echo voltages it receives from the receiving transducer. Next step is demodulation. In the mixer circuit, the received echo frequency is combined with the transmitted frequency. (zagzebski,1996).

The mixer yields the sum and difference of these two frequency inputs and sends this new signal to the low pass frequency filter circuit (high frequency rejection) which extracts the Doppler shift. The Doppler shift is the difference between the transmitted and received frequencies, which is typically one-one thousandth of the transmitted or source frequency and in the audio range. Following demodulation and acquiring the Doppler shift, the signal is sent to the audio-frequency (AF) amplifier for signal boosting. The amplified AF signal drives a loudspeaker and the Doppler signal can be heard. (zagzebski,1996).

2.5.8 Pulsed Doppler:

The poor range resolution of CW Doppler can be overcome by using a pulse of ultrasound energy and only acquiring the returning signal at a known time after the pulse has been transmitted. Thus, by knowing the speed of sound in tissue, the depth from which the signal has returned can be calculated, in the same way as described for pulsed echo imaging(zagzebski,1969).

2.5.8.1 Pulsed wave Doppler instrumentation:

The PW transducer is fundamentally different in design than the CW transducer. The transducer need only contain one crystal or element which functions intermittently in both transmit and receive mode as for pulse-echo imaging . Most modern transducers are arrays which use groups of elements to generate the sound beam and may function simultaneously in imaging and PW Doppler
modes. With single crystal mechanical transducers, the transducer is operated alternatively between imaging and PW Doppler. With PW instruments, the oscillator and receiver are gated since the transducer is pulsed rather than continuous. The signal flow out of the receiver is similar. (zagzebski, 1969).

Gating allows for sampling of echoes from specific tissue depths which are operator controlled and selectable. Therefore, gating provides range or depth resolution which is lacking with CW Doppler. Doppler shifts from specific tissue depths can be detected based on pulse-echo go-return time. Receiver gate length (also known as sample volume) and depth are controlled by the operator during the examination. (zagzebski, 1969).
2.5.8.2 Size of the pulsed Doppler Sample Volume:

The sample volume (SV) orange gate is the flow sensitive region of the sound beam during PW Doppler operation. See atlas figure 2-4. The axial length of the SV is determined by the length of the receiver gate and the spatial pulse length. The width of the SV is determined by the beam width and is thus dependent upon all the parameters that affect formation of the sound beam including the transducer aperture, operating frequency, and focusing. In general, a long SV is helpful for locating Doppler shifts whereas a short SV is better to perform spectral analysis. (zagzebski, 1969).

Sample sizes between 5 and 10 mm usually produce adequate sensitivity, and flow velocities within these ranges vary only slightly. The spatial resolution of PW Doppler is determined by the sample volume. Axial resolution of the transducer when operated in PW Doppler mode is proportional to the length of the sample volume. However, that the length of the sample volume is determined not only by the pulse length but also by the receiver gate. Typically one-half of the pulse length is added to the receiver gate length to produce the effective sample volume length.

Sample volume lengths usually range from 1 mm to 15 mm. The lateral resolution of a transducer operated in PW Doppler mode is the same as the transducer operated in imaging mode since both are determined by the beam width. (zagzebski, 1969).
2.5.9 Extracting the Doppler Signal:

The simplest Doppler systems consist of a transducer with two piezoelectric elements, one continuously transmitting ultrasound and the other continuously receiving back-scattered signals from both stationary tissue and flowing blood. This received signal therefore consists of both the transmitted frequency reflected by stationary objects and the Doppler-shifted frequencies back-scattered from moving blood cells. As the returning echoes are of low amplitude, first they must be amplified. The Doppler shift frequency can then be extracted from the received signal by a process known as demodulation. (zagzebski, 1969).
One method of demodulation used in Doppler systems is the received signal multiplied by the transmitted signal and the product is filtered to remove the high frequencies, thus providing the Doppler shift frequency. The received signal has a different frequency from the transmitted frequency, owing to the Doppler effect, and a lower amplitude, owing to attenuation of the signal by overlying tissue, once the Doppler shift frequency has been extracted (by demodulation) and amplified, it can simply be output to a loudspeaker or investigated using a spectrum analyzer. (zagzebski, 1969).

Figure 37: shows Doppler signal processing (Vaisala 2005)
2.5.10 Duplex ultrasound:

Duplex ultrasound systems, combining pulse echo imaging with Doppler ultrasound. Combining the pulse echo imaging with Doppler ultrasound allows interrogation of a vessel in a known location and permits close investigation of the hemodynamics around areas of atheroma visualized on the image. Ideally, to produce a good image of a vessel wall, the vessel should be at right angles to the ultrasound beam. This is the case in the majority of peripheral vessels, as they mainly lie parallel to the skin. However, the Doppler equation shows that no Doppler signal will be obtained when the angle of insonation is at right angles to the direction of flow (as $\cos \theta = 0$). (zagzebski,1969).

The greatest Doppler shift is detected when the beam is parallel to the direction of flow. Therefore, there is a conflict between the ideal angle of the beam used for imaging and that used for Doppler recordings. A compromise would involve the ability to steer or angle the Doppler beam independently of the imaging beam. Some early duplex systems did this by mounting a separate Doppler element, with an adjustable angle, next to the imaging element. Modern linear array and phased array transducers overcome this by producing a steered beam.

The transducer elements are most sensitive to the returning signals that are at right angles to the front face of the element. This means that, as the beam is steered, the sensitivity of the Doppler transducer will fall to some extent, and therefore the Doppler beam can only be steered by about 20° left and right of center. There is thus a compromise between the choice of Doppler angle and sensitivity. (zagzebski,1996).
2.5.11 Doppler spectral analysis:

There are three types of flow observed in the normal arteries:

- **Laminar**

- **Disturbed**

- **Turbulent**

The term laminar flow refers to the fact that the blood cells move in layers, one layer sliding over another, with the different layers being able to move at different velocities. In laminar flow, the blood cells remain in their layers.

Turbulent flow occurs when laminar flow breaks down, which is unusual in normal healthy arteries but can be seen in the presence of high-velocity flow caused by stenoses. When flow enters a vessel from a reservoir (in the case of blood flow, this is the heart), all the fluid is moving at the same velocity, producing a flat velocity profile. This means that the velocity of the fluid close to the vessel wall is similar to that at the center of the vessel. As the fluid flows along the vessel, viscous drag exerted by the walls causes the fluid at the vessel wall to remain motionless, producing a gradient between the velocity in the center of the vessel and that at the walls. (zagzebski,1996).

As the total flow has to remain constant (as there are no branches in our imaginary tube), the velocity at the center of the vessel will increase to compensate for the low velocity at the vessel wall. This leads to a change in the velocity profile from the initial blunt flow profile to a parabolic flow profile. This is often known as an entrance effect. The distance required for the flow profile to develop from the blunt to the parabolic profile depends on vessel diameter and velocity, but it
is usually several times the vessel diameter. With blood flow, the velocity profiles are complicated by the pulsatile nature of the flow.

Figure 38: shows characteristic of blood flow (Dubiel, M., et al 2000)

2.5.11.1 Spectral analysis

The Doppler shift signal extracted from the echoes returning from moving blood is a complex signal containing a range of frequencies. This is because all the RBCs in a sample volume are very rarely moving at exactly the same velocity. Friction between the layers of moving blood and even between individual RBCs causes the cells to move at a range of velocities. Thus, even with a constant angle and output frequency, the returning signal from a volume of RBCs will contain a range of frequencies referred to as a frequency spectrum. An analysis of this spectrum involves
separating this complex signal into its component parts - its component frequencies. (zagzebski,1996).

The analyser used to separate the complex Doppler shift signal into its component frequencies. After this analysis is done, the component frequencies can be converted into velocities allowing a quantitative analysis of the range of RBC's velocities in the sample volume to be obtained. Several methods have been devised to analyse the Doppler shift frequency spectrum. These include older analog methods such as multi-filter analysis and the zero-crossing detector. Modern Doppler systems use a digital method of spectrum analysis called fast Fourier Transform or FFT.

Fast Fourier Transformer (FFT) is a mathematical technique developed earlier this century by which a complex wave can be broken down into a series of simpler sine waves. However, it was not until the advent of the computer that this technique could be done fast enough to permit analysis of a constantly changing signal such as the Doppler shift signal from RBCs. The modern FFT is a digital process performed by a microprocessor. First, the analog Doppler signal is digitized an analog - digital converter (ADC). Next, short 5 - 10 microsecond samples of the signal are processed using the FFT algorithm to extract the component frequencies. Finally the digital component frequencies are converted back into an analog signal by a digital - analog converter (DAC) for spectral display. The output from the FFT consists of a range of frequencies of varying amplitudes per unit of time (zagzebski,1969).
2.5.11.2 Spectral Display:

The Doppler spectral display provides a readout of the distribution of frequencies and hence, reflector velocities contributing to the signal. Velocity versus time flow patterns for arteries and many large veins have been established. Deviation of these patterns from normal are evaluated using spectral Doppler, where the sample volume was placed at the distal margin of the stenotic region, other important characteristics of flow pattern may also be gleaned from the spectral display, for example with pulsed Doppler and short sample gate positioned in the center of a vessel, a narrow band Doppler frequency spectral display is usually obtained. (zagzebski, 1996).

![Diagram of Doppler flow](www.u/s image.com)

**Figure 39:** shows the sample volume (www.u/s image.com)

The area beneath the peak of the spectral trace is called the spectral window, partial or total fill in of the spectral window can occur in the presence of turbulence. These disturbances in the Doppler spectrum are also called spectral broadening because they are related to a wider range of Doppler frequencies from the sample volume. The presence of the obstructions may sometimes be detected.
from spectrum. If the vessel is large compared to the sample volume, a fairly narrow velocity range is sampled. This results in a narrow frequency band and the spectral window on the display. In presence of mild or several turbulence caused by obstruction, this spectral window is filled in partially or entirely.

**Figure 40: showed spectral window (Dubiel, M., et al 2000)**

Some instruments display additional information related to the instantaneous distribution of velocities in the spectrum. The mean is the average value of all signals in the spectrum at any given time, where the mean frequency trace is super imposed on spectral trace from the artery. The mode is the most likely velocity, or the value in the spectrum that is the whitest shade of gray, this correspond the most prevalent red blood cell velocity in the sample volume. The spectral width indicates the range of Doppler frequencies, and hence, reflector velocities contributing to the Doppler signal, and the peak is the top of the spectral envelope. (Corbett et al, 2005)

2.5.11.3 Diagnostic Spectral Display Features and Measurements:
Duplex and triplex Doppler systems can provide many characteristics of blood flow which can be grouped as qualitative or quantitative. Qualitative features are descriptive whereas quantitative are numerical and obtained by making manual or automatic measurements of the spectral waveform. Both types of information are helpful in assessing the circulatory system and understanding hemodynamics. (Corbett et al, 2005)

- **Qualitative features include:**
  - Absence or presence of flow
  - Direction of flow
  - Flow phasicity
  - Presence or absence of spectral broadening
  - Strength or magnitude of the Doppler signal

- **Quantitative measurements include:**
  - Velocity (peak, mean, etc.)
  - Systolic/diastolic ratio (A/B)
  - Resistive index (RI)
  - Pulsatility index (PI)
  - Acceleration time (AT)
  - Acceleration index (AI)
2.5.12 Flow Velocity:

Blood velocity can be estimated from the Doppler frequency shift if the Doppler angle is known. With CW Doppler, the transducer is manipulated to obtain the highest Doppler shift and therefore the high velocity in the sampled vessel. Peak or maximum velocity is obtained only when the sound beam is parallel to the direction of flow (Doppler angle is 0°; cosine of the angle is 1). With duplex and triplex scanners, the sonographer manipulates the transducer to direct the sound beam at an angle of 30 to 60 degrees to the direction of flow and activates the system’s angle correction which tells the system the Doppler angle. (Corbett et al, 2005)

The conversion of Doppler shift to flow velocity is only accurate if the sonographer sets the angle correction cursor truly parallel to the axis of flow. The dashed line in the center of the vessel represents the angle correction line which is parallel to the vessel axis in this example. Velocity data can be measured on spectral display and is expressed in m/s or cm/s. Doppler Indices All of the Doppler indices are independent of the Doppler angle and the direction of blood. Doppler frequency shift may be substituted with flow velocity in all of the index equations.

Resistive Index (RI) or Pourcelot index is described as the maximum systolic Doppler frequency shift or velocity minus the minimum end diastolic Doppler frequency shift or velocity divided by the maximum systolic Doppler frequency shift or velocity.

\[
RI = \frac{\text{peak systolic velocity} - \text{end diastolic velocity}}{\text{peak systolic velocity}}
\]
Depending on the downstream resistance to flow (as well as other factors), diastolic flow can be relatively high, relatively low, absent, or reversed in part or all of diastole. The greater the difference between the maximum systolic and minimum ends diastolic Doppler frequency shifts or velocities, the greater the RI. Values range from 0 to 1, with 1 representing the highest resistance to forward flow and 0 indicating no difference between maximum systolic and end diastolic Doppler frequency shifts or velocities. RI values greater than 1 occur when the end diastolic flow is reversed. In general, RI values greater than 0.7 are interpreted as high and values less than 0.4 are considered low. (Corbett et al, 2005).

Pulsatility Index (PI) is defined as the maximum systolic Doppler frequency shift or velocity minus the minimum end diastolic Doppler frequency shift or velocity divided by the mean Doppler frequency shift or velocity from the beginning of systole to the end of diastole. (Corbett et al, 2005)

$$PI = \frac{\text{peak systolic velocity} - \text{end diastolic velocity}}{\text{time averaged velocity}}$$

PI is considered by some investigators to be a better physiologic parameter since all of the frequency shifts in the waveform during a complete cardiac cycle are taken into account. All modern Doppler instruments have the technical capability of measuring the mean Doppler shift (with older equipment, this had to be done by an off-line computer method and was too impractical
for daily clinical use). Like RI, the higher the value of PI, the greater the downward resistance to flow. PI values greater than 1.2 are considered high and values below 0.8 are considered low. (Corbett et al, 2005)

Systolic/Diastolic Ratio (S/D), also known as the A/B ratio, is defined as the maximum systolic Doppler frequency shift or velocity divided by the minimum end diastolic Doppler frequency shift or velocity. This ratio is less commonly used as problems arise interpreting values when end diastolic flow is absent or reversed. (Corbett et al, 2005)

\[
S/D \text{ ratio} = \frac{\text{max. systolic shift}}{\text{min. end diastolic shift}}
\]

2.5

2.5.13 Acceleration Time (AT):

Is defined as the time interval from the onset of systole to the initial systolic peak. The unit for AT is seconds (s). This time interval is typically short. It increases downstream to a significant flow obstructing lesion. Tardus Parvus Waveform Schematic diagram showing the difference in time rise to peak systolic velocity (t) and the lower peak systolic velocity (v) seen in a tardus-parvus waveform compared to a normal waveform. (Corbett et al, 2005)
2.5.14 Acceleration Index (AI):

Is the relationship between the slope of the systolic upstroke and the acceleration time (rise over run). (Corbett et al, 2005)

\[
AI = \frac{\text{peak systolic velocity}}{\text{acceleration time}}
\]

On the velocity display, it is calculated by dividing the peak systolic velocity (m/s or cm/s) over the acceleration time (s). The unit of acceleration index on this display is m/s² or cm/s². AI on the frequency display is calculated by dividing the slope of the systolic upstroke (kHz/s) by the carrier Doppler frequency (MHz). The unit for AI on the frequency display is kHz/s/MHz. Both AT and AI are values which reflect flow status downstream or distal to a stenosis. In the absence of any significant flow obstruction, the AT is relatively rapid and the AI is relatively high. With a significant or high grade stenosis (>80%), the waveform downstream from a proximal flow obstruction is dampened or attenuated and is associated with an increased AT and a decreased AI. (Dubiel, M., et al 2000)

2.5.15 Nyquist Limit and Aliasing:
As previously indicated, PW Doppler transducers inherently have good range or depth resolution because any pulsed system has a time base or clock by which to reference events like the depth of Doppler shifted echoes. The pulsing rate of a PW Doppler is determined by the PRF of the gated oscillator. This may be considered the sampling frequency - if it is too low, the receiving information will be sampled too infrequently and incorrectly measured. The PRF determines how high a Doppler shift can be detected - the higher the PRF, the higher the detectable Doppler shift, and vice versa. As for imaging, the maximum PRF that can be used is governed by the time it takes for echoes to return to the transducer from specific tissue depths. The time is referred to as the go-return time and depends on the speed of sound in tissue and the path length or depth of the reflector. (Corbett et al, 2005)

The speed of sound in tissue is considered a constant and the system is calibrated to assume it is 1.54 mm/µs. The only variable left is the go-return time. The longer it is, the lower the maximum PRF, and vice versa. The system must wait for all echoes to return to the transducer before sending out the next pulse otherwise range ambiguity occurs (the system assumes that deep echoes are related to the current pulse timing rather than the previous and incorrectly locates deep echoes too close to the transducer on the display. The inability of a PW Doppler transducer to detect large Doppler shifts is known as aliasing.

Aliasing is a phenomenon that can occur when dealing with sampled signals. A continuous signal can only be represented by discrete periodic samples if the samples are acquired at a high enough rate. If the sampling rate is too low for a given signal, large signal changes can occur between samples and the acquired samples may lack any information regarding these fast changes. Most of us have seen an example of aliasing when watching a speeding stage coach in a cowboy movie.
The motion of the wheels is captured (sampled) on film at a rate of 24 frames per second. When the rotation speed of the wheels increases, that sampling rate becomes inadequate.

Figure 42: Image demonstrating aliasing (A) and flow reversal (R) in an internal carotid artery. Aliasing can be recognized as a color change that wraps around from the top to the bottom of the color scale, or vice versa. A change in color due to a relative change in the direction of flow can be recognized as a change in color across the baseline, at the center of the color scale, passing through black (see color scale on right of image) (Dubiel, M., et al 2000).

Figure 43: demonstrate the aliasing (Dubiel, M., et al 2000)
The result is that the wheels appear to rotate at a lower speed in the opposite direction. In other words, the low sampling rate causes fast motion in one direction to be disguised in the form of slow motion in the opposite direction. This disguise is what gives rise to the term aliasing. Exactly the same phenomenon occurs with PW Doppler transducers. Short bursts or pulses of ultrasound waves are emitted to sample the velocity of RBCs. (Corbett et al, 2005)

The sampling rate is the PRF. To examine a deep vessel, sufficient time must be allowed for a pulse to reach the vessel and return to the transducer before the next pulse is emitted. This means that for deeper vessels, lower PRF rates must be used. If blood is moving at such a high velocity that it cannot be adequately sampled by the PRF used, the Doppler shift will alias and appear as a low frequency shift. The maximum detectable Doppler shift with PW Doppler is known as the Nyquist limit, and is defined as one-half the PRF.

What this equation indicates is that the system PRF must be twice the frequency of the Doppler shift frequency. If the Doppler shift exceeds one-half the system PRF or Nyquist limit, then aliasing occurs and it is no longer possible to quantify peak flow velocity accurately. Aliasing is commonly called "wrap around" because the flow that exceeds the Nyquist limit appears as if it were flowing in the opposite direction. This type of display "wrap around" can be overcome on modern equipment by merely shifting the baseline so the entire waveform can be displayed on the same side of the baseline. (Corbett et al, 2005)

\[
\text{Nyquist limit} = \frac{\text{PRF}}{2}
\]
2.5.16 Eliminating aliasing:

The most straightforward way to eliminate aliasing when it occurs is to adjust the velocity or frequency scale on the Doppler spectral display. Most instruments have the PRF of the pulsed Doppler unit linked to the scale setting. As the scale setting is increased, the PRF is automatically increased to satisfy the Nyquist rate for the maximum scale setting. If the spectral scale as its maximum setting, another method to eliminate the appearance of aliasing is to adjust the spectral baseline, if neither of these methods succeeds, aliasing may sometimes be eliminated by using a lower frequency ultrasound transducer. Another possible method is to locate a window to the region of interest for which the incident sound beam angle is closer to 90 degree (Zagbaski, 1996).
Figure 44: Images of Aliasing. A: This will lead to the assignment of the incorrect color to represent the velocity present within the vessel, shown here in blue. B: Increasing the PRF may overcome aliasing. C: If the PRF is set too high, it may prevent low velocities, present at the vessel walls, from being detected.

2.5.17 Poiseuille’s Law and Equation:

So far in our discussion of energy we have noted that two types of energy exist in a flowing blood stream and that this energy can be lost due to frictional and directional changes in the vessels. We have also stated that the loss of energy due to friction is related to the size of the vessel, and that
disturbed flow results in increased energy loss. We also stated earlier, that several factors besides the pressure gradient and resistance to flow affect the flow rate of our circulation. Let’s review these factors now as we examine an equation that helps us to quantify the energy lost in a given vessel under various flow states. The most important law governing the flow of fluids through cylindrical tubes is called Poiseuille’s law which relates velocity and flow volume in the following equation:

\[ V = \frac{Q}{A} \text{ or } Q = V \times A \]

Where,

- \( V \) = velocity (cm/sec)
- \( Q \) = volume flow (cm\(^3\)/sec)
- \( A \) = cross-sectional area of a vessel (cm\(^2\))

Flow velocity in a tube (vessel) is directly related to the volume of fluid and inversely related to tube area. Thus, the higher the flow volume, the greater the flow velocity, and the smaller the vessel, the higher the velocity (assuming other factors remain constant). (Corbett et al, 2005) Flow volume is the product of flow velocity and vessel area and directly proportional to these two factors. It is important to note that flow volume in different segments of the vessel remains the same. This
occurs because fluid cannot be created or destroyed as it flows through the vessel (tube or phantom). It is the velocity that changes as the blood the passes through different segments of the vessel.

The velocity at any point in the circulatory system is dependent not only on cross-sectional area but also on the magnitude of the blood flow (Q), and the magnitude of flow (Q) depends on many factors, including pressure gradient, the properties of the fluid and the dimensions of the entire circulatory system. We have already discussed how the pressure gradient changes in the circulatory system, thus accounting for the low flow velocity in the capillary bed. (Corbett et al, 2005)

Poiseuille's Law describes the "viscous" or frictional loss of energy that occurs with changing vessel area and is modelled on continuous (non pulsatile) laminar flow of a simple fluid in a rigid tube of uniform size. Fortunately, it also applies to the flow of blood in the circulatory system which can be pulsatile and in compliant vessels of varying dimensions. Let's examine Poiseuille's equation

\[ Q = \frac{\pi (P_1 - P_2) r^4}{8L\eta} \]
Where:

\[ Q = \text{volume flow rate} \]
\[ P_{1} - P_{2} = \text{pressure differential (from proximal to distal end of tube)} \]
\[ r = \text{radius of the vessel} \]
\[ L = \text{length of the vessel} \]
\[ n = \text{viscosity of the fluid} \]

\((\pi/8 \text{ is the constant of proportionality})\)

Poiseuille's law states that flow \((Q)\) varies directly as the pressure difference \((P_{1} - P_{2})\) power of the radius of the vessel, and varies inversely as the length of the vessel and the viscosity of the blood.

### 2.6 Previous studies:

Currently, Doppler ultrasonography (DU) velocimetry of uteroplacental, umbilical, and fetal vessels has become the established method for antenatal monitoring (Baschat and Gembruch, 2003, Dubiel et al., 2000).

Circulatory changes, reflected in certain fetal Doppler waveforms, predict adverse perinatal outcome (Arduini and Rizzo, 1993). Recent studies have shown the efficacy of the middle cerebral artery (MCA) Doppler assessment (Bahlmann et al., 2002).

Recently, with the advancement of pulsed and color-coded DU combined with better reproducibility, the MCA has emerged as the vessel of choice in the Doppler assessment of fetal intracranial as well as other organs perfusion (Mari et al., 1989).

Also A. S. M. et al 2004 had studded fetal heart rate and umbilical artery flow velocity variability in intrauterine growth restriction; Doppler velocity waveforms were collected from long-lasting
umbilical artery recordings in 15 fetuses with growth restriction and 15 normal age matched controls at 23-35 weeks of gestation. Absolute heart rate and umbilical artery blood flow velocity as well as the coefficient of variation were determined. Using power spectral analysis the and high frequency bands of heart rate variability and blood flow velocity variability were calculated. The low to high *(LH) ratio of heart rate variability and blood flow velocity variability were examined as a measure of sympathovagal balance. The results in growth restricted fetuses umbilical artery velocities were significantly reduced. Heart rate variability was significantly reduced in the presence of growth restriction, but no significant difference was demonstrated for blood flow velocity variability, the LH ratio for heart rate variability was significantly reduced in the presence of growth restriction.

Applicability of Doppler indices in the diagnosis of abnormalities is possible only when there are reference normal values for each index. Although various investigators have described and established gestational age-related reference curves, this is the first study performed in Iran (Manning et al., 1980, Wellek and Merz, 1995).

The (C/U) ratio, is considered as an indicator of IUGR, it is also an accurate parameter for prediction of poor perinatal outcome (Schneider and Loos, 1990)
Chapter three

Material and methods
Chapter three

3. Material and methods

3.1 Material of Study

3.1.1 Tools and equipment:

The Umbilical (UA) and Middle cerebral (MCA) arteries should be performed only with appropriate instrumentation. The current standard of practice in this research includes the following tools and equipments which used effectively and accurately to give the desired expected results planed previously in the hypothesis and objective articles in chapter one.

3.1.2 Ultrasound system:

The applied ultrasound unit was a General Electric (GE) medical system, logic 5 expert

Figure 3.1: shows General Electric (GE) medical system, logic 5expert (zweibel, 2000)
1. **Ultrasound Transducer:**

The applied ultrasound Transducer was a convex probe with a frequency of 3.5MHz, made by yokogawa medical system, Ltd.7-127 Asahigaoka 4-home Hino-shi Tokyo, Japan. Model 2302650 with serial of 1028924YM7 and manufactured date of April 2005.

![Image of convex probe](http://www.usimage.com)

**Figure 3.2:** shows convex probe with a frequency of 3.5MHZ, made by the yokogawa medical system (http://www.usimage.com).
2. Ultrasound gel:

The ultrasound gel was a higeen ultrasound transmission gel made by households and toiletries company (Sukhitan) Amman, Jordan.

![Ultrasound Gel Image]

Figure 3.3: shows Higeen ultrasound transmission gel made by households and Toiletries Company (Sukhitan) Amman, Jordan. (Remi, 1995)

Ultrasound gel is prepared by using these ingredients with the following quantities in grams unit:

a. Carbomer (10.0g) a synthetic high molecular weight polymer, it is chemical structure.

b. EDTA (0.25g) (Ethelyen Diamine Tetraetiec Acid) a white crystalline powder, very slightly soluble in water which been added to form the ultrasound gel.

c. Propylene glycol (75.0g), a colorless, viscous liquid with slight sweet taste which form a part of ultrasound gel components

d. Trolamine (12.5g) a mixture of bases, colorless or slightly yellow as a part of ultrasound gel (Remi, 1995)

e. Distilled water (500g), which is additive the previous mention constitution.
3. Ultrasound printer:

Ultrasound printer used is digital graphic printer, 100V, 15 A and 50/60 Hz made by Sony corporation-Japan, with serial number of 3-619-GBI-01

Figure 3.4: illustrates digital graphic Sony printer with addition to high quality printing thermal paper recording (http://www.u/s image .com).

4. Thermal papers:

Ultrasound images were documented in thermal papers of high quality printing thermal papers type I (normal) UPP_110S,110mmx20m, Sony Corporation, Tokyo, Japan
3.1.3 Patient preparation:

The Doppler ultrasound of umbilical and middle cerebral arteries in Intra Uterine Growth Restriction (IUGR) has been scanned without previous preparation; only short orientation and aware of the nature of the study and had to willingly, provide informed consent before entering the study.

3.2 Method of the study:

3.2.1 Examination protocol:

An examination or the techniques protocol should meet or exceed the standards established by the American Institute of Ultrasound in medicine (AIUM). The standard is the same which was our guide for sonographic scanning in this research.
3.2.2 Sample selection:

This study has been carried out in Soba Hospital affiliated to University of Khartoum. The population of study is pregnant women with high risk pregnancy and diagnosed as intrauterine growth restriction. Sample selection and negligence depend on two criterions which are inclusion and exclusion criterions, the included subjects are patients in the 3rd trimester with high risk pregnancy pregnant women who have clinical history(e.g. BH) and diagnosed as intrauterine growth restriction; the excluded are gestational age less than 3rd trimester, congenital malformation and chromosomal abnormalities, twin’s pregnancy and oligohydramnios caused by peri- rupture membrane.

Due to extended scope of our exclusion criteria the sample size was hundred (100) pregnant women with high risk pregnancy at 3rd trimester, they were scanned and compared with control group fifty (50) patients with normal pregnancy, the total number of subjects was (150).

3.2.3 Patient position:

The sample under study has been scanned to visualized the umbilical and middle cerebral arteries in the supine position with knee support with head of bed elevated 30 degree, and a coupling medium (e.g., gel) is applied to the transducer to reduce the interference that may be introduced by air between the transducer and the skin.

TAS: Performed by placing the transducer in contact with the skin just above the symphysis pubis. Pulsed wave ultrasound is used to provide data for Doppler sonograms and color flow images.
3.2.4 Transducer position:

A scanner with a carrier frequency of 3.5 MHZ and color Doppler, transabdominal (TA) curve linear transducer will be used. The angle of insonation will be kept at 55 degree in all cases. Several transducer positions were used in this research to examine the umbilical and middle cerebral arteries in long-axis (longitudinal) planes as illustrated in figure 3.10 A, B ,C and D and short-axis(transverse),the planes was obtained from an anterior and lateral or posterolateral approach, depending on which best shows the vessels.

TAS: Performed by placing the transducer in contact with the skin just above the symphysis pubis, the subjects were scanned after recording of the height, weight and ages. Pulsed wave ultrasound is used to provide data for Doppler sonograms and color flow images. The Doppler signal is then obtained by placing the Doppler gate directly over the vessel of interest simple manipulation of the transducer angle will capture the best waveform.
The umbilical arteries will be study by identifying within the amniotic fluid by the presence of parallel line echoes, which displayed a pulsatile activity on real time image, the Power Doppler (PD) followed by Pulse Wave Doppler (PWD) modes were applied for the spectral analysis and determination the values of peak systolic velocity (PSV) in cm/sec, end diastolic velocity(EDV) in cm/sec, resistive index(RI) and pulsatility index (PI) for each artery respectively. In addition using Doppler angle of 60 degree or less could help in making Doppler signal waveform stronger and clear.

Figure 3.7: determine accurate and normal Umbilical Artery (UA) Doppler measurement (zweibel, 2000)
The obtained numerical values of the above different variable were taken from the middle part of each artery because flow pattern seems to be steady and uniform, which actually help in avoid any misleading or wrong values. the recordings will taken close to the fetal insertion in quite fetal breathing. The flow velocity waveforms obtained from umbilical and MC arteries will computed automatically, the program identified individual cardiac cycles and computed peak systolic velocity. End diastolic velocity and S/D ratio.

The middle cerebral artery is the most studied cerebral artery because it is easy to sample and it can be sampled at an angle of 0° between the ultrasound beam and the direction of the blood flow. Therefore, for the middle cerebral artery we are able to determine angle-independent indices (the most used is the pulsatility index) and also the real velocity of blood flow.

**Figure 3.8**: determine accurate Middle Cerebral Artery (MCA) Doppler (Zweibel, 2000)
E. Color flow imaging, practical guidelines:

(1) Select the appropriate applications/set-up key. This optimizes parameters for specific examinations.

(2) Set power to within fetal study limits. Adjust color gain. Ensure focus is at the region of interest and adjust gain to optimize color signal.

(3) Use probe positioning/beam steering to obtain satisfactory beam/vessel angle.

(4) Adjust pulse repetition frequency/scale to suit the flow conditions. Low pulse repetition frequencies are more sensitive to low flows/velocities but may produce aliasing. High pulse repetition frequencies reduce aliasing but are less sensitive to low velocities.

(5) Set the color flow region to appropriate size. A smaller color flow ‘box’ may lead to a better frame rate and better color resolution/sensitivity.

3.3 Data analysis:

The collected data arranged in master sheet and enter the computer and analyzed by excel and frequency tables and presented in form of graphs, table and figures.

3.3.1 Data storage:

The data collected during this study should be stored on CD, data collection sheets and hard copy of Doppler ultrasound image was additionally obtained and also the data stored in my personal computer.
CHAPTER FOUR

The Results
CHAPTER FOUR

4. Results

Table 4.1 the fetal gender frequency and percentage

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>44</td>
<td>44.0</td>
</tr>
<tr>
<td>Female</td>
<td>56</td>
<td>56.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 4.2: the Descriptive Statistics of UA and MCA indices

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Statistic</td>
<td>Statistic</td>
<td>Std. Error</td>
</tr>
<tr>
<td>PI Umbilical Artery</td>
<td>100</td>
<td>1.299</td>
<td>.0633</td>
</tr>
<tr>
<td>RI Umbilical Artery</td>
<td>100</td>
<td>.843</td>
<td>.0277</td>
</tr>
<tr>
<td>S/D Umbilical Artery</td>
<td>100</td>
<td>5.137</td>
<td>1.0630</td>
</tr>
<tr>
<td>PI Middle Cerebral Artery</td>
<td>100</td>
<td>1.347</td>
<td>.0394</td>
</tr>
<tr>
<td>RI Middle Cerebral Artery</td>
<td>100</td>
<td>.723</td>
<td>.0116</td>
</tr>
<tr>
<td>S/D Middle Cerebral Artery</td>
<td>100</td>
<td>3.833</td>
<td>.1481</td>
</tr>
<tr>
<td>Fetal Weight</td>
<td>100</td>
<td>1.8656</td>
<td>.06257</td>
</tr>
</tbody>
</table>
Table 4.3: the Umbilical Artery EDF frequency and percentage

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Decreased</td>
<td>37</td>
<td>37</td>
</tr>
<tr>
<td>Positive</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Reversed</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 4.4: the Middle Cerebral Artery EDF frequency and percentage

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Positive</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 4.5: the liquor volume in IUGR

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased</td>
<td>15</td>
<td>15.7</td>
</tr>
<tr>
<td>Oligo</td>
<td>38</td>
<td>37.3</td>
</tr>
<tr>
<td>Poly</td>
<td>4</td>
<td>3.9</td>
</tr>
<tr>
<td>Normal</td>
<td>43</td>
<td>43.1</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Table 4.6: the IUGR Classification

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Symmetric</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>symmetric</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 4.7: the maternal clinical history

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>58</td>
<td>58</td>
</tr>
<tr>
<td>Hypertension</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>SLE</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Figure 4.1: demonstrate the relationship between fetal weight and RI of UA.
Table 4.8: the Correlation between RI Umbilical Artery and Fetal Weight

<table>
<thead>
<tr>
<th></th>
<th>RI Umbilical Artery</th>
<th>Fetal Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>RI Umbilical Artery</td>
<td>Pearson Correlation</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed)</td>
<td>.013</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>100</td>
</tr>
<tr>
<td>Fetal Weight</td>
<td>Pearson Correlation</td>
<td>-.345*</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed)</td>
<td>.013</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>51</td>
</tr>
</tbody>
</table>

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

Table 4.9: the Correlation between the Fetal Weight and RI Middle Cerebral Artery

<table>
<thead>
<tr>
<th></th>
<th>Fetal Weight</th>
<th>RI Middle Cerebral Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal Weight</td>
<td>Pearson Correlation</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>100</td>
</tr>
<tr>
<td>RI Middle Cerebral Artery</td>
<td>Pearson Correlation</td>
<td>.230</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed)</td>
<td>.104</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>100</td>
</tr>
</tbody>
</table>
### Table 4.10: the EDF Umbilical Artery vs. Liquor Volume Crosstabulation

<table>
<thead>
<tr>
<th>EDF Umbilical Artery</th>
<th>Decreased</th>
<th>Oligo</th>
<th>Poly</th>
<th>Normal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>Decreased</td>
<td>8</td>
<td>16</td>
<td>2</td>
<td>14</td>
<td>40</td>
</tr>
<tr>
<td>Positive</td>
<td>2</td>
<td>11</td>
<td>2</td>
<td>21</td>
<td>36</td>
</tr>
<tr>
<td>Reversed</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>37</td>
<td>4</td>
<td>43</td>
<td>100</td>
</tr>
</tbody>
</table>

### Table 4.11: GA estimation Paired Sample T- Test

<table>
<thead>
<tr>
<th>Paired Differences</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>95% Confidence Interval of the Difference</th>
<th>T</th>
<th>df</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA Ultrasound - GA LMP</td>
<td>-3.588</td>
<td>1.577</td>
<td>.221</td>
<td>-4.032, -3.145</td>
<td>-16.249</td>
<td>100</td>
<td>.000</td>
</tr>
</tbody>
</table>
Figure 4.2: demonstrate the difference between fetal GA by Ultrasound and GA by LMP

(a strike indicates the significant difference (p < 0.001))

<table>
<thead>
<tr>
<th>Table 4.12: the Descriptive Statistics of UA and MCA indices for control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>**</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>PI Umbilical Artery</td>
</tr>
<tr>
<td>RI Umbilical Artery</td>
</tr>
<tr>
<td>S/D Umbilical Artery</td>
</tr>
<tr>
<td>PI Middle Cerebral Artery</td>
</tr>
<tr>
<td>RI Middle Cerebral Artery</td>
</tr>
<tr>
<td>S/D Middle Cerebral Artery</td>
</tr>
</tbody>
</table>
Figure 4.3 Umbilical artery Doppler indices in control group and IUGR, data presented as mean (a strike indicates the significant difference (p < 0.001))

Figure 4.4 MCA Doppler indices in control group and IUGR, data presented as mean (a strike indicate the significant difference (p < 0.001))
Chapter Five

5. Discussion, conclusion and recommendations

5.1 Discussion:

This study has been carried out in Soba Hospital affiliated to University of Khartoum, with general aim to explore and record the Doppler Ultrasound assessment of the fetal umbilical and middle-cerebral arteries in Intrauterine Growth Restriction (IUGR) during third trimester. 150 patients were enrolled in the study (100 patients in Intrauterine Growth Restriction (IUGR), 100 patients in prenatal outcome and 50 patients as a control group).

The results of the study showed that the mean Umbilical artery (UA) indices (PI 1.299, RI 0.843, S/D 5.137), on the other hand, the mean middle cerebral artery (MCA) indices (PI 1.347, RI 0.723, S/D 3.833), while the mean Umbilical artery (UA) indices in the control group was (PI 0.862, RI 0.582, S/D 2.51), the mean middle cerebral artery (MCA) indices (PI 1.782, RI 0.829, S/D 5.531). It is clearly seen that these indices found to be significantly higher in umbilical artery and lower in middle cerebral artery compared with the control group. Furthermore the mean fetal weight was (1.866 kg). This result in line with Mehmet Ozeren et.al study, which stated that the mean of UA and MCA indices were higher in preeclamptic patients without IUGR than normal pregnancies, these prove that Doppler Indices had a good predictive value among severe intrauterine growth restriction than in the mild cases, because in severe cases the values of indices become more obviously higher.

Regarding the End diastolic flow (EDF) of Umbilical artery, the study revealed that decreased in EDF seen in 40% of cases, absent of EDF represents 17%, positive EDF (37%) and the reversed EDF was (6%). Decreased, absent or reversed EDF underlying in vascular stress in case of placental insufficiency in which a higher vascular resistance exist, as a results diastolic flow
decreased. The absent or reversed EDF depend on severity of placental insufficiency (Krishna and Bhalerao, 2011)

The end diastolic flow (EDF) of middle cerebral artery, it was increased in 75% of cases and positive in 25%. The cerebral resistance index values decrease as a result of cerebral vasodilatation, this phenomenon is called the brain sparing effect, increased blood flow in vital organs in case of growth restriction as a result of redistribution of blood flow.

The Liquor volume has been assessed, the study showed that (38%) of cases have an oligohydramnios, (15%) decreased liquor, (4%) polyhydramnios and (43%) within the normal range of liquor volume. In growth-restricted fetuses, chronic hypoxia results in shunting of fetal blood away from the kidneys to more vital organs. (Luton et al., 2004)

The study showed that the majority of cases of IUGR were Asymmetrical IUGR (75%), and (25%) symmetrical IUGR. Asymmetric IUGR results from any cause of placental insufficiency affecting the delivery of oxygen and vital nutrients to the fetus, AC affected, symmetrical IUGR caused by fetal chromosome anomalies or infections, thus the sensitivity of the umbilical artery Doppler indices increases in asymmetrical growth retardation. Since placental insufficiency and the cerebral adaptation mechanism are considered together (aKaradeniz at.el European Journal of Obstetrics &Gynecology and Reproductive Biology82 (1999) 11–16, 1998)

As noticed in this study most of cases who have clinical history were hypertensive women (PIH) (30%) this due to narrowing and restricted lumen of blood vessels which will lead to low blood flow, pregnant women with heart disease (4%), pregnant women with epilepsy (6%), pregnant women with SLE (2%),while the normal pregnant women are (58%).
The result of the study showed a significant negative relationship between RI of umbilical artery and fetal weight in IUGR cases, \( p < 0.05, r = 0.35 \). The fetal weight decreased when the Resistive Index of umbilical artery was increased. (Borges et al., 2013)

Also the survey showed there is a significant difference between gestational age (GA) obtained by last minstrel period (LMP) and gestational age (GA) calculated with biometrical ultrasound \( p < 0.01 \).
5.2 Conclusion:

This study has been carried out in Soba Hospital affiliated to University of Khartoum, with general aim to explore and record the Doppler Ultrasound assessment of the fetal umbilical and middle-cerebral arteries in Intrauterine Growth Restriction (IUGR) during third trimester.

The results conclude that the mean Umbilical artery (UA) indices (PI 1.299, RI 0.749, S/D 5.137), on the other hand, the mean middle cerebral artery (MCA) indices (PI 1.347, RI 0.723, S/D 3.833), while the mean Umbilical artery (UA) indices in the control group was (PI 0.862, RI 0.582, S/D 2.51), the mean middle cerebral artery (MCA) indices (PI 1.782, RI 0.829, S/D 5.531). Furthermore the mean fetal weight was (1.866 kg).

Regarding the End diastolic flow (EDF) of Umbilical artery, the study revealed that decreased in EDF seen in 40% of cases, absent of EDF represents 17%, positive EDF (37%) and the reversed EDF was (6%). The end diastolic flow (EDF) of middle cerebral artery, it was increased in 75% of cases and positive in 25%.

The Liquor volume has been assessed, the study showed that (38%) of cases have an oligohydramnios, (15%) decreased liquor, (4%) polyhydramnios and (43%) within the normal range of liquor volume.

The study showed that the majority of cases of IUGR were symmetrical IUGR (75%), and (25%) Asymmetrical IUGR., in this study most of cases who have clinical history were hypertensive women (PIH) (30%) this due to narrowing and restricted lumen of blood vessels which will lead to low blood flow, pregnant women with heart disease (4%), pregnant women with epilepsy (6%), pregnant women with SLE (2%), while (58%) without any history of disorders.
The study showed a significant negative relationship between RI of umbilical artery and fetal weight in IUGR cases, (p < 0.05, r = 0.35). The fetal weight decreased when the Resistive Index of umbilical artery was increased, Also the survey showed there is a significant difference between gestational age (GA) obtained by last minstrel period (LMP) and gestational age (GA) calculated with biometrical ultrasound (p < 0.01).

In summary, the umbilical artery Doppler indices provide better values for predicting IUGR or adverse perinatal outcome in second and third trimester.

The correlation between abnormal Doppler indices of fetal vessels, adverse perinatal outcome and fetal distress or IUGR has been demonstrated by several investigators, an abnormal umbilical artery Doppler waveform is a strong and independent predictor of fetal distress or IUGR.
5.3 Recommendations:

After the enumeration of the results that related to the following thesis, there are some ideas which could help further in the field of research and better to be recommended as follows:

- Doppler U/S could be used as routine checkup, follow up in high risk pregnancy suspected of IUGR, to help management and control of IUGR.
- Doppler U/S is very important to pregnant women who have any complications to detect the IUGR, thus fetal problem could be avoided.
- Doppler assessment is a non invasive test, and thus is acceptable to patients and serial assessments should be done in last of third trimester to improve the outcome.
- Early screening of the UA Artery and MCA waveform should be performed, this may help in early diagnosis IUGR and may decrease the fetal and maternal morbidity and mortality rate.
- Doppler ultrasound should be part of setup of every units that provides antenatal medical services with good expertise and well trained examiners
- It would be better to do more studies in Doppler Ultrasound assessment of the fetal umbilical and middle-cerebral arteries in Intrauterine Growth Restriction (IUGR) during third trimester by using large sample and further modalities, and concentrate on combining UA&MCA Doppler ultrasound with other tests that used in clinical care, this may improve the predictive accuracy and the clinical important value of the tests and study the relation of tests that used in clinical care with Doppler of IUGR.
References:


ACC/SCN 2000 The fourth report on the world nutrition situation: nutrition throughout the life cycle.Geneva: Administrative Committee on Coordination,Subcommittee on Nutrition


Coleman MM, Spear ML, Finkelstein M, et al: Short-Term use of umbilical artery catheters may not be associated with increased risk of thrombosis. Pediatrics 2004 APR;113(4):770-4{Mid Line}

(Chudleigh T., Thilaganathan, Obstetric ultrasound how, why and when, 3rd, London Elsevier, B.2004;109)


D. G. Jang, Y. S. Jo, S. J. Lee, N. Kim, and G. S. R. Lee, “Perinatal outcomes and maternal clinical characteristics in IUGR with absent or reversed end-diastolic flow velocity in the umbilical artery,” Archives of Gynecology and Obstetrics. In press. View at Publisher · View at Google Scholar · View at PubMed


Guideline for the screening and treatment of retinopathy of prematurity; Royal College of Ophthalmologists (2008)


Iams JD, Romero R, Culhane JF, et al; Primary, secondary, and tertiary interventions to reduce the morbidity and mortality of preterm birth. Lancet. 2008 Jan 12;371(9607):164-75.


Nosarti C, Al-Asady MH, Frangou S, et al; Adolescents who were born very preterm have decreased brain volumes. Brain. 2002 Jul;125(Pt 7):1616-23


Perinatal Management of Pregnant Women at the Threshold of Infant Viability (The Obstetric Perspective), Scientific Impact Paper No. 41; Royal College of Obstetricians and Gynaecologists, Feb 2014


Quiram PA, Capone A Jr; Current understanding and management of retinopathy of prematurity. Curr Opin Ophthalmol. 2007 May;18(3):228-34.

Royal College of Obstetricians and Gynaecologists. Green-top Guideline No. 31: The investigation and management of the small-for-gestational-age fetus. 2013 [cited 2013 July 1]. (Evidence based guideline)


APPENDICES

APENDIX 1

Data collection sheet

<table>
<thead>
<tr>
<th>Fetal</th>
<th>Maternal</th>
<th>Doppler</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA</td>
<td>Weight</td>
<td>Umbilical arteries velocimetry</td>
</tr>
<tr>
<td>F.wt</td>
<td>Height</td>
<td>PI</td>
</tr>
<tr>
<td>Gender</td>
<td>Parity</td>
<td>RI</td>
</tr>
<tr>
<td>Amount of liquor</td>
<td>History</td>
<td>S/D</td>
</tr>
<tr>
<td>AC</td>
<td></td>
<td>MCA velocimetry PI</td>
</tr>
<tr>
<td>HC</td>
<td></td>
<td>RI</td>
</tr>
<tr>
<td>FL</td>
<td></td>
<td>S/D</td>
</tr>
<tr>
<td>BPD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The mean of normal and abnormal values of GA and indices

<table>
<thead>
<tr>
<th>Variables</th>
<th>Abnormal mean±SD</th>
<th>Normal mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA</td>
<td>31.9±3.2</td>
<td>33.4±3.5</td>
</tr>
<tr>
<td>RI</td>
<td>0.7±0.1</td>
<td>0.6±0.1</td>
</tr>
<tr>
<td>PI</td>
<td>1.2±0.3</td>
<td>0.8±0.1</td>
</tr>
<tr>
<td>S/D</td>
<td>3.4±1.1</td>
<td>2.4±0.4</td>
</tr>
</tbody>
</table>
Umbilical Artery velocity. Spectral Doppler of the UA in the third trimester (36 weeks) shows an arterial waveform with forward flow throughout the cardiac cycle and relatively high end-diastolic flow resulting in low Doppler indices. PI =0.61; RI = 0.45, S/D ratio = 1.81.
**Umbilical Artery velocity.** Spectral Doppler of the UA in the third trimester (31 W+3D) shows an arterial waveform with forward flow throughout the cardiac cycle and relatively high end-diastolic flow resulting in low Doppler indices. $PI = 0.79; Rl = 0.55, S/D ratio = 2.21.$
Umbilical Artery velocity. Spectral Doppler of the UA in the third trimester (36W) shows an arterial waveform with forward flow throughout the cardiac cycle and relatively high end-diastolic flow resulting in low Doppler indices. PI = 0.78; RI = 0.57, S/D ratio = 2.33.
**Umbilical Artery velocity.** Spectral Doppler of the UA in the third trimester (34 W+6D) shows an arterial waveform with forward flow throughout the cardiac cycle and relatively high end-diastolic flow resulting in low Doppler indices. PI = 0.87; RI = 0.57, S/D ratio = 2.34.
**Umbilical Artery velocity.** Spectral Doppler of the UA in the third trimester (32W) shows an arterial waveform with forward flow throughout the cardiac cycle and relatively decrease end-diastolic flow resulting in high Doppler indices. PI = 1.25; RI = 0.76, S/D ratio = 4.25.
**Umbilical Artery velocity.** Spectral Doppler of the UA in the third trimester (29W+5D) shows an arterial waveform with forward flow throughout the cardiac cycle and relatively decrease end-diastolic flow resulting in high Doppler indices. PI = 1.013; RI = 0.70, S/D ratio = 3.39.