Sudan University of Science and Technology
College of Graduate Studies

Study of Umbilical Arteries in Diabetic Mothers using Doppler
دراسة شرايين الحبل السري في الامهات المصابات بالسكري باستخدام الدوبلير

A Thesis submitted for the fulfillment of PhD degree in Medical diagnostic Ultrasound

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بسم الله الرحمن الرحيم

قال تعالى:

وَيَسَّأَلُونَكَ عَنِ الْرُّوحِ ﴿ۖ قُلِ الْرُّوحُ مِنْ أَمْرِ رَبِّي وَمَا أُوْتِيَ مِنَ الْعَلِيمِ إِلَّا قَلِيلًا﴾

سورة الإسراء الآية 85
صدق الله العظيم
DEDICATION

This project is dedicated to my great Parents who have never failed to give me all supports, for giving all need during the time and for teaching 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 daughter, sister, and brothers.
Acknowledgement

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

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<td>US</td>
<td>Ultrasound</td>
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<td>AIUM</td>
<td>American Institute of ultrasound medicine</td>
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<td>WHO</td>
<td>World health organization</td>
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<td>CD</td>
<td>Color Doppler.</td>
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<td>CI</td>
<td>Cephalic index</td>
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<td>CRL</td>
<td>Crown rump length</td>
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<td>AC</td>
<td>Abdominal circumference</td>
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<td>CT</td>
<td>Computed tomogram</td>
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<tr>
<td>EFW</td>
<td>Estimation of fetal weight.</td>
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<td>EDD</td>
<td>Expected date of delivery</td>
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<tr>
<td>FL</td>
<td>Femur length.</td>
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<tr>
<td>GA</td>
<td>Gestational age.</td>
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<tr>
<td>IUGR</td>
<td>Intrauterine growth retardation</td>
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<tr>
<td>LMP</td>
<td>Last menstrual period</td>
</tr>
<tr>
<td>MM</td>
<td>Millimeter.</td>
</tr>
<tr>
<td>MHZ</td>
<td>Megahertz</td>
</tr>
<tr>
<td>C/S</td>
<td>Cesarean section</td>
</tr>
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<td>SRI</td>
<td>Systolic /diastolic</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>PI</td>
<td>Resistance index</td>
</tr>
<tr>
<td>FVW</td>
<td>Pulsatility index</td>
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<td>AEDV</td>
<td>Flow velocity waveform</td>
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<tr>
<td>REDV</td>
<td>Absent end diastolic velocity</td>
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<tr>
<td>UA</td>
<td>Reversed end diastolic velocity</td>
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<td>DM</td>
<td>Umbilical arteries</td>
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<td>IDDM</td>
<td>Diabetic mellitus</td>
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<td>NIDDM</td>
<td>Insulin dependent diabetic mellitus</td>
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<td>GDM</td>
<td>Non insulin dependent diabetic mellitus</td>
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<td>IFG</td>
<td>Gestational diabetic mellitus</td>
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<td>IGT</td>
<td>Impaired fasting glucose</td>
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<td>Impaired glucose tolerance</td>
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<td>HAPO</td>
<td>Oral glucose tolerance test</td>
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<td></td>
<td>Hypoglycemia &amp; adverse pregnancy outcome</td>
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<td>NICU</td>
<td>Neonatal intensive care unit</td>
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<td>IUFD</td>
<td>Intrauterine fetal death</td>
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<tr>
<td>CO2</td>
<td>Carbon dioxide</td>
</tr>
<tr>
<td>O2</td>
<td>Oxygen</td>
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Abstract

The main objective of this study was to evaluate the S/D ratio and resistance index of the umbilical artery at a free loop in patients with diabetic pregnancy and those with normal pregnancies, also Develop national guidelines on the use of fetal Doppler in obstetrics. And To evaluate if the Doppler follow up of the umbilical artery can improve the clinical diagnosis of patients with diabetic pregnancy. A total 325 consecutive pregnant women 100 normal for control and 225 diabetic women in the second & third trimesters were enrolled in this study from maternity clinic in the maternity hospital – Alqassim-Buriada. The duration of the study extended from May 2012 to November 2016. From this study, it has been found that (41.8%) of the diabetes was Type 1 diabetes, since (48%) of diabetes was Gestational, while only (10.2%) of them was Type 2 diabetes, also shown that most (49.8%) of diabetics uses medications to control their sugar since (30.2%) of them uses Insulin and (20%) of them Dose not use any treatment to control their sugar. For family history find that (45.4%) of diabetics have no diabetes in their families history, since (41.3%) of them have diabetes in their family history, while only (13.3%) of them have Hypertension in their family history. & find shown that the most (69.8%) of diabetics have non maternal risk, since (25.8%) of them were Cesarean Section, while only (3.6%) of them were Preeclampsia and (0.9%) of them Eclampsia. Fetal risk shown that (41.8%) of diabetics have non fetal risk, since (24%) of them were IUGR, (17.3%) of them were Polyhydramnios, (16%) were Macrosomia, while only (0.9%) of them were IUFD. And shown that the most (43.1%) of diabetics fetal outcome were Discharged, since (16%) of them were Hypoglycemia or LGA, (14.2%) of them were IUGR, while only (5.3%) of them were RDS, (3.1%) of them were Poor sucking, (0.9%) of them were Sepsis or IUFD and (0.4%) of them were DM. Notes, that (0.6%) participants were No blood flow (IUFD cases) as same as (0.6%) were Absent of end diastolic cases, since the most (89.2%) of participants were Normal, while (9.5%) of participants were Reduce of end diastolic cases. Also I find no statistically significant correlation between (RI and S/D Ratio) and Random Blood Sugar, while there are statistically significant negative relationships between Fetal weight and Doppler indices (RI and S/D Ratio) which means Fetal weight decreases as Doppler indices increase. The chi-square test and Likelihood Ratio test statistics are (chi-square= 8.041 with Sig. = 0.782 and Likelihood Ratio = 8.399 with Sig. = 0.753), therefore, statistically non-significant association between Fetal Risk and Diabetes Type and there is statistically significant difference between the mean of RI, but there is no statistically significant difference between the mean of S/D Ratio for those people who diabetic and those who are not.
المستخلص

تهدف هذه الدراسة إلى تقييم دقة الدوبلر في الموجات فوق الصوتية، ولتطوري المنهج العلمي المتبع. وأيضاً تحليل تشكيل نتائج فحوصات سريان الدم غير مؤكد من الجنين للإملام والحال عن طريق فحص شريان الحبل السري في الثلاث الثاني والثالث من الحمل، وذلك باستخدام دقة سريان الدم من الممارسة وقوة سريان الدم والنسخة بين الانقباض والانسياق في طويلة سرير الدم. في هذه الدراسة تم دراسة ثلاث مائة وخمسون وثاني امرأة حبلى في الثلاث الثاني والثالث من الحمل، ومنحها محلة من مسارات الموجات فوق الصوتية في الحمل الحرج في الفترة من مارس 2011 - نوفمبر 2016. كل الحالات تتمييزها بواسطة الدارس حسب البروتوكولات العالمية. المنهج العلمي المتبع للكشف بدءًا من الموجات فوق الصوتية عن طريق قياس درجة الاختلاف والانباض في سريان الدم ودرجة تأثير مرض السكر على الامام من أم حامل ونسبة بالسكر وذلك باستخدام دوبلر ونسيج دوبلر موجات صوتية ومسار في اتصال 3.5 ميگاهيرتز وذلك باستخدام حالات علاجات السريرية لتنقيح سرير الدم في تقييم المخاطر للجنين من سرير الأم. وجدت الدراسة أن الحالات مرضي السكر في الام يحسن تعلاج نسبة (49.8%). أخذ النتائج الأولي المرضي السكر (30.2%) عند تأجيل الامام (20%) لا يوجد سكر، و يوجد بنسبة (41.3%) ونسبة (13.3%) الضغط السكري في الحالات (41.8%) منخفض السكر ونسبة (10.2%) منخفض السكر. ونسبة (48%) وتواتر الضغط السكري في الحالات (69.8%) ونسبة (3.6%) ارتفاع ضغط الدم، ونسبة (25.8%) الولادة القصبية.

وايضاً حددت السياسات للجنين بنسبة (41.8%) للنوع أحد المضاعفات، ونسبة (24%) للنوع الثاني. نسبة (17.3%) زيادة الماء حول الجنين، ونسبة (16%) زيادة وزن الجنين، ونسبة (9%) تسبب في موت الجنين. وجدت الدراسة أن معدل المواليد للسيدات الحامل بنسبة 0.9% هو الخروج بوضع مستفرس سيرياً، ونسبة 16% هو حضور السكر الطفيلي، ونسبة 3.2% من الحالات نسبة (9.3%) listens the للعمل مضغوطة في الرضاعة. تسمى لديناء حالات. نسبة حدوت المضاعفات لأدم الجنين نجد نسبة (62%) لا يوجد مرضي السكر في الام، ونسبة (31%) يوجد مرضي السكر، ونسبة (4%) يوجد مرضي السكر في الام.

وقد كانت دراسة سوق Pipes السكري في الحمل، ولكن توجد علاقة عكسية بين وزن الجنين ومقياس دبوس الشريان السكري النجمي ومعدل الاربطة =. (0.417 - 0.165). إيجار الدراسة قيمة معادلة للجرعة، وتوجد علاقة عالية، هيئة الإحصائية بين مستوى قياس الموجات فوق الصوتية الشريان السكري وعينة التحكم. وذلك بواسطة اختبار ت. بينما لا يوجد فرق بين متوسط معدل الانقباض والانساقة. تقدمت الدراسة بمقترح هيئة الدوبلر متخذ في قياس مؤشر الموجات ومعالج الانقباض والانساقة في شريان الحبل السري في تشخيص ونياقة. والاضطرابات في السكر للإملام السكري لام الحامل على نمو وصحة الجنين، وبالتالي تحسين فرصة ولاقة وتأمين أفضل الوضع للجنين.
CHAPTER ONE

INTRODUCTION
Chapter one: Introduction

1.1 Diabetes Mellitus:
Diabetes mellitus is a condition in which the pancreas no longer produces enough insulin or cells stop responding to the insulin that is produced, so that glucose in the blood cannot be absorbed into the cells of the body. Symptoms include frequent urination, lethargy, excessive thirst, and hunger. The treatment includes changes in diet, oral medications, and in some cases, daily injections of insulin. Diabetes mellitus is chronic disease that causes serious health complications including renal (kidney) failure, heart disease, stroke, and blindness.

1.1.1 Diabetes mellitus and Pregnancy:
Diabetes mellitus complicating pregnancy is one of the most common antenatal complications that are associated with significant perinatal mortality and morbidity (Magee et al., 1993; Platt et al., 2002; Schmidt et al., 2001). Diabetic pregnancies can be divided into two categories: those with pre-gestational or pre-existing diabetes mellitus in which the diagnosis is made in the pre-pregnancy state, and those with gestational diabetes mellitus. (GDM). Pre-existing diabetes consists of type I (insulin-dependent) diabetes mellitus (IDDM) with an incidence of around 2-3% (Kapoor et al 2007).
1.1.2 Classification – the classification and description of diabetic has changed over time. 1-insulin-dependent diabetic (IDDM) 2- noninsulin dependent diabetic (NIDDM) 3-gestational diabetic (GDM), impaired glucose tolerance (IGT) (3).

1.2 Screening for diabetes mellitus during pregnancy

1.2.1 Gestational diabetes:

The following 2-step screening system for gestational diabetes is currently recommended in the United States:

50-g, 1-hour glucose challenge test (GCT)

100-g, 3-hour oral glucose tolerance test (OGTT) - For patients with an abnormal GCT result, alternatively, for high-risk women or in areas in which the prevalence of insulin resistance is 5% or higher (eg, the southwestern and southeastern United States), a 1-step approach can be used by proceeding directly to the 100-g, 3-hour OGTT.

The US Preventive Services Task Force (USPSTF) recommends screening for gestational diabetes mellitus after 24 weeks of pregnancy. The recommendation applies to asymptomatic women with no previous diagnosis of type 1 or type 2 diabetes mellitus. The recommendation does not specify whether the 1-step or 2-step screening approach would be preferable.

1.2.2 Type 1 diabetes:

- The disease is typically diagnosed during an episode of hyperglycemia, ketosis, and dehydration
• It is most commonly diagnosed in childhood or adolescence; the disease is rarely diagnosed during pregnancy
• Patients diagnosed during pregnancy most often present with unexpected coma. Early pregnancy may provoke diet and glycemic control instability in patients with occult diabetes

1.2.3 Type 2 diabetes:

According to the American Diabetes Association’s "Standards of Medical Care in Diabetes-2010," the presence of any one of the following criteria supports the diagnosis of diabetes mellitus:

• **Hemoglobin A1C** (HbA1C) = 6.5%
• Fasting plasma glucose = >126 mg/dL (7.0 mmol/L)
• A 2-hour plasma glucose level = 200 mg/dL (11.1 mmol/L) during a 75-g OGTT
• A random plasma glucose level = 200 mg/dL (11.1 mmol/l) in a patient with classic symptoms of hyperglycemia or hyperglycemic (47).

1.3 Incidence of diabetic:

In 1997 and 2003, The Expert Committee on Diagnosis and Classification of Diabetes Mellitus (12,13) recognized an intermediate group of individuals whose glucose levels, although not meeting criteria for diabetes, are nevertheless too high to be considered normal. These persons were defined as having impaired fasting glucose (IFG) (FPG levels 100 mg/dL [5.6 mmol/L] to 125 mg/dL [6.9 mmol/L]), or impaired glucose tolerance (IGT) (2-h values in the OGTT of 140
mg/dL [7.8 mmol/L] to 199 mg/dL [11.0 mmol/L]). It should be noted that the WorldHealth Organization (WHO) and a number of other diabetes organizations define the cutoff for IFG at 110 mg/dL (6.1 mmol/L).1.

1.4 Complications:

The two main risks GDM imposes on the baby are growth abnormalities and chemical imbalances after birth, which may require admission to a neonatal intensive care unit. Infants born to mothers with GDM are at risk of being both large for gestational age (macrosomic) and small for gestational age. Macrosomia in turn increases the risk of instrumental deliveries. (8).

1.4.1 Macrosomia:

Macrosomia may affect 12% of normal women compared to 20% of patients with GDM. However, the evidence for each of these complications is not equally strong; in the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study for example, there was an increased risk for babies to be large but not small for gestational age.[5] Research into complications for GDM is difficult because of the many confounding factors (such as obesity). Labelling a woman as having GDM may in itself increase the risk of having a caesarean section.[6][7].
This from previous research. Complications for mothers, high blood sugar, premature birth and cesarean birth.

1.4.2. Intrauterine Growth Restriction:

The IUGR fetus is a fetus that does not reach its potential growth. Environmental factors responsible may be due to maternal, uteroplacental and fetal factors. Many authors have reported on the association between an abnormal UA Doppler FVW and IUGR differentiating the fetus with pathologic growth restriction that is at risk for perinatal complications from the constitutionally small but healthy fetus has been an ongoing challenge in obstetric. Not all infants whose birth weight is below the 10th percentile have been exposed to a pathologic process in utero; in fact, most small newborns are constitutionally small and healthy. Doppler sonography has become the most important investigation method to differentiate between these fetuses.(24)

1.5 Epidemiology:

Gestational diabetes affects 3-10% of pregnancies, depending on the population studied. (9) Gestational diabetes generally resolves once the baby is born. Based on different studies, the chances of developing GDM in a second pregnancy are between 30 and 84%, depending on
ethnic background. A second pregnancy within 1 year of the previous pregnancy has a high rate of recurrence.(11)

There are scarce statistical data on the risk of other conditions in women with GDM; in the Jerusalem Perinatal study, 410 out of 37962 patients were reported to have GDM, and there was a tendency towards more breast and pancreatic cancer, but more research is needed to confirm this finding.(23)(24).

1.6 Importance of Doppler U/S for umbilical arteries:

The aim of Doppler ultrasound studies of the umbilical arteries in diabetic pregnancies is to determine whether impedance to flow is related to maternal glycemic control and whether impedance is increased in patients with diabetic nephropathy and vasculopathy. This section also examines whether impedance in the umbilical arteries can provide useful prediction of subsequent development of preeclampsia and/or intrauterine growth restriction in the same way that it does in non diabetic pregnancies(1).

Diabetes mellitus is associated with an increased risk of fetal death, and data from cordocentesis have demonstrated an association between maternal hyperglycemia and fetal acidemia. The aim of Doppler ultrasound studies of the umbilical arteries is to examine whether the compromised fetus of a diabetic pregnancy demonstrates the same
features of circulatory redistribution as seen in fetal hypoxemia due to uteroplacental insufficiency (1).

1.7 Problem of the study:
Diabetic may adversely affect and have consequences to both the mother and the fetus therefore optimal care and management benefits both. Maternal diabetes mellitus is associated with a high risk of fetal death. The major source of fetal glucose is the mother and there is a good correlation between maternal and fetal blood glucose concentrations. In pregnancies complicated by diabetes mellitus, the maternal hyperglycemia causes fetal hyperglycemia and hyper insulinemia. Furthermore, the fetal insulin to glucose ratio is increased because hyperglycemia and/or the other metabolic derangements associated with maternal diabetes mellitus act on the fetal pancreas to cause β-cell hyperplasia and precocious pancreatic maturation. Fetal hyperinsulinemia causes macrosomia, either directly through its anabolic effect on nutrient uptake and utilization, or indirectly through related peptides such as insulin-like growth factors.

Doppler ultrasound studies of the umbilical and uterine arteries in diabetic pregnancies is vital to determine whether impedance to flow is related to maternal glycemic control and whether impedance is increased
in patients with diabetic nephropathy and vasculopathy. The diabetic pregnancy increases the fetal mortality and morbidity, and the using of Doppler umbilical artery indices might decrease the fetal mortality and morbidity.

1.8 Objectives:

The general objective of this study was to study umbilical arteries blood flow indices in diabetic mothers using Doppler

Specific objective:

- To evaluate the S/D ratio and Resistance index of the umbilical artery at a free loop in patients with diabetic pregnancy and those with normal pregnancies.

- To establish reference ranges of S/D ratio and Resistance index of umbilical artery.

- To evaluate fetal outcome in patients with diabetic pregnancy and in normal control group through Doppler indices of the umbilical artery.

- To evaluate if the Doppler follow up of the umbilical artery can improve the clinical diagnosis of patients with diabetic pregnancy.

- To determine the accuracy of UA indices in predicting the fetal outcome.
1.9 Significance of the study

This study will improve the prediction of prenatal outcome through the using of Doppler umbilical artery indices in patients with diabetic pregnancy.

1.10 Hypothesis

1- The S/D ratio, Resistance index of the umbilical artery are excellent tools in predicting the fetal outcome in diabetic pregnancy.

2- S/D ratio more sensitive than Resistance index of the umbilical artery.

3- High perinatal morbidity and mortality rates have been report in association with absent or reverse end-diastolic flow velocities in the umbilical artery.

4- The patients who have followed up in Doppler of the umbilical artery have improving S/D ratio, and RI suggested good fetal outcome.

1.11 Thesis overview:

This study is concerned with study of umbilical arteries in diabetic mothers accordingly; it is divided into the following chapters: Chapter one, Introduction, diabetic mellitus & pregnancy, importance of Doppler u/s for umbilical arteries, contains statement of the problem and thesis...
objectives, significant of the study, hypothesis. Chapter two, Background: Literature Review, Properties of ultrasound and ultrasound instrumentations; and protocols of Doppler parameters. Chapter three, Materials and Methods. Chapter four, Results. Chapter 5, Discussion, Conclusions, Recommendations and Future works
CHAPTER TWO

BACKGROUND
Chapter two: Background

2.1 Ultrasound imaging:
Ultrasound is sound with a frequency above the audible range which ranges from 20 Hz to 20 kHz. Sound is mechanical energy that needs a medium to propagate. Medical imaging uses frequencies that are much higher than 20 kHz; the range normally used is from 3 to 15 MHz. (Trish Chudleigh ,2004.) Ultrasound imaging (sonography) uses high-frequency sound waves to view soft tissues such as muscles and internal organs. Because ultrasound images are captured in real-time, they can show movement of the body's internal organs as well as blood flowing through blood vessels.(Morgan, G.E., Mikhail, M.S., and Murray, M.J. (2006).

2.2 Obstetric ultrasound:

Obstetric Ultrasound is the use of ultrasound scans in pregnancy. Since its introduction in the late 1950’s ultrasonography has become a very useful diagnostic tool in Obstetrics. Currently used equipments are known as real-time scanners, with which a continous picture of the moving fetus can be depicted on a monitor screen. Very high frequency sound waves of between 3.5 to 7.0 megahertz are generally used for this purpose(21).
Doppler ultrasound is presently most widely employed in the detection of fetal cardiac pulsations and pulsations in the various fetal blood vessels.

One technology in particular is an advancement that will make patients more comfortable with procedures. It is called Doppler Ultrasound. This is exactly what you might think it is. It is an ultrasound technology that uses sound waves to detect things we cannot see. (4)

Umbilical artery Doppler waveforms provide an estimate of downstream placental vascular resistance and placental blood flow. There is a strong association between reduced end-diastolic umbilical artery blood flow velocity and increased vascular resistance in the umbilical placental microcirculation. As well, abnormal umbilical artery.

The use of Doppler during antenatal fetal surveillance has involved assessment of the umbilical arterial and venous flow velocity waveforms, the fetal cerebral circulation, and the fetal venous circulation, in particular the ductus venosus.

Placental insufficiency can be quantified based on the reduction of end-diastolic Doppler flow velocity into reduced end-diastolic flow velocity, absent end-diastolic flow velocity, and (reversed end-diastolic flow velocity. The risk of perinatal mortality increases up to 60%, with increasing severity from reduced to reversed end-diastolic flow velocity.
Therefore, in the presence of umbilical artery reversed end-diastolic flow velocity, delivery by Caesarean section may be considered if fetal viability is achieved. This decision will be influenced by the estimated fetal weight, gestational age, other Doppler parameters, and other assessments of fetal health, such as fetal anatomical and chromosomal anomalies(4).

2.3 Anatomy of uteroplacental circulation:

The blood supply to the uterus comes mainly from the uterine arteries, with a small contribution from the ovarian arteries. These vessels anastomose at the cornu of the uterus and give rise to arcuate arteries that run circumferentially round the uterus. The radial arteries arise from the arcuate vessels and penetrate at right angles into the outer third of the myometrium. These vessels then give rise to the basal and spiral arteries, which nourish the myometrium and decidua and the intervillous space of the placenta during pregnancy, respectively. There are about 100 functional openings of spiral arteries into the intervillous space in a mature placenta, but maternal blood enters the space in discrete spurts from only a few of these. (21, 22, 23).
Figure 2-1 placental insertion & fetal abdominal insertion of umbilical cord.

2.4 Placental and umbilical vessels

The umbilical cord vessels can be followed from their placental insertion (Figure 2.1) to their attachment on the fetal abdominal wall and their extension into the fetal abdomen. (21).

Figure (2.2) shows the umbilical cord into an anterior placenta but an umbilical vessel extends into the amniotic membranes.
2.5 fetal circulation:

The fetal circulation differs greatly from the postnatal circulation. The site of gas exchange in the fetus is the placenta as opposed to the lungs post-natally. In the normal postnatal circulation there is no mixing of oxygen rich pulmonary venous blood with less rich systemic venous blood whereas the fetal circulation contains several sites where blood with different oxygen concentrations mix.

2.5.1. The Umbilical Arteries

The umbilical cord is the life line between the fetus and placenta. It is formed by the fifth week of development and it functions throughout pregnancy to protect the vessels that travel between the fetus and the placenta. Compromise of the fetal blood flow through the umbilical cord vessels can have serious deleterious effects on the health of the fetus and newborn. (25, 26)

The umbilical cord contains three vessels; two arteries and a vein. Blood flowing through the umbilical arteries originates from the fetus and enters the placenta. (25, 27) The flow of blood through the arteries is dependent upon the strength of the fetal heart contraction and the health of the placenta. Blood returning from the placenta goes through the umbilical vein to the fetus. (26)

Numerous medical studies conducted during the past few years have found that measurement of the umbilical artery using Doppler ultrasound identifies high risk fetuses. When these fetuses are identified and management is altered by the physician, the fetal death rate as well as other severe complications is markedly reduced. (25, 28)

2.5.2. Formation and structure of the umbilical cord
By the end of the third week of development the embryo is attached to placenta via a connecting stalk (Figure 2.2). At approximately 25 days the yolk sac forms and by 28 days at the level of the anterior wall of the embryo, the yolk sac is pinched down to a vitelline duct, which is surrounded by a primitive umbilical ring (Figure 2.3). By the end of the 5th week the primitive umbilical ring contains:

1. A connecting stalk within which passes the allantois (primitive excretory duct), two umbilical arteries and one vein.
2. The vitelline duct (yolk sac stalk).
3. A canal which connects the intra- and extraembryonic coelomic cavities.

By the 10th week the gastrointestinal tract has developed and protrudes through the umbilical ring to form a physiologically normal herniation into the umbilical cord (Figures 2.4). Normally these loops of bowel retract by the end of the third month. Occasionally residual portions of the vitelline and allantoic ducts, and their associated vessels, can still be seen even in term umbilical cords, especially if the fetal end of the cord is examined (Figure 2.5).\(^{(25, 26)}\)

The umbilical cord normally contains two umbilical arteries and one umbilical vein. These are embedded within a loose, proteoglycan rich matrix known as Wharton’s jelly (Figure 2.6). This jelly has physical properties much like a polyurethane pillow, which—if you have ever tried twisting such a pillow you know—is resistant to twisting and compression. This property serves to protect the critical vascular life line.
between the placenta and fetus (Figure 2.7).  

Figure (2.3) shows the umbilical cord beginning. By 21 days the embryo has begun to separate from the developing placenta by a connecting stalk.  

Figure (2.4) shows contents and development of the umbilical cord at 5 weeks of developing the embryo.
Figure (2.5) shows UA insertions (21.5 mm) crown-rump length.\textsuperscript{(25, 26)}

Figure (2.6) shows Remnants of the yolk sac stalk (A) and the allantois (B) can often be identified, especially near the fetal end of the cord.\textsuperscript{(25, 26)}
Figure (2.7) shows Cross section of normal umbilical cord. Embedded within a spongy, proteoglycan rich matrix know as Wharton’s jelly (W) is normally two arteries (A) and one vein (V).\(^{(26)}\)

![Cross section of normal umbilical cord](image)

Figure (2.8) shows the umbilical cord protects the fetal vessels that connect the placenta and fetus. A) Fetus and placenta from a 17 week gestation. B) Diagram of the circulation within the fetus, umbilical cord and placenta.\(^{(26)}\)

The human umbilical cord, which is also sometimes referred to as the funiculusumbilicalis or birth cord, connects the developing embryo/fetus to the placenta and literally acts as a ‘life line’ supplying the fetus with oxygen and nutrients that support its growth and development throughout the duration of pregnancy.

The umbilical cord originates from the same zygote as the fetus, comprising remnants of the yolk sac and allantois.

It develops during the fifth week of pregnancy and replaces the yolk sac as the provider of the nutrients that are required by the developing embryo/fetus.\(^{(1)}\)

The umbilical cord is attached to the placenta which transfers oxygen, nutrients and waste products, such as carbon dioxide (CO2) to and from
the maternal blood circulatory system without any direct contact between fetal and maternal blood. In the full-term healthy neonate the cord has a spiral twist and is normally around 50-60 cm in length, with a diameter of approximately 1-2 centimeters (4).

Figure 2.9  The Human Umbilical Cord.

2.6 The umbilical cord and fetal circulation

The umbilical cord enters the developing fetus through the lower abdominal wall, at the level which, following cord separation, becomes the umbilicus or navel. Once inside the fetus, the umbilical vein continues towards the transverse fissure on the visceral surface of the liver (ie where the portal vein and hepatic artery enter and the hepatic ducts leave). At this point it separates into two branches; the first joins with the hepatic portal vein, connecting to its left branch. The other, which is known as the ductus venosus, allows the majority of the incoming blood
(around 80% of blood volume) to bypass the liver and flow via the left hepatic vein into the inferior vena cava, which carries blood towards the fetal heart. The two umbilical arteries branch from the internal iliac arteries, passing on each side of the urinary bladder of the fetus before joining the umbilical cord (8).

**Figure 2.10** fetal–placental circulation.

### 2.7 Diabetes mellitus:

Diabetes mellitus is a chronic illness that requires continuing medical care and ongoing patient self-management education and support to prevent acute complications and to reduce the risk of long-term complications. Diabetes care is complex and requires that many issues, beyond glycemic control, be addressed. A large body of evidence exists that supports a range of interventions to improve diabetes outcomes.
Diabetes mellitus complicating pregnancy is one of the most common antenatal complications that are associated with significant perinatal mortality and morbidity (Magee et al., 1993; Platt et al., 2002; Schmidt et al., 2001). Diabetic pregnancies can be divided into two categories: those with pre-gestational or pre-existing diabetes mellitus in which the diagnosis is made in the pre-pregnancy state, and those with gestational diabetes mellitus (GDM). Pre-existing diabetes consists of type I (insulin-dependent) diabetes mellitus (IDDM) with an incidence of around and type 2 (non-insulin-dependent) diabetes with an incidence of 2-3% (Kapoor et al., 2007).

The incidence of gestational diabetes mellitus differs in different populations (Gunton et al., 2001) and ethnic groups, and was shown to be as high as 13% in Chinese populations (Ko et al., 2002). Effective treatment of pre-existing as well as gestational diabetes mellitus was shown to improve outcome and reduce perinatal mortality, as compared to untreated patients (Lao et al., 2001; Langer et al., 2005).

2.7.1. Diagnosis:
In 1997 and 2003, The Expert Committee on Diagnosis and Classification of Diabetes Mellitus (12,13) recognized an intermediate group of individuals whose glucose levels, although not meeting criteria for diabetes, are nevertheless too high to be considered normal. These persons were defined as having impaired fasting glucose (IFG) (FPG levels 100 mg/dL [5.6 mmol/L] to 125 mg/dL [6.9 mmol/L]), or impaired glucose tolerance (IGT) (2-h values in the OGTT of 140 mg/dL [7.8 mmol/L] to 199 mg/dL [11.0 mmol/L]). It should be noted that the World Health Organization (WHO) and a number of other diabetes organizations define the cutoff for IFG at 110 mg/dL (6.1 mmol/L) (9).
The recommendations for diagnosis and treatment of GDM of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus (Metzger et al., 2007) suggest consideration of fetal growth patterns to guide metabolic management of pregnant women with GDM. However, estimation of fetal weight, particularly at term and in fetuses with high neonatal weight, is not as precise as desirable (Sacks et al., 2000). Fetal overgrowth and accelerated growth velocity of the abdominal circumference in the third trimester is known to predict large for gestational age babies (Kehl et al., 1996). Fetal overgrowth with macrosomia and associated polyhydramnios is associated with higher risks of near term stillbirth, as well as various neonatal metabolic derangements, including neonatal hypoglycaemia, electrolyte disturbances and neonatal jaundice. Previous randomized studies have demonstrated that measurement of fetal abdominal circumference through pregnancy in women with GDM is useful to identify pregnancies at high risk for fetal overgrowth and thus in need of more vigilant treatment including insulin therapy (Bonomo et al., 2004)(7).

2.7.2 Management:

2.7.2.1 Diet:

The goal of dietary therapy is to avoid single large meals and foods with a large percentage of simple carbohydrates. The diet should include foods with complex carbohydrates and cellulose, such as whole grain breads and legumes(46).
2.7.2.2 Insulin:
The goal of insulin therapy during pregnancy is to achieve glucose profiles similar to those of nondiabetic pregnant women. In gestational diabetes, early intervention with insulin or an oral agent is key to achieving a good outcome when diet therapy fails to provide adequate glycemic control. (46)

2.7.2.3 Glyburide and metformin:
The efficacy and safety of insulin have made it the standard for treatment of diabetes during pregnancy. Diabetic therapy with the oral agents glyburide and metformin, however, has been gaining in popularity. Trials have shown these 2 drugs to be effective, and no evidence of harm to the fetus has been found, although the potential for long-term adverse effects remains a concern. (46)

2.8. Risk Factors.

2.8.1 Maternal Risk


2. Infection such as pyelonephritis

3. Fetal macrosomia.

4. Cesarean section delivery because of the fetal macrosomia.
2.8.2. Fetal Risk

1. Intrauterine demise.

2. Perinatal morbidity from birth injury.

3. Fetal congenital anomalies.

4. IUGR, with vascular disease

Most women who have gestational diabetes deliver healthy babies. However, gestational diabetes that's not carefully managed can lead to uncontrolled blood sugar levels and cause problems for women and her baby, including an increased likelihood of needing a C-section to deliver. Complications that may affect baby, If you have gestational diabetes, your baby may be at increased risk of Excessive birth weight. Extra glucose in your bloodstream crosses the placenta, which triggers your baby's pancreas to make extra insulin. This can cause baby to grow too large (macrosomia). Very large babies — those that weigh 9 pounds or more — are more likely to become wedged in the birth canal, sustain birth injuries or require a C-section birth.

2.8.2.1 Early (preterm) birth and respiratory distress syndrome. A mother's high blood sugar may increase her risk of early labor and
delivering her baby before its due date. Or her doctor may recommend early delivery because the baby is large.

Babies born early may experience respiratory distress syndrome condition that makes breathing difficult. Babies with this syndrome may need help breathing until their lungs mature and become stronger. Babies of mothers with gestational diabetes may experience respiratory distress syndrome even if they're not born early.

2.8.2.2. Low blood sugar (hypoglycemia), Sometimes babies of mothers with gestational diabetes develop low blood sugar (hypoglycemia) shortly after birth because their own insulin production is high. Severe episodes of hypoglycemia may provoke seizures in the baby.

2.9 Type 2 diabetes later in life. Babies of mothers who have gestational diabetes have a higher risk of developing obesity and type 2 diabetes later in life. Untreated gestational diabetes can result in a baby's death either before or shortly after birth.

2.10 High blood pressure and preeclampsia. Gestational diabetes raises your risk of high blood pressure, as well as, preeclampsia — a serious complication of pregnancy that causes high blood pressure and other symptoms that can threaten the lives of both mother and baby.
2.11 Future diabetes. If you have gestational diabetes, you're more likely to get it again during a future pregnancy. You're also more likely to develop type 2 diabetes as you get older. However, making healthy lifestyle choices such as eating healthy foods and exercising can help reduce the risk of future type 2 diabetes.

2.12 IUGR Diagnosis, Doctors have many ways to estimate the size of babies during pregnancy. One of the simplest and most common is measuring the distance from the mother's fundus (the top of the uterus) to the pubic bone. After the 20th week of pregnancy, the measure in centimeters usually corresponds with the number of weeks of pregnancy. A lower than expected measurement may indicate the baby is not growing as it should. Other procedures to diagnose IUGR and assess the baby's health include the following: Ultrasound. The main test for checking a baby's growth in the uterus, ultrasound involves using sound waves to create pictures of the baby. The ultrasound exam lets the doctor see the baby in the uterus with an instrument that is moved over the mother's abdomen.

Ultrasound can be used to measure the baby's head and abdomen. The doctor can compare those measurements to growth charts to estimate the
baby's weight. Ultrasound can also be used to determine how much amniotic fluid is in the uterus. A low amount of amniotic fluid could indicate IUGR.

Doppler flow is a technique that uses sound waves to measure the amount and speed of blood flow through the blood vessels. Doctors may use this test to check the flow of blood in the umbilical cord and vessels in the baby's brain.

2.13 Pathophysiology:

Maternal diabetes mellitus is associated with a high risk of fetal death. In the past, before the introduction of insulin the main cause of death was in association with maternal keto-acidosis, but now most fetal deaths are non-ketoacidotic and occur in association with fetal macrosomia.

The major source of fetal glucose is the mother and there is a good correlation between maternal and fetal blood glucose concentrations 1. In pregnancies complicated by diabetes mellitus, the maternal hyperglycemia causes fetal hyperglycemia and hyperinsulinemia 2,3. Furthermore, the fetal insulin to glucose ratio is increased because hyperglycemia and/or the other metabolic derangements associated with maternal diabetes mellitus act on the fetal pancreas to cause □-cell hyperplasia and precocious pancreatic maturation 2. Fetal
hyperinsulinemia causes macrosomia, either directly through its anabolic effect on nutrient uptake and utilization, or indirectly through related peptides such as insulin-like growth. In pregnant women with diabetes mellitus, despite stringent maternal glycemic control, the fluctuation in maternal glucose concentration is greater than in non-diabetics and it is possible that, during short-lived episodes of hyperglycemia, an already hyperplastic fetal pancreas will respond with a disproportionately high release of insulin.

### 2.14 Benefits of Umbilical Artery Surveillance

Recent studies have found that surveillance of high-risk fetuses with umbilical artery Doppler ultrasound results in a marked decrease in fetal death and morbidity when compared to traditional surveillance (non-stress test). For this reason, all fetuses with suspected intrauterine growth restriction should undergo umbilical artery Doppler evaluation (43).

Doppler ultrasound provides a non-invasive method for the study of fetal hemodynamics. Investigation of the uterine and umbilical arteries gives information on the perfusion of the uteroplacental and fetoplacental circulations, respectively, while Doppler studies of selected fetal organs are valuable in detecting the hemodynamic rearrangements that occur in response to fetal hypoxemia. (44)

### 2.15 Safety of Doppler Ultrasonography

Diagnostic ultrasonography has been used in medicine for many decades. To date, at the intensities allowed by regulations, there has been no solid evidence of any detrimental biologic effects in humans. Literally millions of people around the world are exposed each year to medical
ultrasonography, a technique that continues to boast an excellent safety record.\(^{(45)}\)

In USA, more than three scans per live birth are performed annually. Despite proven safety of the method, ultrasonography does not have some inherent bioeffects that should not be ignored and are therefore addressed below. An important factor that plays a major role in the development of biologic effects is the acoustic power of the ultrasonography device, i.e., the amount of energy produced in a unit of time.

The duration of the ultrasound pulse, the pulse repetition frequency (the reciprocal of the interval between the pulses), and the duty factor (the pulse duration divided by the pulse repetition frequency) are the most important determinants of acoustic power output. In particular, pulsed Doppler ultrasonography has higher duty factors than do conventional imaging facilities. There are two potential mechanisms through which ultrasonography can produce biologic effects: thermal and mechanical.\(^{(45)}\)

2.16 Umbilical artery sonography:

The cord forms between the 7-8 menstrual weeks. The umbilical cord extends from fetal umbilical to the chorionic surface of the placenta. In the early first trimester diastolic blood velocity in the umbilical artery is normally absent.\(^{(3)}\).

After 15 weeks of pregnancy umbilical blood flow is maintained throughout diastole, reflecting the low resistance in fetoplacental circulation with increasing gestational age the RI and S/D ratio values fall as a sign of decreasing resistance to blood flow in placenta. The UA may
be evaluated anywhere along the length of the free-flouting umbilical cord(3). The umbilical artery is evaluated by measuring the blood flow velocity at peak systole (maximal contraction of the heart) and peak diastole (maximal relaxation of the heart).\(^{(43)}\)

These values are then computed to derive a ratio. One of the most common ratios that are used is the Resistance Index. This is computed by measuring the peak of systole and then dividing it by the sum of measurements at peak systole and diastole. RI= systole/(systole+diastole)

In early pregnancy the peak flow at diastole is less than later in pregnancy.\(^{(44)}\)

Therefore, as the duration of pregnancy increases, the amount of blood flowing in the umbilical artery increases during diastole. This means that the placenta is less resistant to blood flow, thus providing more blood to flow from the fetus to the placenta. The following image illustrates Doppler waveforms at 20 and 36 weeks of pregnancy.\(^{(44)}\)

2.16.1 the normal Doppler waveform:

has a rapid upstroke to peak systole and a gradual decline diastole, while maintaining continuous forward flow during diastole until the onset of the next fetal cardiac heart beat.
Figure: 2.11 the normal Doppler waveform.

2.16.2 Abnormal UA Doppler waveform:

depend on the severity of disease initially it is characterized by a decrease in end-diastolic flow resulting in an increase in Doppler indices. In more severe cases, there is absence of end-diastolic flow, and with worst disease there is reversal of end-diastolic flow. The Doppler indices increase in value with increasing severity of disease. An umbilical artery S/D ratio was proposed as being abnormal beyond 30 weeks gestation.
Figure (2.14) shows abnormal Resistance Index\(^{(73)}\)

There are three types or degrees of abnormal waveforms:

2.16.2.1 Abnormal Resistance Index with Blood Flow Present During Diastole:

Once the waveforms are obtained and measured, the results are plotted on graphs to determine if the amount of flow of blood during diastole is normal or abnormal. If the Resistance Index increases to a value above the upper range of normal, this identifies a fetus at risk or who has IUGR. If the Resistance Index that is measured from the Doppler waveform is above the red line, this is abnormal. The gold circle illustrates a measurement of the Resistance Index that is abnormal.

2.16.2.2 Absent Blood Flow during Diastole:
This is a more serious form than Type I because blood flow is absent during diastole. Fetuses with this type of finding should be monitored closely in a hospital setting. The following ultrasound picture illustrates this type of Doppler waveform. This illustrates absent diastolic flow during diastole. When this occurs there is abnormal resistance in the placenta which results in a marked decrease in blood flow from the fetus to the placenta. (72).

Figure: 2.12 Show Absent Blood Flow during Diastole.

2.16.2.3 Reverse Blood Flow During Diastole:

When the resistance in the placenta increases further, absent diastolic flow becomes reverse diastolic flow in which the Doppler waveform is observed to be below the baseline. When the fetus develops this type of abnormality, intense surveillance is required if the fetus is less than 32 to 34 weeks and delivery if it is greater than 32 to 34 weeks. The surveillance that is currently recommended is evaluation of the ducts
venous and/or inferior vena cava, in addition to traditional ante partum testing. The following illustrates reverse diastolic flow during diastole. When this occurs there is abnormal resistance in the placenta which results in a marked decrease in blood flow from the fetus to the placenta.

(73)

![Image: Show Reverse Blood Flow During Diastole]

**2.17 Flow imaging mode:**

**2.17.1 Spectral doppler:**

- Examines flow at one site
- Detailed analysis of distribution of flow
- Good temporal resolution – can examine flow waveform
- Allows calculations of velocity and indices(1).

**2.17.2 Color flow:**

- Overall view of flow in a region
- Limited flow information
• Poor temporal resolution/flow dynamics (frame rate can be low when scanning deep)
• color flow map (different color maps)
• direction information
• velocity information (high velocity & low velocity)
• turbulent flows (1).

2.17.3 power flow:

• Sensitive to low flows
• No directional information in some modes
• Very poor temporal resolution
• Susceptible to noise. Sensitive to low flows

2.17.4 Doppler affect & application in obs:

Non-dimensional analysis of the flow waveform shape and spectrum has proved to be a useful technique in the investigation of many vascular beds. It has the advantage that derived indices are independent of the beam/flow angle.

1) Resistance index (RI) (also called resistive index or Pourcelot’s index);
(2) Systolic/diastolic (S/D) ratio, sometimes called the A/B ratio
These indices are all based on the maximum Doppler shift waveform and their calculation is described in figure below. The PI takes slightly longer to calculate than the RI or S/D ratio because of the need to measure the mean height of the waveform. It does, however, give a broader range of values, for instance in describing a range of waveform shapes when there is no end-diastolic flow.

**figure:2.14 Show Doppler indices**

Umbilical cord displaying umbilical artery (red) and umbilical vein (blue), the gate or sample volume include both signals. Sonogram of the umbilical artery and vein. (1)
figure: 2.15 Show Sonogram of the umbilical artery and vein.

2.18: Ultrasound machine:

The parameters preset on the machine will enable you to start scanning but use the following information to help understand the controls and modify settings to obtain the best diagnostic image in individual patients. Images are viewed from the patient’s right for longitudinal scans, and from the patient’s feet for trans axial scans(1).

figure 2.16 Show Ultrasound machine.
2.18.1 Transducer frequency

is the frequency of the signal emitted. On some modern machines this can be selected electronically from a range within the same transducer: however, nowadays most transducers are still single-frequency only and you will have to toggle between transducers or plug a new one into the socket on the front or side of the machine.

High frequency probes have a better longitudinal resolution but less penetrating power through tissues, and are typically used for children and small organs or ones close to the transducer face. Low frequency probes can be used to penetrate deep into large areas such as adult abdomens but at the cost of a somewhat lower resolution.

Figure 2.17 Show modern ultrasound transducer of type 8820e (BK Medical, Denmark) with frequency range 2 - 6 MHz. From www.bkmed.com.
2.18.2 Equipment

High resolution grey scale ultrasound machine

Colour Doppler reduces scan times significantly

Spectral Doppler assessment for velocity measurements

Frequency - 7.5 megahertz linear array vascular probe().

2.19: u/s scanning technique:

2.19.1 OBSTETRIC SCANNING:

The following guidelines apply to trans abdominal scanning in patients undergoing routine examination during pregnancy. Record the first day of the patient's last menstrual period (LMP), and ask about previous pregnancies. Should wear comfortable, loose-fitting clothing for your ultrasound exam. You may need to remove all clothing and jewelry in the area to be examined. May be asked to wear a gown during the procedure.
Figure: 2.18 Show u/s scanning technique

Other preparation depends on the type of examination you will have. For some scans may instruct you not to eat or drink for as many as 12 hours before your appointment. For others you may be asked to drink up to six glasses of water two hours prior to your exam and avoid urinating so that your bladder is full when the scan begins. (13).

Ultrasound scanners consist of a console containing a computer and electronics, a video display screen and a transducer that is used to do the scanning. The transducer is a small hand-held device that resembles a microphone, attached to the scanner by a cord. The transducer sends out inaudible high frequency sound waves into the body and then listens for the returning echoes from the tissues in the body. The principles are similar to sonar used by boats and submarines.

The ultrasound image is immediately visible on a video display screen that looks like a computer or television monitor. The image is created based on the amplitude (strength), frequency and time it takes for the sound signal to return from the area of the patient being examined to the transducer and the type of body structure the sound travels through (4). for making non-invasive velocity measurements of blood flow. Christian Doppler was the first to describe the frequency shift that occurs when
sound or light is emitted from a moving source and the effect now bears his name. For the velocity measurement of blood, ultrasound is transmitted into a vessel and the sound that is reflected from the blood is detected. (4)

2.19.2 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.

2.19.3 Umbilical artery waveform:

Although umbilical artery waveforms are invaluable in the management of fetal growth restriction, they are of little or no value as a screening test.
for the small-for-gestational-age fetus. Additionally, umbilical artery Doppler does not to predict unexplained ante partum stillbirths or placental abruption. Despite being commonly requested, umbilical artery Doppler is not of established value in the management of ante partum hemorrhage, preterm rupture of membranes or rhesus is oimmunized, diabetic ,post-term or multiple pregnancies, unless these coexist with fetal growth restriction (30).

2.20 : previous studies:

1.Johnstone et al. measured impedance to flow in the umbilical artery in 128 pregnancies complicated by diabetes mellitus 24. There was no significant association between impedance to flow and either short-term or long-term glycemic control. Although, in some cases that subsequently developed fetal distress, there was increased impedance, fetal compromise also occurred in association with normal impedance(27).

2.Bracero et al. performed Doppler studies of the umbilical artery during the third trimester of pregnancy in 43 women with diabetes mellitus . They found a significant association between impedance to flow and maternal serum glucose concentration. Furthermore, high impedance was associated with an increased number of stillbirths and neonatal morbidity.
It was suggested that maternal hyperglycemia causes placental vasoconstriction by impairing prostacyclin production (28).

3. Bracero et al. evaluated 207 singleton pregnancies complicated by maternal diabetes mellitus within 1 week of delivery. In 36% of cases, there was an adverse outcome (defined as delivery before 37 weeks, or fetal risk requiring Cesarean delivery, or fetal growth restriction, or neonatal hypocalcemia, hypoglycemia, hyperbilirubinemia, or respiratory distress syndrome) 18. The relative risk of adverse outcome was 2.6 for increased impedance in the umbilical artery, which was higher than the risk of 1.7 for abnormal biophysical profile score or a non-reactive non-stress test (29).

4. Landon et al. performed serial measurements of impedance to flow in the umbilical artery in 35 insulin-dependent diabetic women, during the second and third trimesters, and found no significant association between this index and maternal blood glucose or glycosylated hemoglobin level(30) .

5. Ishimatsu et al. performed Doppler studies of the umbilical artery during the third trimester of pregnancy in 16 women with diabetes mellitus. They found no significant association between impedance to flow and maternal serum glucose or fructosamine levels 23. However, in
two patients with serum glucose levels of over 300 mg/dl, impedance was increased and returned to the normal range when the serum glucose level decreased to below 200 mg/dl (31).

6. Reece et al. examined 56 diabetic pregnancies and reported that the umbilical artery PI was higher in patients with diabetic vasculopathy than in non-diabetic controls or in diabetic patients without vasculopathy. Intrauterine growth restriction and neonatal metabolic complications were also significantly correlated with elevated umbilical artery PI. There was, however, no correlation between Doppler indices and maternal glucose values, although most were within a euglycemic range (32).

7. Mermann et al. carried out serial measurements of impedance to flow in the umbilical artery in 53 women with insulin-dependent diabetes. Impedance was within the normal range and there was no significant association with maternal blood glucose or glycosylated hemoglobin level or maternal vascular disease (22). This group also measured impedance to flow in the uterine arteries in 43 pregnancies complicated by insulin-dependent diabetes mellitus and found no significant differences from normal or significant associations with short- and long-term glycemic control, maternal vasculopathy, or diabetes-specific fetal morbidity (33).
8. Kofinas et al. examined 31 pregnant women with gestational diabetes and 34 with insulin-dependent diabetes mellitus. Impedance to flow in the umbilical and uterine arteries during the third trimester was not different between patients with good glycemic control and those with poor control. In contrast, impedance was significantly higher in patients with pre-eclampsia than in those without pre-eclampsia, regardless of glycemic control. It was concluded that Doppler investigation may be clinically useful only in diabetic pregnancies complicated by pre-eclampsia(34).

9. Ishimatsu et al. measured impedance to flow in the fetal middle cerebral artery in 43 pregnant women with well-controlled diabetes mellitus at 24–38 weeks of gestation. The PI was within the normal range and was not significantly associated with maternal serum glucose, fructosamine or glycosylated hemoglobin level(35).

10. Reece et al. Examined 30 pregnant women with insulin-dependent diabetes mellitus at 2-week intervals between 18 and 38 weeks of gestation. They found no significant association between impedance to flow in the fetal aorta and fetal outcome. They concluded that fetal aortic Doppler velocimetry cannot be used as a means of assessing impending fetal compromise in offspring of diabetic mothers(36).
11. Alvesen et al. carried out a longitudinal Doppler study in 48 relatively well-controlled diabetic pregnancies (27). With the exception of three pregnancies complicated by pre-eclampsia and/or intrauterine growth restriction, the uteroplacental and fetoplacental circulations were essentially normal. Thus, impedance to flow in the uterine and umbilical arteries and the PI or mean velocity in the middle cerebral artery or descending thoracic aorta were not significantly different from normal. It is of particular interest that normal Doppler results in the uterine and umbilical arteries and the fetal middle cerebral artery and aorta were also observed in five of six patients with diabetic nephropathy (37).

12. Reece et al. Examined 30 pregnant women with insulin-dependent diabetes mellitus at 2-week intervals between 18 and 38 weeks of gestation. They found no significant association between impedance to flow in the fetal aorta and fetal outcome. They concluded that fetal aortic Doppler velocimetry cannot be used as a means of assessing impending fetal compromise in offspring of diabetic mothers (38).

13. Ishimatsu et al. measured impedance to flow in the fetal middle cerebral artery in 43 pregnant women with well-controlled diabetes mellitus at 24–38 weeks of gestation. The PI was within the normal range and was not significantly associated with maternal serum glucose, fructosamine or glycosylated hemoglobin level (39).
CHAPTER THREE

MATERIALS AND METHOD
Chapter Three: Materials and Methods

3.1 Doppler Ultrasound:

Doppler Ultrasound is considered the best modality for detection of fetal UA during normal and diabetic pregnancy.

3.2 Instrumentation:

Ultrasound machine used is Doppler parameters in ultrasound clinic in maternity and children hospital.

3.3 Type of the study:

This is a prospective experimental study deals with the patients who were come to the department for obstetrical ultrasound investigation.

3.4 Inclusion criteria:

1. Single pregnancy
2. Non diabetic Pregnant women for control group
3. Second & third trimester of pregnancy
4. Diabetic pregnant women with all of diabetic types

3.5 Exclusion criteria:

1. Twins, triplets pregnancy
2. Congenital malformation of pregnancy
3- First trimester

**3.6 Area of the study:**

This study performed in OB/ gynecological ultrasound department in maternal and children hospital in Buraidah, Alqassim.

**3.7 Duration of the study:**

The duration of study from April (2012) to April (2017)

**3.8 Population of the study:**

Patients who had come to the ultrasound department for obstetrical investigation.

**3.9 Sampling of the study:**

The target population amount for this study had three hundred patients at doppler ultrasound department clinic.

**3.10 Methods of data collections:**

For ultrasound examination each patient had scanned twice, firstly by student and then by qualified sonographer to confirm the accurate measurement to estimate gestational age in second trimester.

**3.11 Technique:**
The one technique generally used in the second trimester is transabdominal sonography.

Trans abdominal probes they are typically 3.5 -5MHZ

TAS: performed by placing the transducer in contact with skin just above symphysis pubis.

### 3.11.1 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.

### 3.11.2 Patient preparation:
Explanation of examination to the patient

3.11.3 Patient position:

Pt in supine position

3.11.4 Plane section;

Longitudinal scanning

Transverse scanning

All above by anterior approach

3.11.5 Contra indication:

No clinical contra indications for the use of TAS to study fetal umbilical arteries in diabetic mothers.

3.12 Data collection:

A had been executed by using data collection sheet and ultrasound image.

3.13 Data storage method:

Data in correspondence with the thesis procedure had been storage in personal computer (PC).

3.14 Data analysis method:
This had been solved by using computer analysis (SPSS).

### 3.15. Facilities and resources:

Studies were identified using several search strategies such as using available electronic databases and references of either published articles or chapters from textbooks. The electronic databases used were MEDLINE and other data at the Library of Medicine.

Practical in Obstetric and Gynecological ultrasound units in Sudia Arabia at buriada maternal & children hospital, a well qualified and well expert consultant Obstetricians and Sonologists were supporting the results of ultrasound screening in this study.
CHAPTER FOUR

Results
Chapter Four: Result

**Statistical Methods:** The use of comparative analytical method using the SPSS statistical program based descriptive statistics and comparative and association hypothesis tests (0.05 sig. level), to demonstrate the relationship between (Doppler Indices) and (Maternal age, Weight, Parity, Random blood sugar, Sugar control method, Family history of sugar and Diabetic type) and (Gestational age, Fetal weight, Fetal Risk and Maternal risk) and (Doppler Indices) among. The tests were used for correlation, t-test, Chi-square test, and ANOVA table to study the hypothesis which states no there are significant relationships.

Table (4.1) distributions of (Sugar control Treatment) for diabetics:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non</td>
<td>45</td>
<td>20.0</td>
<td>20.0</td>
<td>20.0</td>
</tr>
<tr>
<td>Medication</td>
<td>112</td>
<td>49.8</td>
<td>49.8</td>
<td>69.8</td>
</tr>
<tr>
<td>Insulin</td>
<td>68</td>
<td>30.2</td>
<td>30.2</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>225</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Figure (4.1) distributions of (Sugar control Treatment) for diabetics.

Table (4.2) distributions of (Family History) for diabetics:
<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non</td>
<td>102</td>
<td>45.3</td>
<td>45.3</td>
<td>45.3</td>
</tr>
<tr>
<td>Diabetic</td>
<td>93</td>
<td>41.3</td>
<td>41.3</td>
<td>86.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>30</td>
<td>13.3</td>
<td>13.3</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>225</strong></td>
<td><strong>100.0</strong></td>
<td><strong>100.0</strong></td>
<td></td>
</tr>
</tbody>
</table>

Figure (4.2) distributions of (Family History) for diabetics:

Table (4.3) distributions of (Diabetes Type) for diabetics:

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>94</td>
<td>41.8</td>
<td>41.8</td>
<td>42.2</td>
</tr>
<tr>
<td>Gestational</td>
<td>108</td>
<td>48.0</td>
<td>48.0</td>
<td>89.8</td>
</tr>
<tr>
<td>Type 2</td>
<td>23</td>
<td>10.2</td>
<td>10.2</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>225</strong></td>
<td><strong>100.0</strong></td>
<td><strong>100.0</strong></td>
<td></td>
</tr>
</tbody>
</table>
Figure (4.3) distributions of (Diabetes Type) for diabetics:

Table (4.4) distributions of (Maternal Risk) for diabetics:

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non</td>
<td>157</td>
<td>69.8</td>
<td>69.8</td>
<td>69.8</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>8</td>
<td>3.6</td>
<td>3.6</td>
<td>73.3</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>2</td>
<td>.9</td>
<td>.9</td>
<td>74.2</td>
</tr>
<tr>
<td>Cesarean Section</td>
<td>58</td>
<td>25.8</td>
<td>25.8</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>225</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>
Figure (4.4) distributions of (Maternal Risk) for diabetics:

<table>
<thead>
<tr>
<th>Maternal Risk</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non</td>
<td>94</td>
<td>41.8</td>
<td>41.8</td>
<td>41.8</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>36</td>
<td>16.0</td>
<td>16.0</td>
<td>57.8</td>
</tr>
<tr>
<td>IUFD</td>
<td>2</td>
<td>.9</td>
<td>.9</td>
<td>58.7</td>
</tr>
<tr>
<td>IUFD</td>
<td>54</td>
<td>24.0</td>
<td>24.0</td>
<td>82.7</td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>39</td>
<td>17.3</td>
<td>17.3</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>225</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>
Table (4.6) distributions of (Fetal Outcome) for diabetics:

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>1</td>
<td>.4</td>
<td>.4</td>
<td>.4</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>36</td>
<td>16.0</td>
<td>16.0</td>
<td>16.4</td>
</tr>
<tr>
<td>LGA</td>
<td>36</td>
<td>16.0</td>
<td>16.0</td>
<td>32.4</td>
</tr>
<tr>
<td>IUGR</td>
<td>32</td>
<td>14.2</td>
<td>14.2</td>
<td>46.7</td>
</tr>
<tr>
<td>Discharged</td>
<td>97</td>
<td>43.1</td>
<td>43.1</td>
<td>89.8</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2</td>
<td>.9</td>
<td>.9</td>
<td>90.7</td>
</tr>
<tr>
<td>IUFD</td>
<td>2</td>
<td>.9</td>
<td>.9</td>
<td>91.6</td>
</tr>
<tr>
<td>RDS</td>
<td>12</td>
<td>5.3</td>
<td>5.3</td>
<td>96.9</td>
</tr>
<tr>
<td>Poor sucking</td>
<td>7</td>
<td>3.1</td>
<td>3.1</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>225</strong></td>
<td><strong>100.0</strong></td>
<td><strong>100.0</strong></td>
<td></td>
</tr>
</tbody>
</table>

Figure (4.6) distributions of (Fetal Outcome) for diabetics:

The table and Figure above shown that the most (43.1%) of diabetics fetal outcome were Discharged, since (16%) of them were Hypoglycemia or LGA, (14.2%) of them were IUGR, while only (5.3%) of them were RDS, (3.1%) of them were Poor sucking, (0.9%) of them were Sepsis or IUFD and (0.4%) of them were DM.
Table (4.7): Association of RI with respect to S/D Ratio:

<table>
<thead>
<tr>
<th>RI</th>
<th>Count</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2</td>
<td>.6%</td>
</tr>
<tr>
<td>0.01 and less than 0.7</td>
<td>0</td>
<td>.0%</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>.6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S/D Ratio</th>
<th>0</th>
<th>0.01 to 3.0</th>
<th>More than 3.0</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>0.01 to 3.0</td>
<td>290</td>
<td>89.2%</td>
<td>9.5%</td>
<td>321</td>
</tr>
<tr>
<td>More than 3.0</td>
<td>31</td>
<td>98.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>89.2%</td>
<td>9.5%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Notes from the table above, that (0.6%) participants were No blood flow (IUFD cases) as same as (0.6%) were Absent of end diastolic cases, since the most (89.2%) of participants were Normal, while (9.5%) of participants were Reduce of end diastolic cases.

Table (4.8): Relations between Doppler Indices (RI and S/D Ratio) and Random Blood Sugar, (Fetal Weight) and (Doppler Indices) for diabetics:

<table>
<thead>
<tr>
<th></th>
<th>RI</th>
<th>S/D Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random Blood Sugar</td>
<td>Pearson Correlation</td>
<td>.041</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed)</td>
<td>.540</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>225</td>
</tr>
<tr>
<td>Fetal Weight</td>
<td>Pearson Correlation</td>
<td>-.417</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed)</td>
<td>.000</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>225</td>
</tr>
</tbody>
</table>
Shown from table above that the Correlation coefficients between (RI and S/D Ratio) and Random Blood Sugar are (0.041, 0.005) respectively, with corresponding significance values of Pearson Correlation Coefficients (0.540, 0.937), the Correlation coefficients between Fetal Weight and (RI and S/D Ratio) are (-0.417, -0.165) respectively, with corresponding significance values of Pearson Correlation Coefficients (0.000, 0.013), that indicates there are no statistically significant correlation between (RI and S/D Ratio) and Random Blood Sugar, while there are statistically significant negative relationships between Fetal weight and Doppler indices (RI and S/D Ratio) which means Fetal weight decreases as Doppler indices increase.

Table (4.9): Association of Fetal Risk and Diabetes Type:

<table>
<thead>
<tr>
<th></th>
<th>Fetal Risk</th>
<th>Non</th>
<th>Macrosomia</th>
<th>IUFD</th>
<th>IUGR</th>
<th>Polyhydramnios</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>45</td>
<td>15</td>
<td>1</td>
<td>19</td>
<td>14</td>
<td>94</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Diabetes Type</td>
<td>47.9%</td>
<td>16.0%</td>
<td>1.1%</td>
<td>20.2%</td>
<td>14.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gestational</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>45</td>
<td>17</td>
<td>1</td>
<td>23</td>
<td>21</td>
<td>107</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Diabetes Type</td>
<td>42.1%</td>
<td>15.9%</td>
<td>.9%</td>
<td>21.5%</td>
<td>19.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Type 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>12</td>
<td>4</td>
<td>23</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Diabetes Type</td>
<td>13.0%</td>
<td>17.4%</td>
<td>.0%</td>
<td>52.2%</td>
<td>17.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>94</td>
<td>36</td>
<td>2</td>
<td>54</td>
<td>39</td>
<td>225</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Diabetes Type</td>
<td>41.8%</td>
<td>16.0%</td>
<td>.9%</td>
<td>24.0%</td>
<td>17.3%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Notes from the table Above, that 47.9% of type one diabetics had non fetal risk, while 16.0% of them were Macrosomia, 1.1% of them were IUFD, 20.2% of them were IUGR and 14.9% of them were Polyhydramnios compared with 42.1% of Gestational diabetics had non fetal risk, while 15.9% of them were Macrosomia, 0.9% of them were IUFD, 21.5% of them were IUGR and 19.6% of them were Polyhydramnios and 13.0% of type two diabetics had non fetal risk, while 17.4% of them were Macrosomia, there were no IUFD, 52.2% of them were IUGR and 17.4% of them were Polyhydramnios.

The chi-square test and Likelihood Ratio test statistics are (chi-square = 8.041 with Sig. = 0.782 and Likelihood Ratio = 8.399 with Sig. = 0.753), therefore, statistically non-significant association between Fetal Risk and Diabetes Type.

Table (4.10): ANOVA table for difference between (different types) diabetics in mean of Doppler Indices (RI and S/D Ratio):

<table>
<thead>
<tr>
<th></th>
<th>Sum of Squares</th>
<th>Df</th>
<th>Mean Square</th>
<th>F</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>RI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between Groups</td>
<td>.051</td>
<td>2</td>
<td>.026</td>
<td>1.118</td>
<td>.329</td>
</tr>
<tr>
<td>Within Groups</td>
<td>5.105</td>
<td>222</td>
<td>.023</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5.156</td>
<td>224</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S/D Ratio</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between Groups</td>
<td>5.716</td>
<td>2</td>
<td>2.858</td>
<td>.581</td>
<td>.560</td>
</tr>
<tr>
<td>Within Groups</td>
<td>1086.864</td>
<td>221</td>
<td>4.918</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1092.580</td>
<td>223</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
It shows the results of the 1-Way between Subjects (Diabetics) ANOVA that be conducted. We take a look at the Sig. values in the last column; these values determine if the different diabetics were relatively the same in Doppler indices or if they were significantly different from one another. The Sig. values are 0.329 and 0.560 for RI and S/D Ratio respectively and we can conclude that the differences between Doppler indices are likely due to chance with respect to diabetes type.

Table (4.11): Distributions of two groups (Diabetic and Control group):

<table>
<thead>
<tr>
<th>TYPE</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Std. Error</td>
<td>Mean</td>
</tr>
<tr>
<td>RI</td>
<td>225</td>
<td>.5893</td>
<td>.14663</td>
<td>.00978</td>
</tr>
<tr>
<td>Control</td>
<td>100</td>
<td>.5398</td>
<td>.07304</td>
<td>.00730</td>
</tr>
<tr>
<td>S/D Ratio</td>
<td>225</td>
<td>2.6078</td>
<td>2.18622</td>
<td>.14575</td>
</tr>
<tr>
<td>Control</td>
<td>100</td>
<td>2.2813</td>
<td>.37813</td>
<td>.03781</td>
</tr>
</tbody>
</table>
The table and figures above provides useful descriptive statistics for the two groups that you compared, including the mean and standard deviation mean confidence intervals for RI and S/D Ratio.
Table (4. 12): t-test for Equality of Means of two groups:

<table>
<thead>
<tr>
<th></th>
<th>t-test for Equality of Means</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t</td>
<td>Df</td>
<td>Sig. (2-tailed)</td>
<td>Mean Difference</td>
<td>Std. Error Difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RI</td>
<td>3.785</td>
<td>321.013</td>
<td>0.000</td>
<td>0.04722</td>
<td>0.01248</td>
</tr>
<tr>
<td>S/D Ratio</td>
<td>1.763</td>
<td>250.696</td>
<td>0.079</td>
<td>0.26915</td>
<td>0.15265</td>
</tr>
<tr>
<td></td>
<td>Equal variances not assumed</td>
<td>Equal variances not assumed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

T-test results will tell us if the Means for the two groups were statistically different (significantly different) or if they were relatively the same.

We can see that the group are significantly different in means for (RI) "Sig. (2-tailed = 0.000)" is less than 0.05, while does not for (S/D Ratio) "Sig. (2-tailed = 0.079)" is less than 0.05. Looking at the Distribution of two groups table (12) above, we can conclude that there is statistically significant difference between the mean of RI, but there is no statistically significant difference between the mean of S/D Ratio for those people who diabetic and those who are not.
CHAPTER FIVE

Discussion,

Conclusions Recommendation and

Future works
Chapter Five

5-1 Discussion:

This study has been carried out in maternity & children Hospital in al qassim – buriada , with general aim to explore and record the Doppler Ultrasound assessment of the fetal umbilical artery in diabetic mothers during second & third trimester. 325 patients were enrolled in the study (225 patients in diabetic mothers , and 100 patients as a control group).

Statistical Methods: the use of comparative analytical method using the SPSS statistical program based descriptive statistics and comparative and association hypothesis tests (0.05 sig. level), to demonstrate the relationship between (Doppler Indices) and (Maternal age, Wight, Parity, Random blood sugar, Sugar control method, Family history of sugar and Diabetic type) and relationship between (Gestational age, Fetal weight, Fetal Risk and Maternal risk) and(Doppler Indices) among.

The tests were used for Correlation, t-test, Chi-square test, and ANOVA table to study the hypothesis which states no there are significant relationships.
The result of the study showed that the table and Figure (1) most (49.8%) of diabetics were use Medications to control their sugar since (30.2%) of them uses Insulin and (20%) of them Dose not use any treatment to control their sugar. the table and Figure (2) shown that (45.4%) of diabetics have no diabetes in their families history, since (41.3%) of them have diabetes in their family history, while only (13.3%) of them have Hypertension in their family history. The tableand Figure (3) shown that (41.8%) of diabetes was Type 1 diabetes, since (48%) of diabetes was Gestational, while only (10.2%) of them was Type 2 diabetes. The table and Figure (4) shown that the most (69.8%) of diabetics have non maternal risk, since (25.8%) of them were Cesarean Section, while only (3.6%) of them were Preeclampsia and (0.9%) of them Eclampsia. The table and Figure (5) shown that (41.8%) of diabetics have non fetal risk, since (24%) of them were IUGR, (17.3%) of them were Polyhydramnios, (16%) were Macrosomia, while only (0.9%) of them were IUFD. The table and Figure (6) shown that the most (43.1%) of diabetics fetal outcome were Discharged, since (16%) of them were Hypoglycemia or LGA, (14.2%) of them were IUGR, while only (5.3%) of them were RDS, (3.1%) of them were Poor sucking, (0.9%) of them were Sepsis or IUFD and (0.4%) of them were DM.
The study showed that from the table (7), that (0.6%) participants were No blood flow (IUFD cases) as same as (0.6%) were Absent of end diastolic cases, since the most (89.2%) of participants were Normal, while (9.5%) of participants were Reduce of end diastolic cases.

The study found from table (8) that the Correlation coefficients between (RI and S/D Ratio) and Random Blood Sugar are (0.041, 0.005) respectively, with corresponding significance values of Pearson Correlation Coefficients (0.540, 0.937), the Correlation coefficients between Fetal Weight and (RI and S/D Ratio) are (-0.417, -0.165) respectively, with corresponding significance values of Pearson Correlation Coefficients (0.000, 0.013), that indicates there are no statistically significant correlation between (RI and S/D Ratio) and Random Blood Sugar, while there are statistically significant negative relationships between Fetal weight and Doppler indices (RI and S/D Ratio) which means Fetal weight decreases as Doppler indices increase.

Notes from the table (9), that 47.9% of type one diabetics had non fetal risk, while 16.0% of them were Macrosomia, 1.1% of them were IUFD, 20.2% of them were IUGR and 14.9% of them were Polyhydramnios compared with 42.1% of Gestational diabetics had non fetal risk, while 15.9% of them were Macrosomia, 0.9% of them were IUFD, 21.5% of them were IUGR and 19.6% of them were Polyhydramnios and 13.0% of
Type two diabetics had non fetal risk, while 17.4% of them were Macrosomia, there were no IUFD, 52.2% of them were IUGR and 17.4% of them were Polyhydramnios.

The chi-square test and Likelihood Ratio test statistics are (chi-square = 8.041 with Sig. = 0.782 and Likelihood Ratio = 8.399 with Sig. = 0.753), therefore, statistically non-significant association between Fetal Risk and Diabetes Type.

It shows the results of the (table 10) 1-Way between Subjects (Diabetics) ANOVA that be conducted. We take a look at the Sig. values in the last column; these values determine if the different diabetics were relatively the same in Doppler indices or if they were significantly different from one another. The Sig. values are 0.329 and 0.560 for RI and S/D Ratio respectively and we can conclude that the differences between Doppler indices are likely due to chance with respect to diabetes type. The table and figures (11) provides useful descriptive statistics for the two groups that you compared, including the mean and standard deviation mean confidence intervals for RI and S/D Ratio.

T-test results will tell us if the Means for the two groups were statistically different (significantly different) or if they were relatively the same.
We can see that the group are significantly different in means for (RI) "Sig. (2-tailed = 0.000)" is less than 0.05, while does not for (S/D Ratio) "Sig. (2-tailed = 0.079)" is less than 0.05. Looking at the Distributions of two groups table (12) above, we can conclude that there is statistically significant difference between the mean of RI, but there is no statistically significant difference between the mean of S/D Ratio for those people who diabetic and those who are not.

Also the survey showed there is accuracy of umbilical artery Doppler in predicting fetal outcome: In this study the Doppler of the umbilical artery indices were considered abnormal when S/D ratio >3 & RI >.64 in predicting adverse fetal outcomes. In this study the main adverse fetal outcome criteria were: cesarean section, IUGR, IUFD, Premature birth, admission to the neonatal intensive care unit, fetal mortality and morbidity. The study considered the tests positive if the umbilical artery Doppler indices were above the cut-off levels, S/D ratio >3, RI >0.64.
5-2 Conclusion:

Several studies have demonstrated that Doppler ultrasound represents an important tool for evaluating fetal outcome in diabetic mothers during second & third trimester.

The study found in normal pregnancies, the flow velocity waveforms (FVWs) showed a good diastolic flow and fall in indices as pregnancy progressed. A low diastolic flow and higher indices characterized the pregnancies with abnormal outcomes. From what is mentioned above the study found that Doppler of the umbilical artery was useful to predict fetal well being in diabetic mothers. percentage of adverse fetal outcome had been reported in absent and reversed end diastolic flow velocity in umbilical artery compared with group of present flow velocity.

The study found significant improvement in fetal performance associated with follow up Doppler examination.

The results conclude that the shown that(41.8%) of diabetics have non fetal risk, since (24%) of them were IUGR, (17.3%) of them were Polyhydramnios,(16%) were Macrosomia, while only (0.9%) of them were IUFD.& the most (43.1%) of diabetics fetal outcome were Discharged, since (16%) of them were Hypoglycemia or LGA, (14.2%) of them were IUGR, while only (5.3%) of them were RDS, (3.1%) of
them were Poor sucking, (0.9%) of them were Sepsis or IUFD and (0.4%) of them were DM.

*The study found that (0.6%) participants were No bloodflow (IUFD cases) as same as (0.6%) were Absent of end diastolic cases, since the most (89.2%) of participants were Normal, while (9.5%) of participants were Reduce of end diastolic cases.

*Also I find no statistically significant correlation between (RI and S/D Ratio) and Random Blood Sugar, while there are statistically significant negative relationships between Fetal weight and Doppler indices (RI and S/D Ratio) which means Fetal weight decreases as Doppler indices increase.

* The chi-square test and Likelihood Ratio test statistics are (chi-square = 8.041 with Sig. = 0.782 and Likelihood Ratio = 8.399 with Sig. = 0.753), therefore, statistically non-significant association between Fetal Risk and Diabetes And there is statistically significant difference between the mean of RI, but there is no statistically significant difference between the mean of S/D Ratio for those people who diabetic and those who are not.
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 follow:

- **Applied Doppler** ultrasound technique should be used routinely in obstetric departments and periodic training for examiner in all types of Doppler techniques is highly recommended.

- **Early screening** of the UA Artery waveform should be performed, this may help in early diagnosis and may decrease the fetal and maternal morbidity and mortality rate.

- **Farther studies** are recommended in Doppler technique to know the relation between umbilical artery and other fetal vessels to reduce the adverse outcome e.g, the ratio between umbilical artery and middle cerebral arteries.

- **Doppler examination** should be used properly and effectively to reduce acoustic exposure to the patients.
QUATETUNARE
Sudan University of Science and Technology

Data collection sheet

PhD medical diagnostic ultrasound

Doppler study of umbilical arteries in diabetic pregnancy

Date: / / 201

Patient No:

GENARAL PATIENT INFORMATION:-

Hospital or clinic names: ( ) maternal age:...( )
maternal weight: ( ) Maternal parity : ( )

Blood Glucose level investigation : RBS ( )

Control: current medication( ) insulin( ) diet( )

Family history: NO H/O: ( ) Diabetic: ( ) hypertension: ( )

Maternal diabetic type: Non-diabetic : ( ) type one: ( )
Gestational diabetic :( ) type two: ( )

SPICIFIC INFORMATION:-

Doppler measurement: RI……( ) S/D ratio ( ).

Gestation Age…( ) Fetal weight: ( )

Diabetic Pregnancy complications:

Maternal complication: high blood sugar: ( ) Cesarean section ( ) Preeclampsia: ( )

Fetal complication: Macrosomai: ( ) hypoglycemia ( )
IUGR ( ) Polyhydramnois: ( ) IfUD ( )

Fetal outcome:

........................................................................................................

........................................................................................................

........................................................................................................
APPENDIX

5-4. appendix images

5-4.1 Sonographic images selected as the sample of the study.

Figure (5.1) shows normal Color Doppler of the umbilical artery waveform at 33Wks.

Figure (5.2) shows normal Color Doppler of the umbilical artery waveform at 35 Wks.
Figure (5.3) shows normal Color Doppler of the umbilical artery waveform at 29 Wks.

Figure (5.4) shows reduced end diastolic of the umbilical artery waveform at 34Wks.
Figure (5.5) shows reduced Color Doppler of the umbilical artery waveform at 33Wks.

Figure (5.6) shows reduced Color Doppler of the umbilical artery waveform at 33Wks.
Figure (5.7) shows normal Color Doppler of the umbilical artery waveform at 33Wks.

Figure (5.8) shows normal Color Doppler of the umbilical artery waveform at 33Wks.
Figure (5.9) shows reduced end diastolic flow of the umbilical artery waveform at 37Wks.

Figure (5.10) shows normal Color Doppler of the umbilical artery waveform at 25Wks.
Figure (5.11) shows normal Color Doppler of the umbilical artery waveform at 36 Wks.

Figure (5.12) shows normal Color Doppler of the umbilical artery waveform at 27 Wks.
Figure (5.13) shows Color Doppler of the umbilical artery waveform demonstrating reduced end-diastolic frequencies at 34Wks. Compare these appearances with the normal appearances of waveform.

Figure (5.14) shows color Doppler of the umbilical artery waveform demonstrates absent end-diastolic frequencies.

Figure (5.15) shows normal Color Doppler of the umbilical artery waveform at 38 Wks.
Figure (5.16) shows reduced end diastolic Color Doppler of the umbilical artery waveform at 32 Wks.

Figure (5.17) shows normal Color Doppler of the umbilical artery waveform at 36 Wks.
Figure (5.18) shows normal Color Doppler of the umbilical artery waveform at 39 Wks.

Figure (5.19) shows normal Color Doppler of the umbilical artery waveform at 29 Wks.

Figure (5.20) shows normal Color Doppler of the umbilical artery waveform at 23 Wks.
Figure (5.21) shows normal Color Doppler of the umbilical artery waveform at 20 Wks.
REFERENCES:

1- Obstetric Ultrasoun, third edition, Trish Chudleigh PhD DMU
Superintendent Sonographer, Fetal Medicine Unit, St Thomas’ Hospital,
London, UKBaskyThilagana than MD MRCOGDirector of Fetal
Medicine, St George’s Hospital, London, UKAn imprint of Elsevier
Science Limited, 2004, Elsevier Limited. All rights reserved.


3. Burwin institute of diagnostic medical ultrasound obstetric and
gynecology.

4. A Comprehensive Guide, Rated among the top 5% of all Internet sites
by Lycos in 1995, and consistently ranked first on Google for the
keyword "Ultrasound"

5. du Plessis JM, Hall DR, Norman K, Odendaal HJ. Reversed end
diastolic flow velocity in viable fetuses: is there time to wait for the effect

6. Clinical obstetric&gynecology ultrasound, second edition, edited by
Medical diagnostic ultrasound, By Jens E. Wilhjelm, Martin Kristensson and Ole Trier Andersen DTU Elektro, Ørstedsplads, building 348
Technical University of Denmark 2800 Kgs. Lyngby (Ver. 3.1 3/9/10) © 2001-2010 by J. E. Wilhjelm & O.T. Andersen.


Standards of Medical Care in Diabetes-2012, doi: 10.2337/dc12-s011
Diabetes Care January 2012 vol. 35 no. Supplement 1 S11-S63.

.neurological system, denissstevenscrna, msn, arnpaugust 2010, florida international university, advanced bioscience in anesthesiology ingr 6405.


correlation of fetal gestational age by biparietal diameter and abdominal circumference in second trimesteter. saramohammedahamed,

Faculty of Radiology Science and Medical Imaging, Alzaiem Alazhari University, P.O.Box 1432 Khartoum North, Sudan- 2010.
13. The Manchester Handbook of Ultrasound Technique, Brennan Wilson
Department of Radiology Royal Manchester Children's Hospital
Pendlebury Manchester M27 4HA, Tel: (0161) 794 4696 (switch) email:
Brennan.Wilson@man.ac.uk.

14. To3-Doppler Studies Second & Third Trimester © 2009 Brayford
Studio Date enter 22.7.2012, from www.google.com. a b Thomas R
Moore, MD et al. Diabetes

15. To4 Mellitus and Pregnancy. med/2349 at eMedicine. Version: Jan
27, 2005 update.-

16. To5- a b c d HAPO Study Cooperative Research Group; Metzger,
1991–2002. doi:10.1056/NEJMoa0707943. PMID 1846337. 6-

"Selective Screening for Gestational Diabetes Mellitus". New England

19. re to 8. The Human Umbilical Cord, anatomy & physiology.

20. re to 9. Doppler in Obstetrics Copyright © 2002 by Kypros Nicolaides, Giuseppe Rizzo, Kurt Hecker and Renato Ximenes Centrus. ® produced at

21. re to 10 Copyright © 2012 Radiological Society of North America, Inc. (RSNA). ( 


Reference of previous studies:

27. Epidemiological studies of exercise in diabetes prevention ,

Authors: Hu, Gang; Lakka, Timo A.; Kilpeläinen, Tuomas O.; Tuomilehto, Jaakko.

Source: Applied Physiology, Nutrition, and Metabolism, Volume 32, Number 3, June 2007 , pp. 583-595(13)

Publisher: NRC Research Press(


Enter date ,23.7.2012.


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