Sudan University of Sciences and Technology

College of Graduate Studies

Evaluation of Doppler indices and Measurement For Umbilical Artery In Patients with pre-Eclampsia

مؤشرات الموجات الطيفية وقياس الشريان السري لمرضى تسمم الحمل

A Thesis submitted for Partial Fulfillment for the Degree of Masters(M. Sc) in Diagnostic Medical ultrasound imaging

By:

Rehab Mohammed Ali Hassan Ahmed

Supervisor:

Dr. Caroline Edward Ayad

Associate Professor

2015

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﴿ اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ ﴾ 1 ﴿ خَلَقَ

الْإِنْسَانَ مِنْ عَلَقٍ ﴾ 2 ﴿ اقْرَأْ وَرَبُّكَ الْأَكْرَمُ

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الْإِنْسَانَ مَا لَمْ يَعْلَمْ ﴾ 5 ﴿

صدق الله العظيم

سورة العلق الآيات (1 – 5)

Dedication

To my mother

To soul of my kind father

To my dear husband

To my lovely Childs

To my friends and colleagues

To everyone who ever help me

To all of them I dedicate this work

Acknowledgment

First of all, I thank Allah the Almighty for helping me complete this project.

I wish to express my deepest appreciation to my friendly teacher and supervisor (Dr. Caroline Edward Ayad) for her guidance unending support during the preparation of this thesis.

I would also like to acknowledge and express my gratitude to Dr. Mohammed Mohammed Amin the head of radiology department in Saqr hospital (U.A.E) for his understanding and helping and also Dr. Hossam for his great help and advice.

Also I would like to thanks my brother Dr.Adel and my collagenus friends Jameela and Ebtisam for their assistant and helping to complete this research.

Abstract

Preeclampsia is one of the leading causes of maternal mortality and is responsible for considerable perinatal morbidity and mortality.

This study aims to evaluate Doppler indices and measure umbilical diameter in patients with pre-eclampsia.

This was a prospective, cross-sectional, hospital-based, case-control study of 30 normotensive (controls) and 30 pre-eclamptic (cases) women at Khartoum Teaching Hospital; between the period of December 2014 – June 2015.

All patients were scanned for obstetric ultra sound and Doppler indices (RI, PI) were evaluate for both control and pre-eclampsia patients.

The mean umbilical cord diameter for control subjects was (14.47 mm +/- 1.87 SD), for subjects with mild pre-eclampsia it was (13.65 mm +/- 1.2 SD). The mean pulsatility index for normotensive participants (controls) was (0.99 +/- 0.17 SD), that of participants with mild pre-eclampsia was (1.68 +/- 0.33 SD) and that of subjects with severe pre-eclampsia was (2.11 +/- 0.06 SD). The mean R.I of normotensive participants (controls) was (0.59 +/- 0.05 SD), it was (0.94 +/- 0.05 SD and 1.14 +/- 0.068 SD) for participants with mild and severe pre-eclampsia, respectively.

The umbilical cord diameter was found to be larger in the normal than the pre-eclampsia patients as well as the Doppler indices were found to be significantly increase in pre-eclampsia patients.

ملخص الدراسة

الكلبش هو أحد الأسباب التي تؤدي إلي وفيات الأمهات وهو المسؤل عن زيادة معدل إصابة ووفيات الأطفال قبل الولادة.

تهدف هذه الدراسة إلي تقويم مؤشرات الدوبلار وقياس قطر الشريان السري لدي مرضي الكلبش.

هذه الدراسة المقطعية المستعرضة أجريت على مجموعه تحكم تتكون من 30 أمراء طبيعية و 30 حاله مصابه بالكلبش بمستشفي الخرطوم التعليمي في الفترة بين ديسمبر 2014م ومايو 2015م.

تم فحص كل المرضي- باستخدام الموجات فوق الصوتية وقياس مؤشر- الدوبلار (مؤشر- المقاومة ومؤشر- النبض) وتم تقيمهم لكل من مجموعه المرضي ومجموعة التحكم.

وجد أن قطر الحبل السري لمجموعه التحكم لدي السودانيين ((14.47 mm 1.87 SD -/+ و المرضي المصابين بالكلبش تساوي (13.65 SD 1.2 -/+ mm). كما وجد أن متوسط مؤشر النبضة للأفراد الطبيعية مجموعه التحكم (0.99 +/- 0.17 SD) والمجموعة المصابة بالكلبش بدرجه بسيطة تساوي 1.68 +/- 0.33 SD)) والمصابين بدرجه حادة تساوي) (2.11 +/- 0.06 SD. ومؤشرات المقاومة لمجموعة التحكم تساوي (0.59 +/- 0.05 SD) وكانت القيم تساوي 0.94 +/- 0.05 SD (0.068 -/+ SD and 1.14))(للمرضي- المصابين بالكلبش البسيط والحاد على التوالي.

أوضحت الدراسة أن قطر الحبل السري أكبر في الحالات الطبيعية عن حالات الكلبش كما أن مؤشرات الدوبلار يزداد في حاله المرضي- المصابين بمرض الكلبش.

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List of Abbreviations

AFI	:	Amniotic Fluid Index
EDV	:	End Diastolic Velocity
FVWs	:	Flow Velocity Wave forms
GA	:	Gestation Age
IUD	:	Intrauterine Death
IUGR	:	Intrauterine Growth Retardation
PE	:	Pre-eclampsia
PI	:	Pulsatility
PSV	:	Peak Systolic Velocity
SD	:	Standard Deviation
S/ D	:	Systolic/ Diastolic
TAMV	:	Time Average Maximum Velocity
RI	:	Resistive Index
UA	:	Umbilical Artery

Chapter One

Introduction

Chapter One

1.1 Introduction

Worldwide pre-eclampsia (PE) is the first cause of maternal mortality, intrauterine growth retardation (IUGR), and fetal prematurity (Crispi, 2008) (Diab, 2008). PE affects 5-10% of pregnancies and is clinically manifested after 20 weeks of gestation (GW) (Baumwell, 2007) (Backes, 2011). The aetiology of PE is still unknown, although an excessive maternal systemic inflammatory response and an imbalance between circulating angiogenic and anti-angiogenic factors have been described (Szarka, et al., 2010).

Pre-eclampsia (PE), defined as de novo hypertension (>140/90 mmHg) appearing after 20 weeks of gestation accompanied by proteinuria (>0.3 g/24 h), remains a major source of perinatal growth restriction, prematurity and death worldwide. Since its introduction practitioners have increasingly utilized fetal ultrasonography for the management of pre-eclampsia. Ultrasonographic diagnostic modalities including fetal biometric growth curves, the biophysical profile and umbilical artery Doppler have been used to detect Pre-eclampsia, fetal growth restriction and assess fetal wellbeing, respectively (Jodicke, 2012).

Umbilical cord plays important role in fetal wellbeing. Several umbilical cord abnormalities are known to cause adverse prenatal outcome. Abnormal cord length, thick or lean umbilical cords, hyper coiling or hypo coiling, marginal or velamentous insertion of cord may be associated with IUGR, IUD or fetal distress (Sbnis, et al., 2012).

Morphologic umbilical cord characteristics, including thickness and the amount of umbilical cord Wharton jelly (Ghezzi, et al., 2001), coiling (Qin, et al., 2002), and the direction of the umbilical cord rotation,

have been reported to be associated with adverse perinatal outcomes, including hypertensive disorders, gestational diabetes (Weissman, et al., 1997), intrauterine growth restriction (Naro, et al., 2002), small- and large-for-gestational-age neonates, fetal distress in labor, and cesarean delivery.

It is common knowledge now that preeclampsia may change the phenotype of umbilical cord vessels (Blanco, et al., 2011) have researched that and concluded that:

“Umbilicalcord in preeclampsia showed significant changes in the structure of umbilical arteries, with increases in wall areas and wall/ lumen ratios”.

Role Of Ultrasound In Pre-Eclampsia

For many years, evaluation of umbilical cord morphology was restricted to the post-partum period and was performed by pathologists who demonstrated that a thin umbilical cord was associated with adverse pregnancy outcome. In normal pregnancies, the feto-placental circulation acts as a low resistance system unit. Thus, the blood velocity waveforms in umbilical artery (UA) show continuous forward flow throughout the cardiac cycle (Divon, et al., 2001).

Goldkranket al documented a steady increase in the blood flow of the umbilical artery as pregnancy progresses. The diameter of the umbilical artery increases until reaching a plateau at 32-34 weeks' gestation, whereas the systolic/ diastolic (S/ D) ratio, resistance index and pulsatility index (PI) decrease throughout pregnancy (Goldkrand, et al., 2000).

(Ertan et al., 2004) also showed that the frequency of preeclampsia, intrauterine growth retardation, oligohydramnios and nicotine abuse were significantly higher in a group of patients with reverse flow of umbilical artery compared to the control group.

In (Arauz et al., 2008) study abnormal umbilical artery Doppler velocimetry was present in 52% of preeclamptic patients and they suffered more from adverse neonatal outcomes than those with normal Doppler indices.

Ultrasonographic evaluation of the fetus is very significant in the obstetrical management. In addition to fetal parameters it includes placental measures such as umbilical cord length, diameter, and degree coiling among others (De Laat, et al., 2005). In a typical three vessel umbilical cord there are two umbilical arteries and one umbilical vein, suspended in a mesodermal mucoid matrix stroma, called Wharton's jelly. There are no nerves or lymphatic vessels in the umbilical cord. Wharton's jelly consists of myofibroblasts and ground substance (Nanaev, et al., 1997).

The umbilical cord diameter depends upon the number of vessels present, size of the umbilical vein and the fluid content of Wharton's jelly. Till date, factors determining the amount of water content in Wharton's jelly are not clearly understood. The normal cord diameter is 1-2 cm and the cord can be oedematous in clinical situations such as maternal diabetes mellitus. The cord diameter can also be decreased in conditions like pre-eclampsia (Arauz et al., 2008).

Umbilical arterial Doppler assessment is used in surveillance of fetal well-being in the third trimester of pregnancy. Umbilical artery Doppler assessment has been shown to improve perinatal mortality and morbidity in high risk obstetric situations. Abnormal umbilical artery Doppler is a marker of utero-placental insufficiency and consequent intrauterine growth restriction (IUGR) or suspected pre-eclampsia (Maulik, et al., 2010). Therefore, it was made the objective of the current study to determine the role of ultrasound imaging in predicting and diagnosing pre-eclampsia.

1.2 Problem of the study:

Worldwide pre-eclampsia (PE) is the first cause of maternal mortality, intrauterine growth retardation (IUGR), and fetal prematurity.

PE develops in about 10% of pregnancies and is a leading cause of perinatal morbidity and mortality. Therefore, it was the very objective of this study to determine the exact role of ultrasonography in diagnosis, prediction and management of this grave disease.

1.3 Justification

Preeclampsia is one of the leading causes of maternal mortality and is responsible for considerable perinatal morbidity andmortality; especially, in developing countries.

Doppler velocimetry studies of placenta and fetal circulation(i.e. Umbilical cord diameter and Doppler indices) can provide important information regarding the diagnosis and progression of preeclampsia, maternal and fetal wellbeinggiving obstetricians a unique opportunity to alleviate maternal suffering and improve foetal outcome.

1.3.1 General Objective:

- To evaluate the Doppler indices and umbilical cord diameter using ultrasonagraphy in patients with pre-eclampsia.

1.3.2 Specific Objectives:

- To compare Doppler parameters of umbilical artery (pulsatility and resistance indices) in patients with preeclampsia with those of normal pregnancies.
- To evaluate the diagnostic characteristics of these parameters in preeclampsia.

1.4 Overview of study

This study consisted of five chapters. Chapter one is an introduction which includes; problem and objective of the study. Chapter two is a literature review which includes; Anatomy, Physiology,

Pathology and previous studies. Chapter three is about research methodology. In Chapter four the results are presented and Chapter five includes; discussion, conclusions and recommendations.

Chapter: Two

Backgrounds

Chapter Two

Background

2.1 Anatomy and Physiology

The umbilical cord normally contains two umbilical arteries, a single umbilical vein, an obliterated allantois duct, all surrounded by Wharton's jelly and contained within an outer layer of amnion. The structure of the umbilical cord can vary in the number of umbilical arteries, the length and diameter of the cord, and the direction and number of spirals of the cord. The umbilical cord vein is the remnant of embryological venous development that results in the obliteration of the right umbilical cord vein and the establishment of two pathways through the liver and heart for oxygenated blood travelling from the placenta to the foetus via the persisting left umbilical cord vein. Pressure gradients caused by foetal heart contractions, foetal breathing and distortions of the umbilical cord arteries transports oxygenated blood from the placenta to the foetus through the umbilical cord vein (Weissman, et al., 1997).

An understanding of the embryology, anatomy and physiology of the umbilical cord, especially the vein, may lead to more comprehensive ultrasound imaging, heighten appreciation of the importance of this structure and encourage further research into this critical blood conduit.

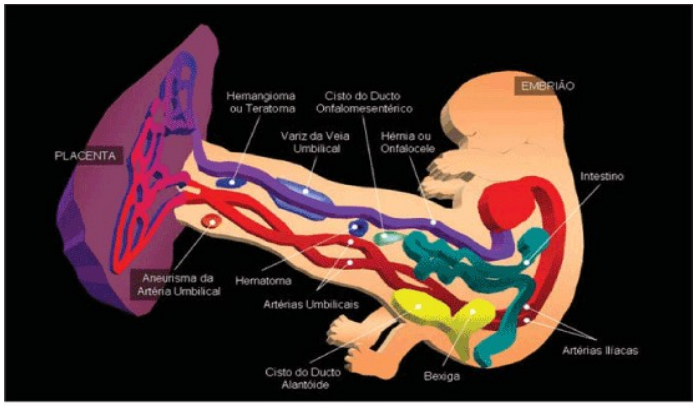

Figure 1. Umbilical cord masses. (Modified from: Callen PW, editor. Ultra-sonografia em obstetrícia e ginecologia. 4ª ed. Rio de Janeiro: Guanabara Koogan; 2002. p. 587).

Figure (2.1): Umbilical cord masses (Weissman, et al., 1997).

2.2 Mechanisms of blood flow in the umbilical cord vein

The placenta provides a large volume of blood awaiting transportation to the foetus. “The quantity of the blood flowing from the fetus to the placenta very nearly equals that flowing from the placenta to the fetus” and as such the foetus can be considered a closed system (Ertan et al., 2004).

Movement of oxygenated blood from the placenta to the foetus occurs by the following methods:

1. The umbilical cord vein pressure increases from 4.5 mmHg at 18 weeks gestation to 6 mmHg at term and the blood pressure distending the umbilical vein is higher than that in the fetal IVC.20 This gradient is due to at least two mechanisms:

- Normal foetal heart contractions producing a pressure gradient between the atria and ventricles, which in turn diminishes the preload in the venous circulation and allows the blood in the umbilical vein to move towards the heart.
- Changes in abdominal and thoracic cavity pressures due to foetal breathing movements causing a pressure gradient between the umbilical vein and the ductus venosus such that there is an increase in the velocity of the blood in the umbilical vein during inspiration.

2. Passive pressure changes in the umbilical cord vein due to longitudinal distortion of the arteries with each foetal heart beat. The pressure peaks in the umbilical cord artery and vein are out of phase by 180° which results in the addition of the effect of numerous, small pressure changes along the length of the cord and the subsequent movement of blood through the umbilical cord vein.

2.3 Normal Sonographic Appearance of Umbilical Cord

Umbilical cord which contains two umbilical veins and one umbilical artery appear as shown below:

Figure (2.2): Ultrasound appearance of a normal umbilical cord (Qin et al., 2002)

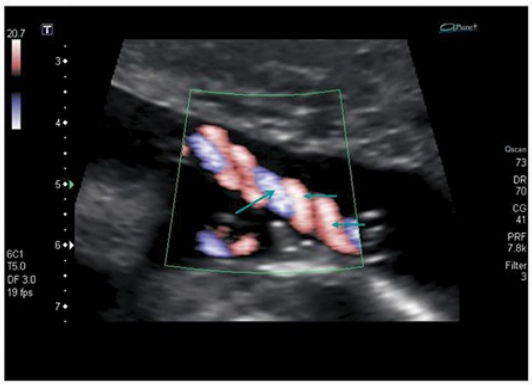

Figure (2.3): Ultrasound appearance of a normal umbilical cord (Qin et al., 2002)

Figure (2.4): Doppler Ultrasound appearance of a normal umbilical cord (Divon et al., 2001)

2.4 Literature Review:

Preeclampsia (PE) is a pregnancy-specific heterogeneous systemic disorder, affecting both the mother and the fetus. Maternal syndrome is characterised with hypertension, proteinuria and oedema, causing fetal syndrome, i.e. growth restriction and chronic hypoxia of the fetus. Premature delivery or abruption placentae may also occur. PE develops in about 10% of pregnancies and is a leading cause of perinatal morbidity and mortality. Although the cause of PE remains unknown, genetic, immunologic and inflammatory factors are considered. In the pathophysiology of PE, impaired trophoblastic invasion and endothelial cell damage plays a crucial role. From this point of view, PE is a two-stage disease. Failure of blastocyst nidation at the beginning of pregnancy (1^{st} stage), causes hypoxic changes in endothelium in the second half of pregnancy (2^{nd} stage). On the other hand, two clinical entities of PE are possible. Early-onset PE with severe course, causing early vasoconstriction of spiral arteries and late-onset PE with mild course with late atherosclerotic changes in spiral arteries (Zahumensky, 2009).

Role For Doppler Flowmetry In Diagnosis of PE

In physiological pregnancies trophoblast invasion transforms the high-resistance spiral arteries into low-

impedance utero-placental circulation. This vascular transformation remains incomplete in PE.

Sonography is the world-wide method of choice for non-invasive examination of pregnancy. B-scan or 3D/ 4D ultrasound can detect structural characteristics of the fetus and other components of gestational sac. However, there are some limitations of this examination (Drobny et al., 2004). Especially in the sonography of placenta, depiction of placental structures alone with the evaluation of the placenta is insufficient. Sonography can visualize structural changes of trophoblast and placenta during pregnancy (Drobny et al., 1994). On the other hand, functional changes of placenta are of great interest for obstetricians. From this point of view, Doppler flowmetry is a suitable non-invasive method for the evaluation of pathological haemodynamic changes not only in utero-placental circulation, but also in subsequent altered feto-placental and fetal circulation.

Doppler velocity indices include; pulsatility index (PI), resistive index (RI) and systolic/ diastolic velocity ratio (S/ D Ratio). PI = (PSV – EDV)/ TAMV, RI = (PSV – EDV) / PSV and S/ D Ratio = PSV / EDV, where; PSV means peak systolic velocity, EDV end-diastolic velocity and TAMV time-averaged maximum velocity (Zahumensky, 2009).

In the first and second trimester of gestation high resistance flow, determined by Doppler flowmetry indices can detect later development of PE. On the other hand,

application of this method for screening of all pregnancies in order to detect risk of PE is questionable.

(Melchiore et al., 2008) found significantly higher Aut RI at 11-14 weeks in women who subsequently developed preterm PE in opposite to those with normal outcome. These findings support, but not prove, a rigid separation between the aetiology of early- and late-onset pre-eclampsia. Finally, this data does not support routine introduction of first trimester Doppler flowmetry into clinical practice.

(Plasencia et al., 2008) measured Aut PI at 11 + 0 to 13 + 6 weeks and 21 + 0 to 24 + 6 weeks of gestation. They detect that the decrease in Aut PI between these two examinations is steeper in pregnancies with normal outcome than in those developing PE. Authors conclude that effective screening for PE can be achieved by the Doppler measurement of Aut PI at 11 + 0 to 13 + 6 weeks and the change in PI between 11 + 0 to 13 + 6 weeks and 21 + 0 to 24 + 6 weeks.

(Detti, 2006) in addition, focused on abnormal Doppler flow indices and the possibility to detect first trimester IUGR in cases, when the last menstrual period and conception time are accurately known.

(Teixeira, 2008) evaluated Ductus venous Doppler flowmetry in the first trimester from the view of trophoblastic migration, partially by PE. Their findings suggest that the first wave of trophoblastic migration may begin at a CRL of 63 mm. Investigation of pulsatility index

for vein behaviour in early pregnancy may be useful as a screening method to evaluate whether placental implantation is adequate.

(Parra et al., 2005) Detected by the examination at 11 to 14 and 22 to 25 weeks a significantly increased Aut PI, plasma level of soublefms-like tyrosine kinase 1 (sFlt1), PAI-1/ PAI 2 ratio and F-2 isoprostane in women who subsequently developed PE compared with control pregnancies. This syudy demonstrated early changes in markers of impaired placentation, anti-angiogenic state, oxidative stress and endothelial dysfunction suggesting that these derangements may play a role in the pathogenesis of PE. Aut PI is the best test to predict PE at 23 weeks of gestation (Parra et al., 2005).

2.5 Appraisal of Similar Studies:

Doppler indices of umbilical artery are used as indicator of fetal well being.

To compare Doppler parameters of umbilical artery including pulsatility index (PI) and resistance index (RI) in patients with preeclampsia with those of normal pregnancies and to evaluate the diagnostic characteristics of these parameters in preeclampsia, (Aali et al., 2010) carried out their case control study.

Umbilical artery pulsatility and resistance indices were calculated at a free loop of umbilical cord in 25 preeclamptic patients and 75 uneventful pregnancies. Measurements were compared and diagnostic characteristics of the indices were determined.

Mean of pulsatility and resistance index were significantly higher in preeclampsia patients than the control group. Besides, patients with severe preeclampsia showed significantly higher values of PI and RI in comparison to those with mild preeclampsia. For PI, the cut-off of ≥0.98 yielded the highest sensitivity and specificity. Also, RI of 0.64 acquired a sensitivity of 100% and specificity of 44%.

(Aali et al., 2010) has finally concluded that umbilical artery pulsatility index and resistance index increase in preeclampsia and these changes tend to be greater in severe preeclampsia. Umbilical artery PI and RI seem to be more appropriate in excluding preeclampsia rather than confirming it, and they propose the cut-off values of 0.98 for PI and/or 0.64 for RI, to rule-out the disease.

Experimental and clinical evidence have shown that the morphometry of the umbilical cord in the second half of gestation might be useful in predicting adverse perinatal outcome. The purposes of this study by (Ghezzi et al., 2001) were to generate a nomogram for the umbilical cord diameter in the first trimester and, in an observational study, to investigate whether the sonographic measurement of the umbilical cord diameter early in gestation has the same clinical value as that late in gestation.

The sonographic umbilical cord diameter, crown-rump length and biparietal diameter were measured in

439 foetuses at between 8 and 15 weeks of gestation. The perinatal outcome was recorded for all patients.

The umbilical cord diameter increased steadily from 8 to 15 weeks of gestation. A significant correlation was found between umbilical cord diameter and gestational age ($r = 0.78$; $P < 0.001$), umbilical cord diameter and crown-rump length ($r = 0.75$; $P < 0.001$) and umbilical cord diameter and biparietal diameter ($r = 0.81$; $P < 0.001$). No correlation was found between umbilical cord diameter values and either birth weight or placental weight. Among patients who had a miscarriage ($n = 7$) and pre-eclampsia ($n = 8$) the umbilical cord diameter was below 2 standard deviations from the mean in three cases (42.9%) and three cases (37.5%), respectively. (Ghezzi et al., 2001) then concluded that the measurement of the umbilical cord diameter in the first trimester is correlated with the growth of the embryo and may be a marker for identifying a subset of fetuses at risk of spontaneous miscarriage and pre-eclampsia.

The appearance of end-diastolic flow velocities (EDF) in the umbilical artery (UA), usually between 10 and 14 weeks of gestation, has been associated with the opening of the spiral arteries and consequently of the intervillous space.

The aim of (Zdanowicz 2013) study was to compare first trimester UA (PI) and EDF between women who developed preeclampsia (cases) and controls.

Database was searched for cases that had UA Doppler between 10-14 weeks. UA PI and EDF were compared between cases and two gestational age (GA) matched controls.

15 cases with severe preeclampsia (PE) were matched to 30 controls. GA with negative EDF was lower than with positive EDF (12.1 ± 0.79 vs. 12.8 ± 0.34; $p = 0.001$). UA PI in cases was higher than in controls, although not significant (cases: 2.18 ± 0.6 vs. controls: 1.92 ± 0.48; $p = 0.12$). However, comparing groups with negative EDF, the difference became significant (PI cases: 2.45 ± 0.57 vs. PI controls: 1.94 ± 0.56; $p = 0.038$), while no difference was found comparing groups with positive EDF.

First trimester UA PI is significantly higher in women which will develop PE than in controls. Interestingly, the timing of screening for PE by UA Doppler seems to play an important issue.

This cross sectional study was carried out by (Ferdousi et al., 2013) on 60 pregnant Bangladeshi women in the department of Radiology and Imaging. Pulsatility Index (PI) of umbilical artery of their foetuses by duplex colour Doppler sonography during 2nd and 3rd trimester of pregnancies.

Considering total 2nd and 3rd trimesters the mean PI value of umbilical artery was 1.24 (SD +/- 0.27). While considering the gestational in separate trimesters, study showed that the value of PI in 2nd trimester was 1.33 (SD +/- 0.29) and in 3rd trimester PI was 1.18 (SD +/- 0.25).

Paired t test shows there was a highly significant (t = 35.79, df = 59, Level of significance = 0.001) difference between mean values of PI in different gestational ages. It was observed that there was gradual decrease of PI value with increase of gestational age (r = -0.207) but this decrease of PI was not statistically significant (p = 0.113). Regression analysis between dependent PI value and independent gestational age showed linear negative relationship but this was not statistically significant (p = 0.11).

This study by (Ferdousi et al., 2013) revealed that the Pulsatility index of umbilical artery was decreased with increase of gestational age from 2nd to 3rd trimester.

Preeclampsia is a pregnancy specific syndrome characterizedby reduced organ perfusion secondary to vasospasm and endothelialpathophysiology. This condition is the leading cause of maternal mortality and is responsible for considerable perinatal morbidity and mortality.

This study by (U Gupta et al., 2008) was conducted to find Doppler velocimetric indices of the uterine and umbilical artery in normotensive and hypertensive pregnancy and to detect SGA foetuses with abnormal velocimetric index.

Two hundred women of third trimester in antenatal clinic were studied: hypertensive and normotensive 100 each. Baseline investigations and Doppler velocimetry of both the uterine arteries and umbilical artery was done.

Statistical analysis of data was done using the EPI-info 6 (CD) (US) / WHO).

The mean SD ratio of Uterine Artery decreased from 6.15 at 32-34 weeks to 3.06 at 38-40 weeks in the hypertensive group.

Abnormal uterine artery Doppler findings were reported in 55% of hypertensives. In the hypertensive group 92.10% of cases with SGA babies and 32.25% of cases with AGA babies had abnormal uterine artery Doppler findings.

(U Gupta et al., 2008) then concluded that abnormal Doppler findings of the uterine and umbilical are more common in SGA foetuses.

Pregnancy induced hypertension results from defective trophoblast invasion and increased umbilical artery resistance which in turn results in decreased blood supply to the placenta and hence to the foetus. This arterial resistance varies in different cases of PIH thus causing variable effects on placenta and foetus.

The objective of this study by (K Borgesetal et al., 2013) was to study the morpho-metric changes in placenta and alterations in birth weight with differences in umbilical artery resistive index in hypertensive pregnancies. Ninety pregnant women with pregnancy induced hypertension were selected with gestational age greater than 35 weeks. Doppler ultrasound examinations were carried out to record umbilical artery resistive index (UARI).

Two groups were made on the basis of median values of UARI. Plain ultrasound examination was then carried out to record presentation, site of placentation, grade of maturity, insertion of the cord, cord thickness, placental thickness, vacuolation and amniotic fluid index (AFI). After delivery, foetal birth weight was noted and placentae examined for placental weight, infarcts, number of cotyledons, umbilical cord insertion, cord thickness and placental thickness were noted. Foetoplacental weight ratio was also calculated.

Significantly higher UARI was seen in the high-resistance group. Significantly lower values of placental thickness, AFI, birth weight, placental weight and placental thickness, whereas greater number of grade-III maturity, infarcts and marginal cord insertion were noted in the high-resistance group.

Increased UARI leads to a spectrum of changes in the placenta and also decreased birth weight. Marginal cord insertion causes greater risk of increased UARI.

During normal pregnancy, physiological modifications of the utero-placental and umbilico-placental bed take place to permit a decrease in vascular resistance and consequent increase in diastolic flow. Failure of this physiological process results in increased vascular resistance and fall in diastolic flow resulting in abnormal pathological conditions.

Doppler US provides a means of studying these circulatory

beds and detecting abnormal vascular resistance patterns in the uterine and umbilical arteries non-invasively.

The purpose of this study by (Lakhkar et al., 1999) was to evaluate the uterine and umbilical arteries at 20, 28 and 34 weeks of gestation using Doppler techniques. The study included various indices such as pulsatility index (PI), resistance index (RI) and systolic/diastolic (S/D) ratio and their usefulness as screening tests.

For the purpose of this study, (Lakhkar et al., 1999) have recruited total of 120 random pregnancies were screened at 20, 28 and 34 weeks of gestation. A colour Doppler scanner with a carrier frequency of 3.5 MHz was used for studying the uterine and the umbilical arteries. Pregnancies with a normal outcome were used for calculating the normal range of various indices and for testing the specificity and negative predictive value (NPV) of the study. Those pregnancies with an abnormal outcome (PIH and SGA babies) were used for calculating the sensitivity and positive predictive value (PPV) of the study.

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 high indices characterized the pregnancies with abnormal outcomes. The uterine artery had a better sensitivity and specificity as compared to the umbilical artery. Among the various uterine waveform parameters, the diastolic notch had the highest sensitivity and specificity. Among the

umbilical indices, the PI had the highest sensitivity and specificity.

Doppler provides a non-invasive method of assessing the fetal and maternal circulation during pregnancy. Both uterine and umbilical arteries have a low sensitivity at 20 weeks and therefore cannot be used as a screening test.

Currently, Doppler ultrasound, an evolved non-invasive technique, is widely used to assess blood flow in both fetal and maternal hemodynamic circulatory function.

Due to its feasibility and safety, this newinnovation has now become an effective instrument for fetal surveillance.

To establish a normative data of the umbilical artery Doppler waveform indices (S/ D ratio, RI and PI) in normal fetus, (Chanprapaph et al., 2000) has done a cross-sectional descriptive study.

A total of 332 normal singleton pregnant women were recruited into the study from theantenatal care clinic between September 1, 1994 and August 1, 1996. Their gestational ages werefrom 21 to 40 weeks. The S/D ratio, RI and PI of the umbilical arteries were obtained by the samesonographer. All foetuses were delivered at term with normal outcomes at birth.

A total of 411 Doppler indices measurements were performed. The values of S/ D ratio, RI,PI declined gradually with gestational age. The mean values decreased from 3.560 to 2.511, 0.756 to0.609 and 1.270 to 0.967, respectively. Doppler indices declined rapidly from 21 to 32 weeks, when compared to that in the last 8

weeks. Notably, the S/D ratio was less than 3 after 30 weeks of gestation.

The nomogram of umbilical artery Doppler waveform indices was constructed and showed the decreasing of Doppler indices with gestational age. These normative data could be served as a basis for evaluation the umbilical artery circulation in that population.

Chapter: Three
Materials and Methods

Chapter Three
Materials and Methods

This was a prospective, cross-sectional, hospital-based, case-control study.

The study was conducted in Khartoum Teaching Hospital (KTH), situated in Khartoum.

The study was conducted in a period of six months; spanning from December 2014 – June 2015.

3.1 Materials:

3.1.1 Equipment

The equipment requirements include 3D Ultra sound machine (Philip - Iu22 medical system) with 3-5 MHz curvilinear transducer.

A: Begin with a new patient

B: Enter Name (ID)

C: Menu Selection: e.g. abdomen, thyroid gland

D: Change of transducer

E: Freeze

F: Gain

G: Depth gain compensation (DGC)

H: Image depth/ Field of View

I: Trackall for positioning the dot or range markers

J: Measurements.

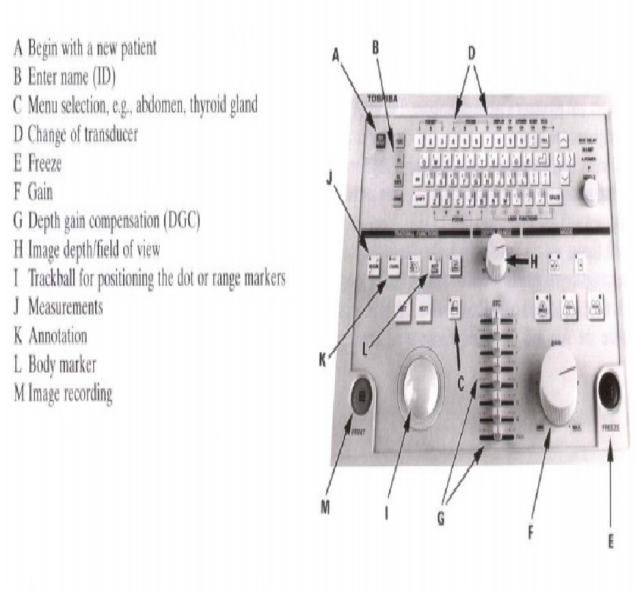

Figure (3.1) 3D Ultrasound Machine

3.2 Methods:

This is an experiment system that deals with hypertensive pregnants with pre-eclamsia, in the second and third trimester - pre-eclamsia divided into mild and sever PE.

3.2.1 Study Population:

30 preeclamptic patients (cases) and 30 women with uneventful pregnancies (controls); attending the designated study area during the study period.

3.2.2 Sampling technique:

Non probability convenient sampling was used for this study.

3.2.3 Sample size:

Sample size = 60, it was calculated using the following equation, the sample size n and margin of error E are given by:

$x=Z(c/100)2r(100-r)$

$n=N\ x/((N-1)E2 + x)$

$E=Sqrt[(N - n)x/n(N-1)]$

Where N is the population size, r is the fraction of responses of interest, and Z(c/100) is the critical value for the confidence level c.

3.2.4 Inclusion Criteria:

- Controls: Low risk, singleton pregnancies with intact membrane, living foetus and gestational age of more than 20 weeks.
- Cases: Preeclampticwomen with singleton gestation, intact membrane, living foetus and gestational age of more than 20 weeks.

3.2.5 Exclusion Criteria:

- Cases with intra-uterine growth restriction (IUGR), fetal anomalies and twin pregnancies were all excluded.
- Women with established diagnosis of chronic hypertension, gestational diabetes and those with isolated single umbilical artery (SUA).

3.2.6 Data collection tools:

Verbal consent was first obtained from all potential participants. The aims, benefits and prospective risks of the present study were explained

to all participants in details. Medical, obstetric and gynaecological history of all study subjects posing as (controls) were thoroughly reviewed (either from clinical records or directly from participants themselves) and those with conditions that may –in any way- alter the findings of the current study were excluded.

(Cases) were carefully selected and matched with their corresponding (Controls); the author did her very best to control possible confounding factors and therefore, cases and controls were of similar age group, parity and socio-demographic profile.

Doppler ultrasound examination of the umbilical artery (UA) was performed on the women in the left lateral recumbent position using a colour Doppler system. The UA was identified and flow velocity waveforms were obtained from a free-floating loop of the cord during fetal quiescence. The first parameter to be measured was umbilical cord diameter.

Doppler parameters including pulsatility index (PI) and resistance index (RI) were calculated by the dedicated software supplied within the Doppler equipment. The average value of at least two waveforms was considered as the final measurement.

Gestational age was measured by an accurate menstrual history and an ultrasonographic examination before 20th week of pregnancy.

Preeclampsia was diagnosed if a blood pressure of ≥140/90 was detected in the pregnant woman after 20th week of gestation with appropriate cuff and supine position in at least two occasions 4 hours apart and random proteinuria of ≥+1 or 24hours proteinuria more than 300m. Rise of blood pressure to ≥160/110 with a proteinuria of >+2 or 24 hours proteinuria of >2 gr, and development of headache, epigastric pain, blurred vision, pulmonary oedema, abnormal liver and renal function test was considered

as severe preeclampsia this was similar to what was found by (Jodicke et al., 2012).

3.3 Data analysis:

Data was analyzed using Statistical Package of Social Sciences (SPSS) version 20 for windows. Results were then displayed in simple frequency and cross-tabulation tables.

3.4 Ethical Consideration:

- An approval from the hospital administration to conduct the current study was first obtained.
- All participants were given informed consents and were asked to sign it, after objectives of this study was clarified.
- Each potential subject participating in the current study was thoroughly informed about aims, methods, the anticipated benefits and potential risks of the study and the discomfort it may entail.
- All subjects were informed about their right to abstain from participation in the current study and their option of withdrawing consent to participate at any time without reprisal.
- No information revealing the identity of any individual was included in the final report or in any other communication prepared in the course of the Project.
- The author’s own personal biases and opinions did not affect the way this study was conducted.

Chapter Four

Results

Chapter Four

Results

In the present study the majority of participants (30 subjects, 50%) had un-eventful pregnancies and served as (controls). Another 30 subjects served as cases; 17 of which (28.3%) had mild pre-eclampsia and 13 subjects (21.7%) had severe pre-eclampsia.

Table (4.1):Shows the different groups of the current study:

Study Group	Frequency	Percentage
Normal (Controls)	30	50%
Mild Pre-eclampsia (Cases)	17	28.3%
Severe Pre-eclampsia (Cases)	13	21.7%
Total	**60**	**100%**

Table (4.2): Shows distribution of study subjects according to their gestational age (in weeks):

Gestational Age * Patient's Group Cross-tabulation

Count

		Patient's Group		Total
		Normal (Control)	Cases (Pre-eclampsia)	
Gestational Age	20-24 wks	16	16	32
	25-29 wks	11	11	22
	> 29 wks	3	3	6
Total		30	30	60

X2 = 0.000, P-value = 1.00

Table (4.3): Shows the mean umbilical cord width for each participant's group:

Participant's Group	N	Mean Umbilical Cord Width	Std. Deviation
Normal	30	14.4720	1.87698
Mild Preeclampsia	17	13.6588	1.20030
Severe Preeclampsia	13	10.5300	.83876
Total	60	13.3875	2.16422

Table (4.4): Shows the significance of differences for the mean cord diameter between different participant's groups (i.e. cases and controls); using Tukey HSD test

(I) Pre-eclampsia		Mean Difference (I-J)	Std. Error	Sig.
Normal	Mild Preeclampsia	.81318	.46487	.196
	Severe Preeclampsia	3.94200*	.50847	.000
Mild Preeclampsia	Normal	-.81318	.46487	.196
	Severe Preeclampsia	3.12882*	.56420	.000
Severe Preeclampsia	Normal	-3.94200*	.50847	.000
	Mild Preeclampsia	-3.12882*	.56420	.000

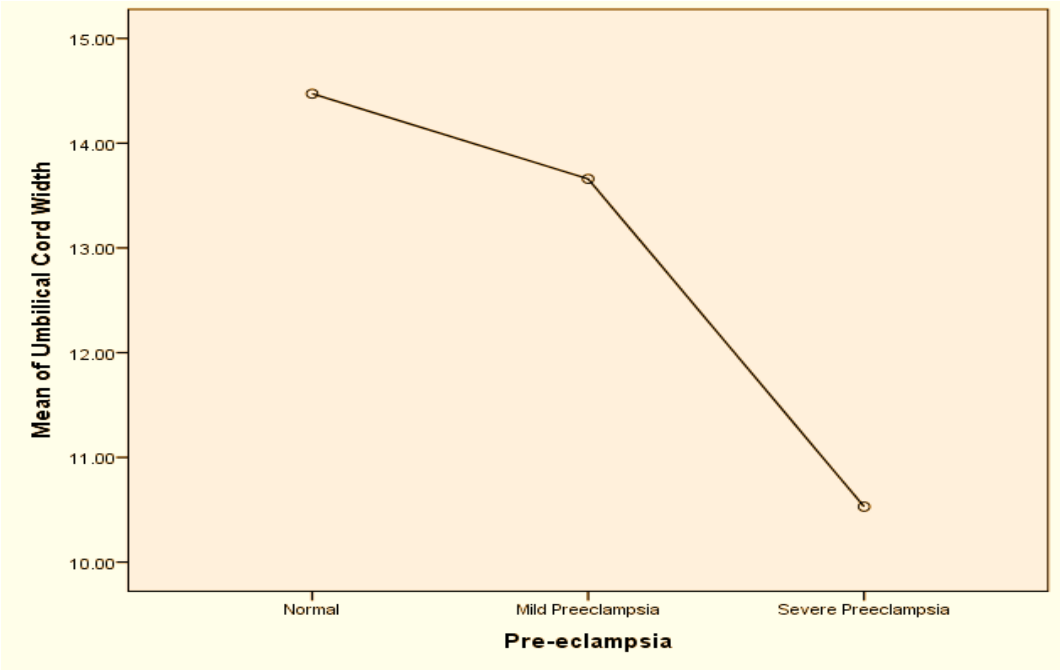

Figure (4.1): Shows the means plot (the different umbilical cord diameters against their correspondent participant's group)

Table (4.5): Shows the mean umbilical cord pulsatility index (PI) for each group:

Participant's Group	N	Mean	Std. Deviation
Normal	30	.9917	.17929
Mild Preeclampsia	17	1.6812	.33247
Severe Preeclampsia	13	2.1115	.06162
Total	60	1.4297	.51456

Table (4.6): Shows the significance of differences for the mean pulsatility index (PI) between different participant's groups (i.e. cases and controls); using Tukey HSD test:

(I) Pre-eclampsia		Mean Difference (I-J)	Std. Error	Sig.
Normal	Mild Preeclampsia	-.68951*	.06664	.000
	Severe Preeclampsia	-1.11987*	.07289	.000
Mild Preeclampsia	Normal	.68951*	.06664	.000
	Severe Preeclampsia	-.43036*	.08087	.000
Severe Preeclampsia	Normal	1.11987*	.07289	.000
	Mild Preeclampsia	.43036*	.08087	.000

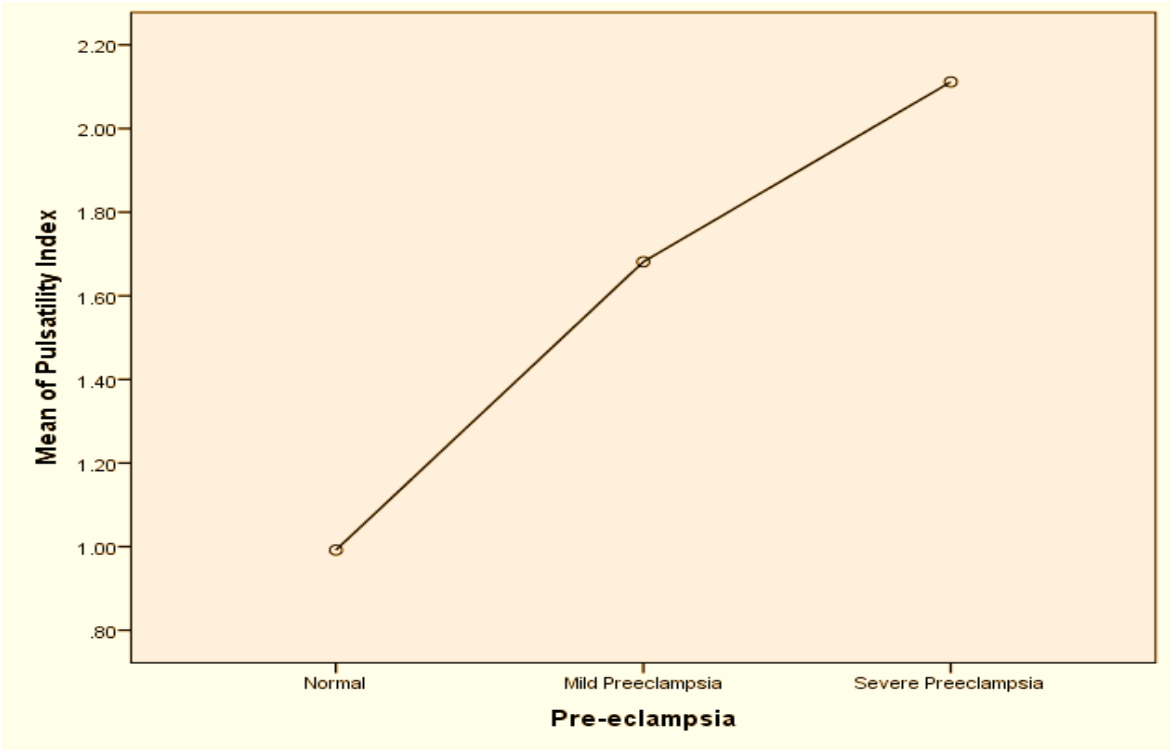

Figure (4.2): Shows the means plot (the different umbilical cord P.I against their correspondent participant’s group)

Table (4.7): Shows the mean umbilical cord resistance index (RI) for each group:

Participant's Group	N	Mean	Std. Deviation
Normal	30	.5943	.05237
Mild Preeclampsia	17	.9476	.05154
Severe Preeclampsia	13	1.1485	.06805
Total	60	.8145	.23946

Table (4.8): Shows the significance of differences for the mean resistance index (RI) between different participant's groups (i.e. cases and controls); using Tukey HSD test:

(I) Pre-eclampsia		Mean Difference (I-J)	Std. Error	Sig.
Normal	Mild Preeclampsia	-.35331*	.01695	.000
	Severe Preeclampsia	-.55413*	.01854	.000
Mild Preeclampsia	Normal	.35331*	.01695	.000
	Severe Preeclampsia	-.20081*	.02057	.000
Severe Preeclampsia	Normal	.55413*	.01854	.000
	Mild Preeclampsia	.20081*	.02057	.000

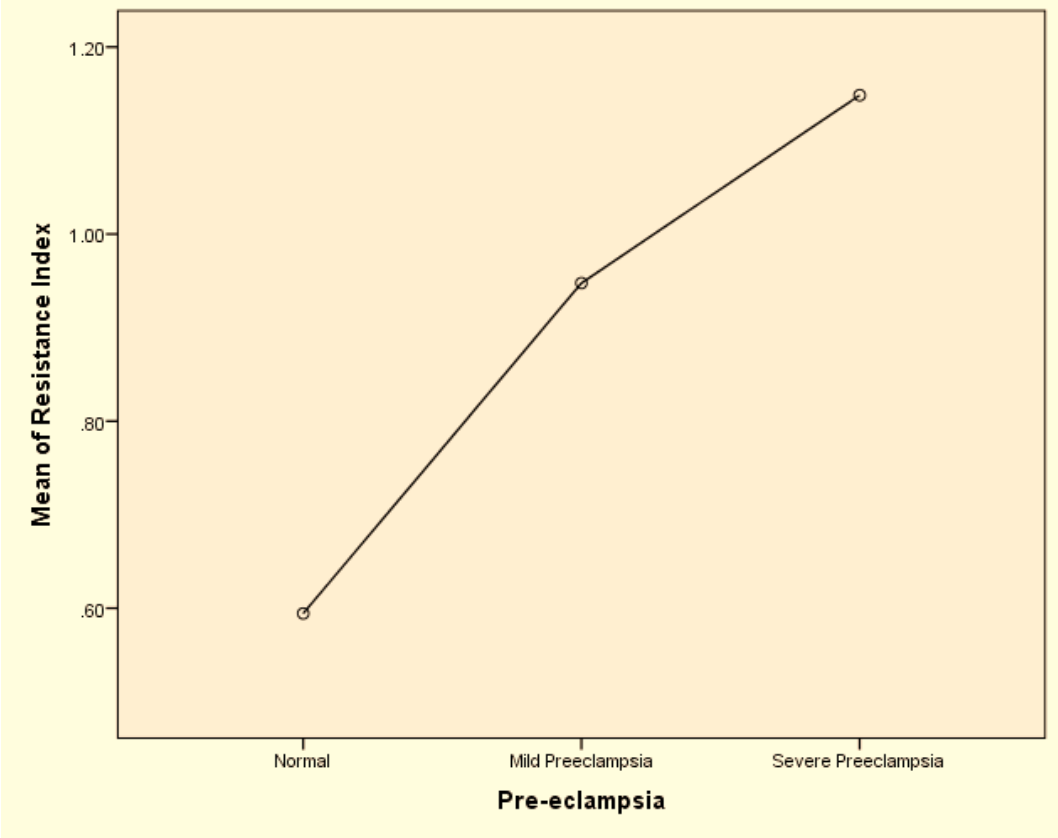

Figure (4.3): Shows the means plot (the different umbilical cord R.I against their correspondent participant's group)

Table (4.9): Shows the mean umbilical cord diameter (mm) plotted against gestational age (weeks):

Participant's Group	N	Mean	Std. Deviation
20-24 wks	32	11.8800	1.52545
25-29 wks	22	14.7795	1.20039
> 29 wks	6	16.3233	1.17326
Total	60	13.3875	2.16422

Figure (4. 4): Shows the means plot (the different umbilical cord diameter (in mm) against their correspondent gestational age (G.A))

Figure (4.5): Shows the means plot (the different umbilical cord pulsatility index (P.I) against their correspondent gestational age (G.A))

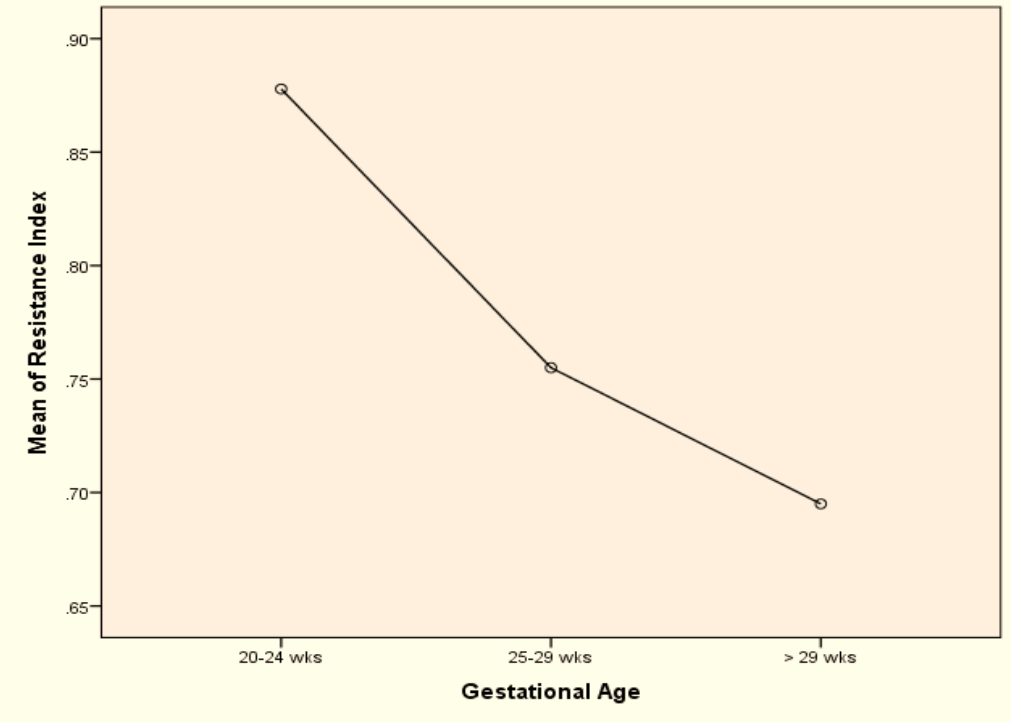

Figure (4.6):Shows the means plot (the different umbilical cord resistance index (R.I) against their correspondent gestational age (G.A))

Table (4.10): Shows the mean umbilical cord diameter (mm) of normal pregnancies (controls) plotted against different gestational age:

Gestational Age	N	Mean	Std. Deviation
20-24 wks	16	12.9944	1.14745
25-29 wks	11	15.8318	.43833

> 29 wks	3	17.3667	.20817
Total	30	14.4720	1.87698

Table (4. 11): Shows the mean umbilical cord diameter (mm) of pregnancies complicated by pre-eclampsia (cases) plotted against different gestational age:

Gestational Age	N	Mean	Std. Deviation
20-24 wks	16	10.7656	.91828
25-29 wks	11	13.7273	.63075
> 29 wks	3	15.2800	.36387
Total	30	12.3030	1.89017

Table (4. 12): Shows the mean pulsatility index of pregnancies complicated by pre-eclampsia (cases) plotted against different gestational age:

Gestational Age	N	Mean	Std. Deviation
20-24 wks	16	2.0963	.06428
25-29 wks	11	1.7545	.13988
> 29 wks	3	1.0633	.04041
Total	30	1.8677	.33107

Table (4.13): Shows the mean resistance index of pregnancies complicated by pre-eclampsia (cases) plotted against different gestational age:

Gestational Age	**N**	**Mean**	**Std. Deviation**
20-24 wks	16	1.1244	.08124
25-29 wks	11	.9473	.02760
> 29 wks	3	.8767	.02082
Total	30	1.0347	.11673

Table (4.14): Shows the mean pulsatility index of normotensive, un-eventful pregnancies (controls) plotted against different gestational age:

Gestational Age	N	Mean	Std. Deviation
20-24 wks	16	1.1513	.02802
25-29 wks	11	.8373	.02611
> 29 wks	3	.7067	.01155
Total	30	.9917	.17929

Table (4.15): Shows the mean resistance index of normotensive, un-eventful pregnancies (controls) plotted against different gestational age:

Gestational Age	N	Mean	Std. Deviation
20-24 wks	16	.6313	.03862
25-29 wks	11	.5627	.02149
> 29 wks	3	.5133	.00577
Total	30	.5943	.05237

Chapter Five

Discussion, Conclusion and Recommendations

Chapter Five

Discussion Conclusion And Recommendations

5.1 Discussion:

Duplex colour Doppler sonography is one of the popular imaging modalities in the department of radiology and imaging as well as to the physian to assay the condition of blood vessel and flow pattern in various diseases. The Doppler technique allows the non-invasive study of umbilical and placental circulation; allowing the early diagnosis of pre-eclampsia, hypoxic states and the prediction of adverse fetal outcomes.

Therefore, it was the very objective of the present study to investigate Doppler indices of both normotensive and pre-eclamptic women to define and set clear cut-off points to what's a normal or abnormal Doppler index in a group of Sudanese population.

In the current study there were no differences between the 30 cases and controls; in terms of maternal characteristics such as; age, parity and gestational age. The author did her best to nullify any potential maternal factors that may –somehow- alter the results of the current study.

In their attempt to measure umbilical cord diameter and establish normal reference values for normal pregnancies, (C. Barbieri et al., 2012) have reported a significant, consistent and practically linear increase in the measurements of the diameters of the umbilical artery and vein, the umbilical cord and the cross-sectional area of the cord until around 32 weeks of gestational age, after

which these measurements remain practically constant until the end of pregnancy. Therefore, the author of the current study adopted a strict policy in matching her cases and controls in regards to their gestational age, (table 4.2).

(C. Barbieri et al., 2012) have reported a mean umbilical cord diameter of (12.8 mm) for normal pregnancies in their 20-25th week of gestation, (16.12 mm) for those in their 26-30th week of gestation and (16.8 mm) for normal pregnancies on their 30th week of gestation. Similarly, in the present study the author reported a men umbilical cord diameter of (12.99 mm) for normotensive, un-eventful pregnancies (controls) in their 20-24th week of gestation, (15.83 mm) for those in their 25-29th week of gestation and (17.36 mm) for those in their >29th week of gestation. The figures might not be exactly the same but they are definitely attuned and comparable. As for pre-eclamptic women (cases) the mean umbilical cord diameter through second and third trimesters of pregnancy was statistically and significantly lower than that of (controls). Which were noted in (table 4.10). These findings support the association between lean umbilical cord diameter, reduced amount of Wharton's jelly (WJ) and hypertensive disorders such as; pre-eclampsia.

For many years, the observation of thin cords or ones with a small amount of Wharton's jelly was related to adverse perinatal effects or even to the presence of Oligohydramnios, pre-eclampsia and fetuses with low birth

weight has been described in the literature which was discussed by (Arauz et al., 2008). This observation was confirmed in the present study (table 4.3).

Doppler ultrasound (cord diameter, P.I, R.I and S/D Ratio) in 2nd and 3rd trimester play vital role in determining foetal outcome. Doppler wave form shows increased resistant to flow in 2nd and 3rd trimesters which are associated with poor pregnancy outcome. Among all those parameters PI is the most important predictor of normal pregnancy outcome.

In (Ferdousi et al., 2013) study of 60 pregnant Bangladeshi women, the mean umbilical artery PI for these women –in their 2nd and 3rdtrimester was (1.24 +/- 0.27 SD). In the present study the overall mean PI for controls was (0.99 +/- 0.17 SD), (table 4.5). It is indeed lower than the figure reported in (Ferdousi et al., 2013) study but still falls within expected normal range of PI. The author of the current study could find no reason to this unforeseen difference in PI mean values; except maybe the difference in the mean gestational age of participants, unanticipated confounding factors and the dissimilar ethnicity of participants in each study.

In (Aali et al, 2010) study, it has been noted that both Doppler parameters of umbilical artery were significantly higher in preeclamptic patients (PI of 1.32±0.23 and RI of 0.77±0.09) when compared to the controls (0.97±0.18 and 0.64±0.08 for PI and RI, respectively) ($p<0.001$). Similarly, when we compared mild and severe preeclamptic patients using their Doppler indices,

significantly higher values were obtained in severe cases than mild ones.

Similarly, for pre-eclamptic participants of the present study (cases); the mean PI was (1.867 +/- 0.33 SD); way higher than the (0.99 +/- 0.17 SD) reported in their matched (controls). Moreover, the mean P.I of participants with mild pre-eclampsia was significantly lower than that of patients with the severe form of the disease (1.68 Vs. 2.11) these were noticed in (table 4.5).

The same observation was noted in resistance index (RI); it was (0.59, 0.94 and 1.14) for normal, mild and severe pre-eclampsia participants, respectively.

In agreement with (Aali et al., 2010) study and other scholars, the current thesis revealed that umbilical artery Doppler indices (PI and RI) are higher in pre-eclamptic women and continues to decreased with advancement of gestational age from 2nd to 3rd trimester.

Our results showed higher pulsatility and resistance indices in patients with preeclampsia than normal pregnancies. As showed in (table 4.6 and 4.7) This confirms a state of high resistance in placental circulation in preeclampsia. Our findings are in line with the study performed by (Chen et a., 2009) which showed not only a higher pulsatility index in preeclamptic patients but also a significantly greater PI in severe cases of preeclampsia.

(Aali et al., 2010) went on to set a cut-off point for the diagnosis of pre-eclampsia from umbilical artery Doppler indices. They have found that for PI, the cut-off of ≥0.58

yielded a sensitivity of 100% and specificity of 1.3%. At the cut-off of ≥0.98 sensitivity was the same but specificity increased to 53.3%. In the present study, the highest PI value to be recorded in a normotensive woman was (1.18) and she had no clinical symptoms or laboratory findings of the disease. Moreover, she was at her 20th week of gestation where higher readings of PI are accepted. Just like the others, her PI reading continued to gradually decline as her pregnancy continued to progress.

With a cut-off of 0.64 for RI, a sensitivity of 100% and specificity of 44.0% was calculated in (Aali et al., 2010) study. Again the dissimilar ethnic group of participants, gestational age and probably several confounding factors have contributed to yet another disparity between findings of this study and that of (Aali et al., 2010). As the author of the present study had normotensive, perfectly healthy (controls) with RI of as high as (0.65). Therefore, the author of the current study can't accept nor apply (Aali et al., 2010) cut-off points to her own population.

In clinical practice; PI lower than 0.98 and/ or RI lower than 0.64 had a negative predictive value of 100% for diagnosing preeclampsia. This implies that if a pregnant woman has negative results from the PI and/or RI tests (i.e., values lower than the abovementioned cut-offs); the clinician can be 100% confident that she does not have preeclampsia (Fletcher et al., 2005). This remark was– somewhat- confirmed in the current study.

On the other hand, (Ozeren et al., 1999) could not find any difference in umbilical PI between normal pregnancies and preeclamptic patients without IUGR whereas, the current study in pre-eclampsia group showed a significantly higher mean umbilical artery PI which was noticed in (tables 4.6 and 4.12).

Early identification of umbilical cord parameters that may be capable of detecting abnormalities in low- or high-risk pregnancies may be useful in the prevention of associated complications or in the more rigorous follow-up of these cases so that timely intervention may be made.

5.2 Conclusion:

There is sample evidence that Doppler indices P.I, R.I, cord diameter, and S/D Ratio from the fetal circulation can reliably diagnose pre-eclampsia in obstetric patients. The normal umbilical artery Doppler indices reference ranges– reported in literature- were confirmed in the present study with slight differences that were attributed to differences in gestational age and ethnic groups.

Umbilical artery Doppler indices have an important role to play in the diagnosis and management of the pre-eclampsia.

5.3 Recommendations:

- Antenatal serial umbilical cord diameter and umbilical artery Doppler indices measurements are mandatory for both normotensive and pre-eclamptic women and should be implemented in regular antenatal care.
- We recommend the following cut-off points for the diagnosis of pre-eclampsia from umbilical artery Doppler indices; PI of (>1.18) and RI of (>0.65).
- Especial attention should be paid to mothers with hypertensive disorders. Serial sonographic measurements of cord diameter are a must; to monitor disease progression and fetal wellbeing.
- Women with severe, early-onset preeclampsia should be labelled as high risk-pregnancies, have frequent umbilical (and probably uterine and middle cerebral

arteries) Doppler U/S and counselled for various treatment options and delivery plans.

- Larger, multi-centric, nation-wide prospective study of umbilical cord diameter and umbilical artery Doppler indices are recommended to set more accurate cut-off points for the diagnosis of pre-eclampsia in Sudanese population.

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Appendices

Appendix (A)

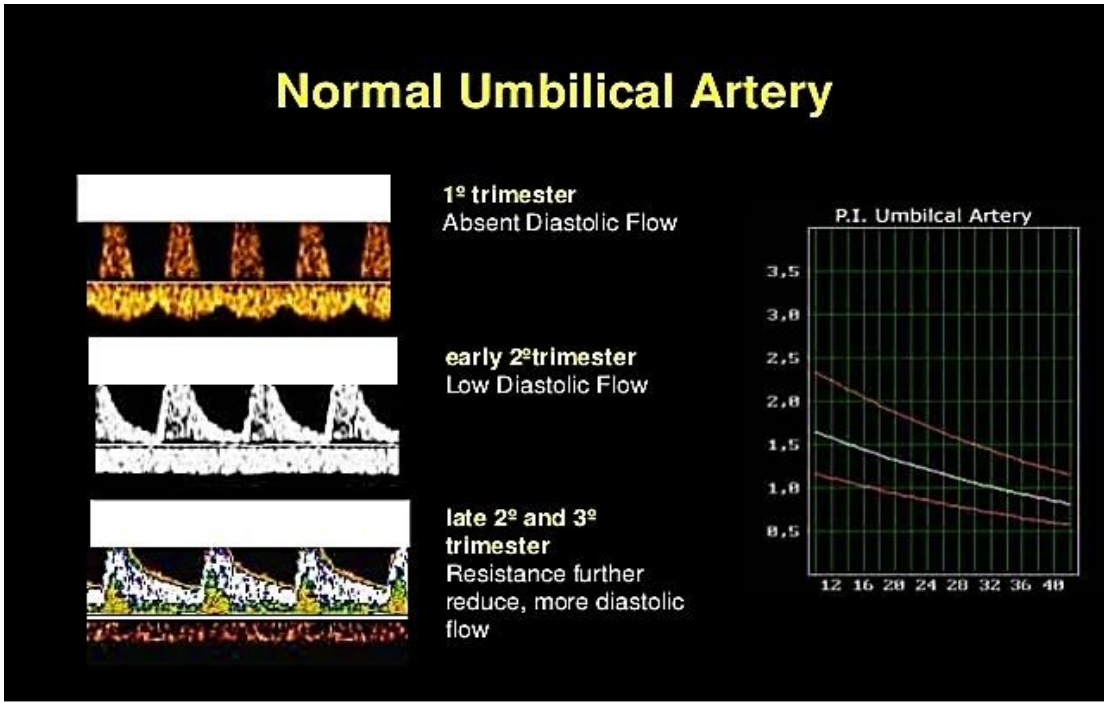
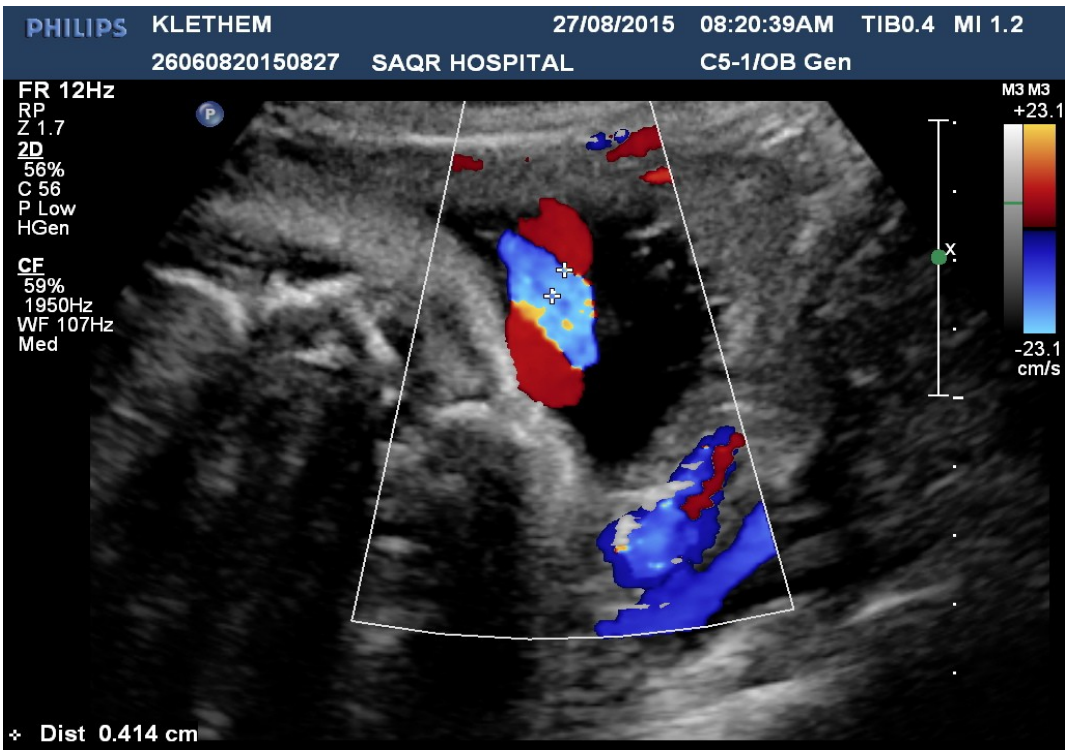


Image (1) Ultra sound appearance of a normal umbilical artery (Sabnis et al., 2012)

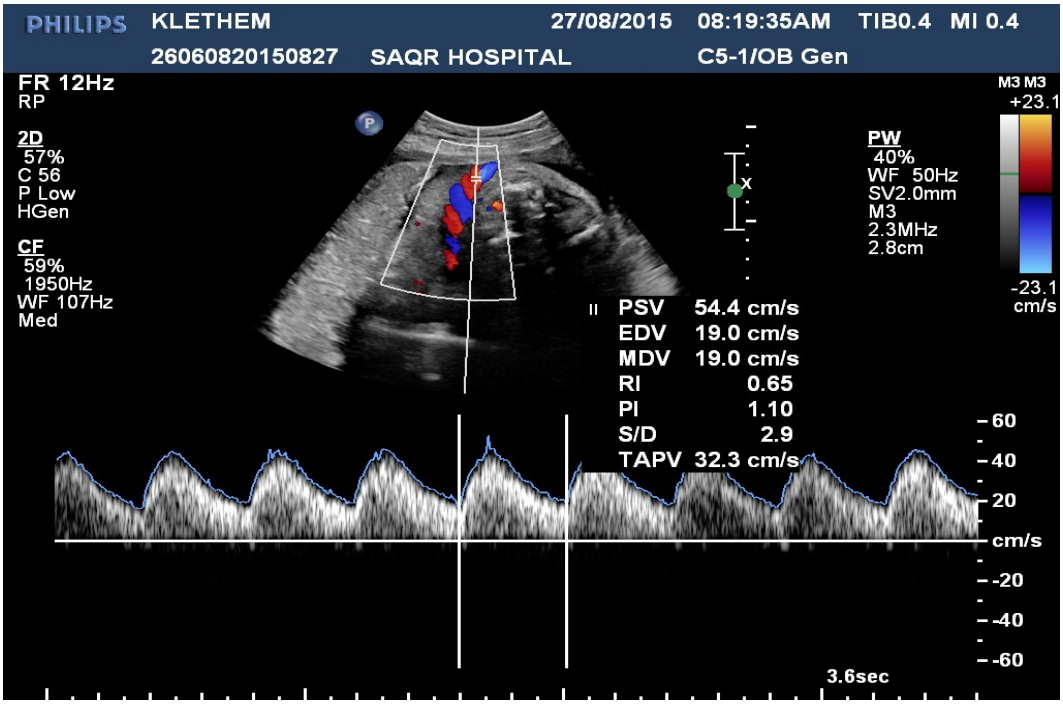
Image (2) Measurement of umbilical artery at 30 weeks pregnant (Ghezzi, et al., 2001)

Appendix (B)

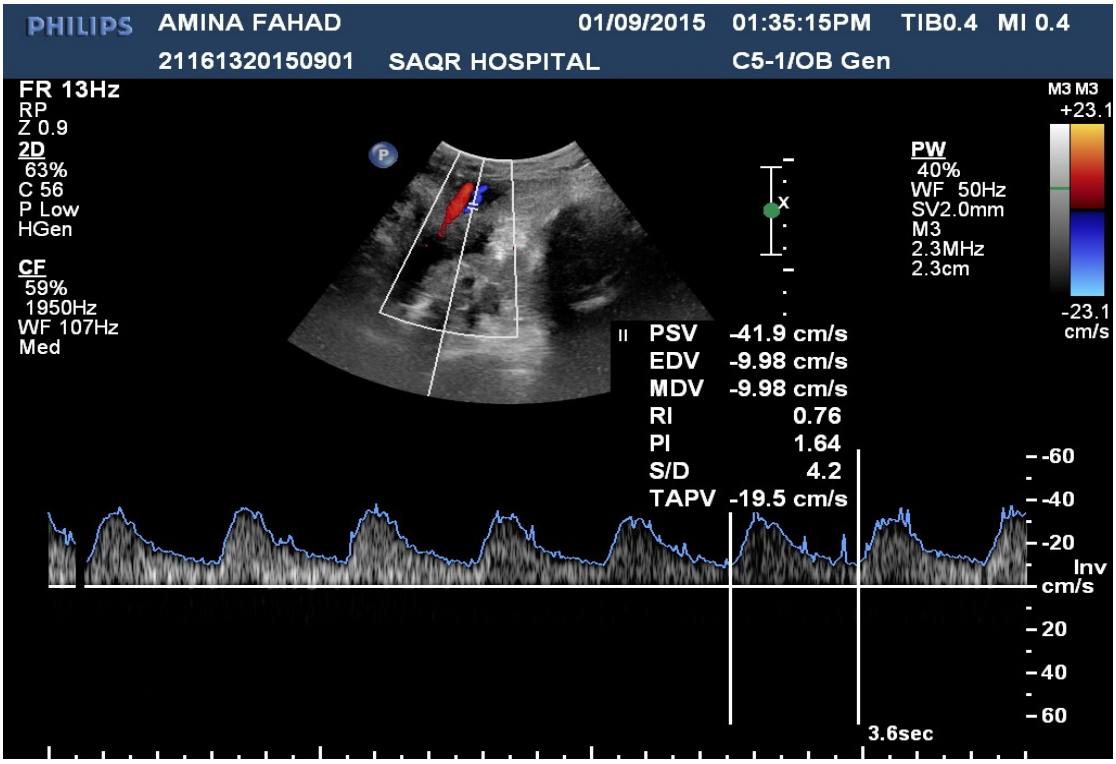
Cases



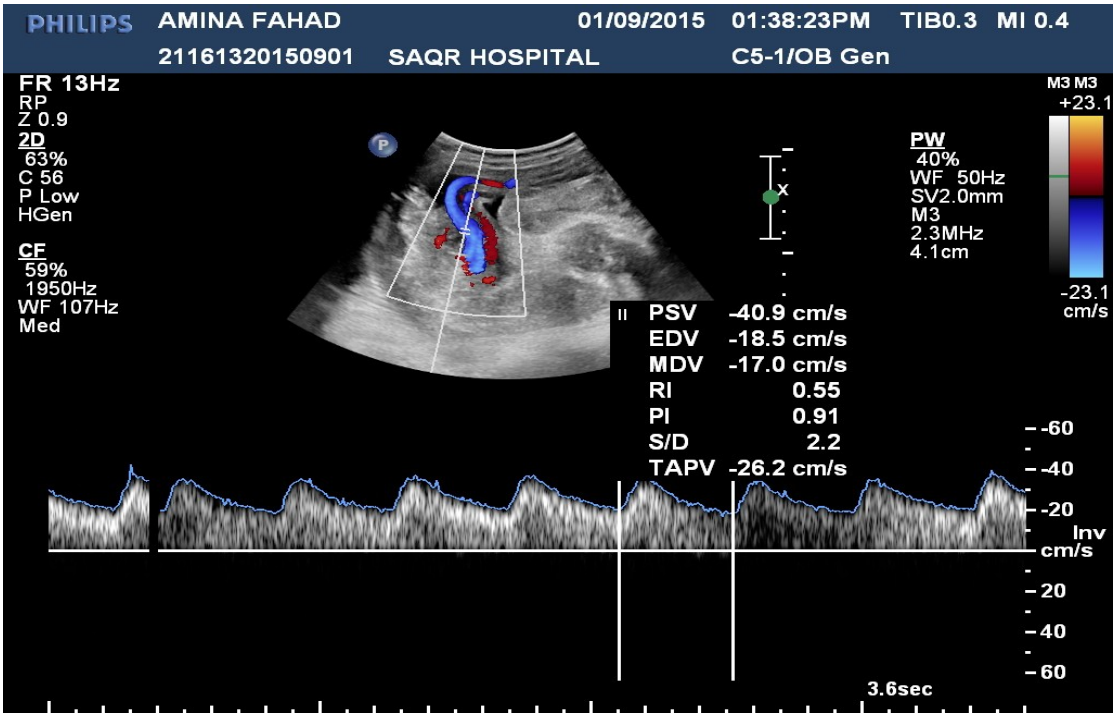
Case (1) Measurement of Umbilical artery at 20 weeks pregnant (0.414cm)



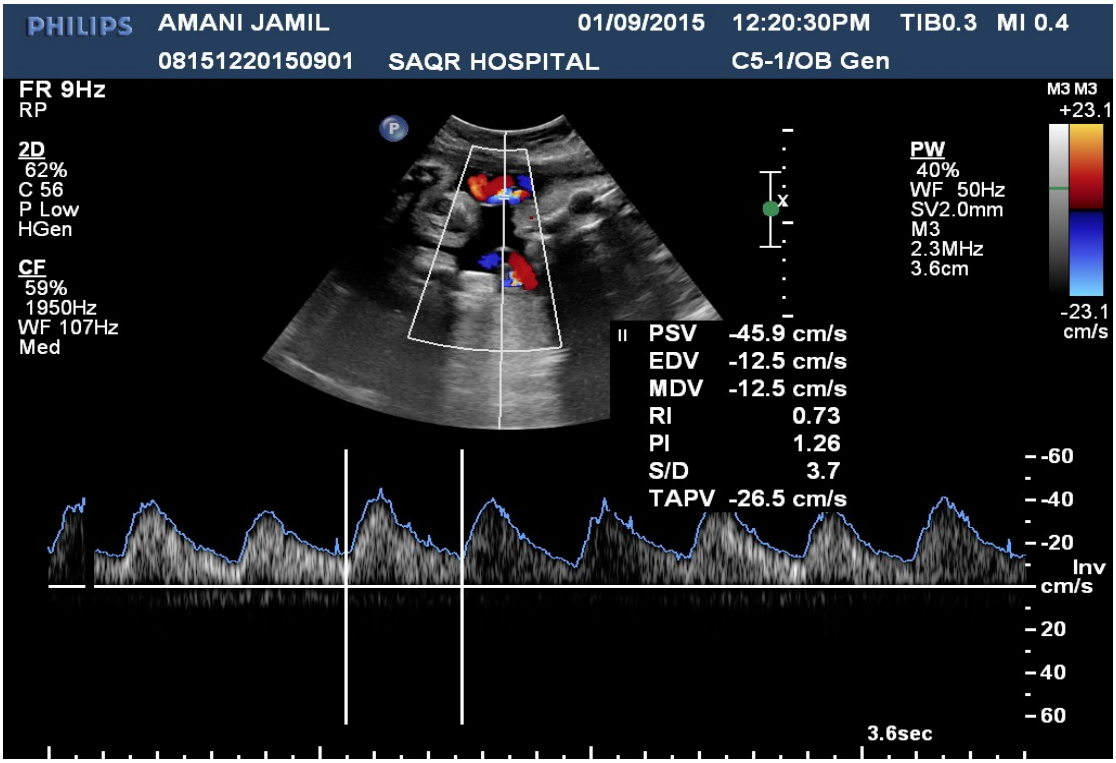
Case (2) Colour Doppler Ultrasound of Umbilical artery at 21 weeks pregnant (RI 0.65 & PI 1.10)



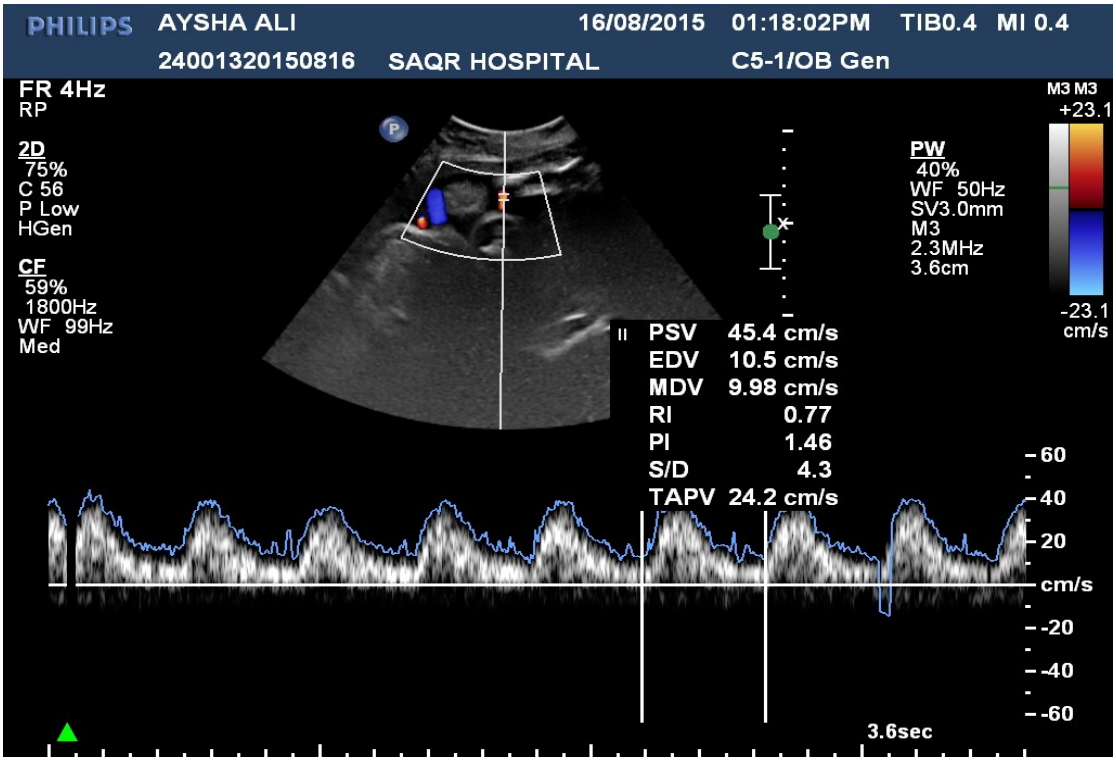
Case (3) Colour Doppler Ultrasound of Umbilical artery at 26 weeks pregnant (RI 0.76 & PI 1.64)



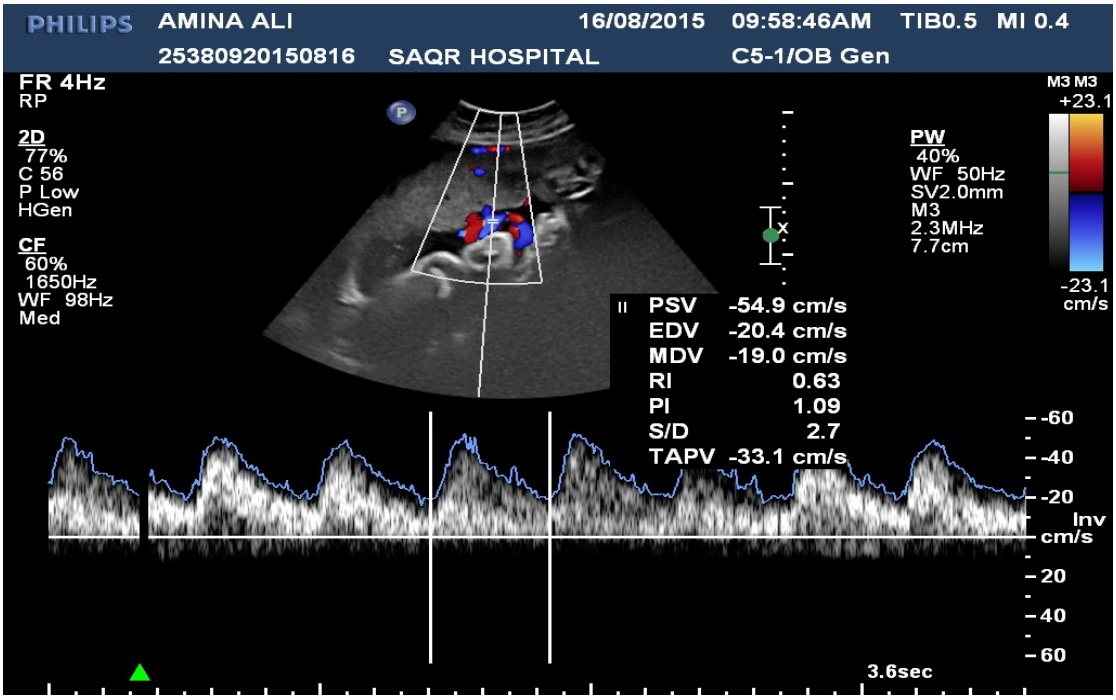
Case (4) Colour Doppler Ultrasound of Umbilical artery at 28 weeks pregnant (RI 0.55 & PI 0.91)



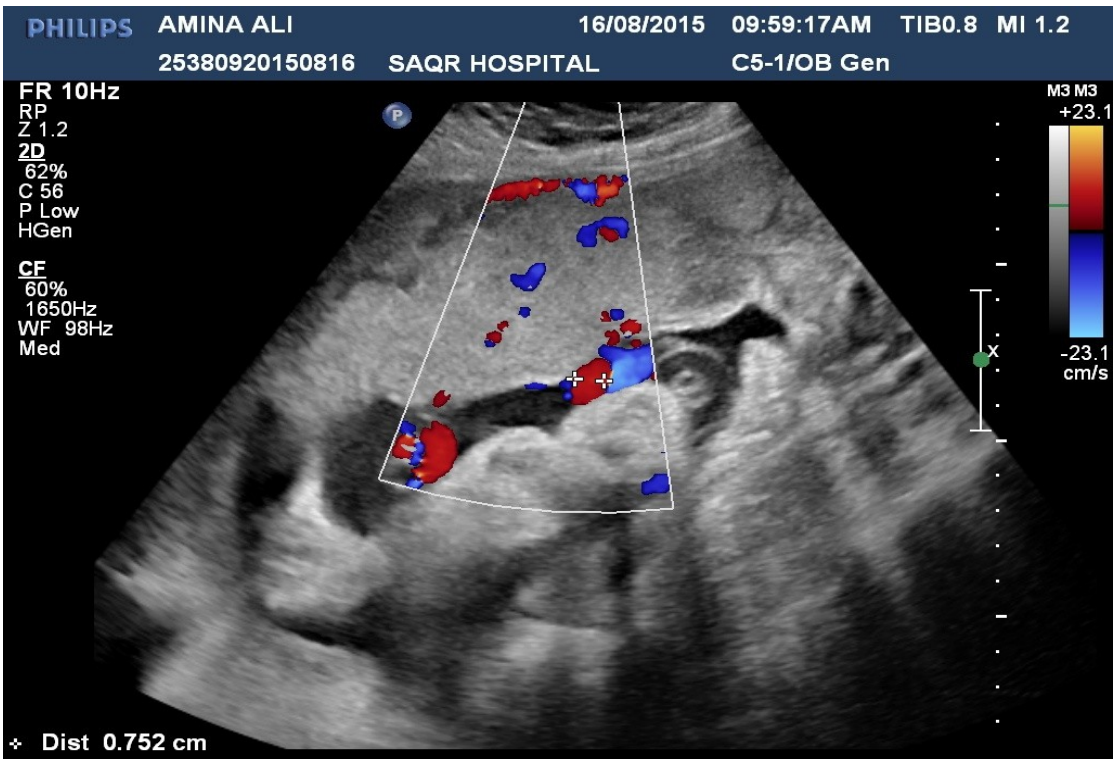
Case (5) Colour Doppler Ultrasound of Umbilical artery at 29 weeks pregnant (RI 0.73 & PI 1.26)



Case (6) Colour Doppler Ultrasound of Umbilical artery at 32 weeks pregnant (RI 0.77 & PI 1.46)



Case (7) Colour Doppler Ultrasound of Umbilical artery at 30 weeks pregnant (RI 0.63 & PI 1.09)



Case (8) Measurement of Umbilical artery at 21 weeks pregnant (0.752cm)