PROSPECTIVE ANALYSIS OF THE ROLE OF UTERINE ARTERY DOPPLER STUDY IN PREDICTING ADVERSE PREGNANCY OUTCOME

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CERTIFICATE

This is to certify that the dissertation entitled "**PROSPECTIVE ANALYSIS OF THE ROLE OF UTERINE ARTERY DOPPLER STUDY IN PREDICTING ADVERSE PREGNANCY OUTCOME"** is the bonafide original work of **Dr. C.C. NANDHINI** in partial fulfilment of the requirements for **M.D. Branch – II (Obstetrics and Gynaecology)** Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in March 2008. The period of study was from June 2006 to July 2007.

Dr. MYTHLI BHASKARAN, M.D., D.G.O.
DEAN
Govt. Stanley Medical College & Hospital,
Chennai-600 001.

Dr. AMRITA PRESCILLA NALINI, M.D. , D.G.O.
Superintendent i/c
Govt. R.S.R.M. Lying-in Hospital
Govt. Stanley Medical College & Hospital,
Chennai-600 001.

DECLARATION

I, **Dr. C.C. NANDHINI,** solemnly declare that dissertation titled, "**PROSPECTIVE ANALYSIS OF THE ROLE OF UTERINE ARTERY DOPPLER STUDY IN PREDICTING ADVERSE PREGNANCY OUTCOME"** is a bonafide work done by me at Govt. Stanley Medical College & Hospital during 2005-2008 under the guidance and supervision of my Unit Chief **Prof. Dr. ANURADHA, M.D. , D.G.O.**

The dissertation is submitted to Tamilnadu, Dr. M.G.R. Medical University, towards partial fulfilment of requirement for the award of **M.D. Degree (Branch – II) in Obstetrics and Gynecology.**

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CONTENTS

INTRODUCTION

Screening, a deliberate examination of substantial segments of the population in search of the disease at its earlier stage is a logical extension of the role of preventive medicine and one which is becoming increasing in vogue . It should increase the predictive value and the prophylactic measure must be effective.

Preeclampsia which is one of the five hypertensive disorders of pregnancy is common with an incidence of 5-8% and form one of the deadly triad, along with hemorrhage and infection ,that contribute greatly to maternal morbidity and mortality. Fetal growth restriction is estimated to occur in 3-10% of the infants. The perinatal morbidity and mortality are significantly increased among these growth restricted infants.

Diseases that may be causes of perinatal mortality and morbidity such as preeclampsia, intrauterine growth retardation (IUGR) are often seen in the third month or even just before the time of birth but the pathophysiologic mechanisms are believed to originate at the earlier times in pregnancy. During the period of a normal pregnancy beginning from the first three months till the 24th week, becoming more evident as time goes by, there is an increase in the diastolic blood flow of the uterine vessels. The above said diseases are associated with increased impedance to blood flow. This can be detected by uterine artery Doppler velocimetry as early as the beginning of second trimester.

Thus Uterine artery Doppler studies are common for both preeclampsia and adverse fetal outcome as a screening test because the impairment of placental perfusion is common in

both. This study is designed to test the efficacy of uterine artery Doppler study done between 22-24 weeks as a single stage screening test for early prediction of preeclampsia and adverse fetal outcome (SGA,IUGR, Prematurity)

AIM OF THE STUDY

To evaluate uterine artery Doppler as an early predictor of preeclampsia and adverse fetal outcome (SGA, IUGR, Prematurity) and elucidate its role in stratifying antenatal care according to the Doppler study.

REVIEW OF LITERATURE

LITERATURE SURVEY

Impaired trophoblastic invasion of the maternal spiral arteries is associated with increased risk for subsequent development of intrauterine growth restriction, preeclampsia and prematurity. A series of screening studies involving assessment of impedance to flow in the uterine arteries have examined the potential value of Doppler in identifying pregnancies at risk of the complications of impaired placentation

1) A pioneering study by Campbell S, Pearce JM, Hacket G *et al* assessing Uterine artery Flow velocity wave forms between 16-18 weeks showed a cutoff level of 0.58 for RI predicted IUGR with a sensitivity of 68 %,the predictive value of positive test was 42% and that of negative test 87%. But prevalence of pregnancy adverse outcome in the study was high almost 25%. This may imply that these impressive figures may not imply to a low risk population.

2) In an attempt to quantify the predictive value of the uterine artery Doppler velocimetry, Bewley, Cooper and Campbell[23] studied 977 unselected women at 16-24 weeks of gestation .The overall risk of pregnancy complications was 67% when an averaged RI value was greater than 95th percentile .In the, prediction of preeclampsia ,the sensitivity was 25%, specificity 95%,positive predictive value was 25% and negative predictive value was96%. In prediction of SGA less than 10th percentile the positivity was 15%, the positive predictive value was 35%.

3) North et al[22] measured RI in a low risk population consisting of 458 primigravidas during 19-24 weeks to predict subsequent preeclampsia and SGA. The authors were able to predict 51% of women who developed preeclampsia later in pregnancy. The positive predictive value was 29%.

4) Harrington K, Carpenter R G, and Goldfrad C[16] et al were able to show that even at 12-16 weeks there were significant differences in the circulatory conditions between women with normal pregnancy outcomes and those who developed subsequent preeclampsia. The preeclamptic women had lower uterine artery volume flow and mean velocity.

5) Irion *et al*[25] in their study for prediction of preeclampsia, low birth weight for gestation and prematurity by uterine artery blood flow velocimetry by uterine artery blood flow velocimetry in low risk nulliparous women concluded that uterine artery Doppler does not qualify as a reliable screening test in low risk pregnancies but may be useful in selected high risk population.

6) Coleman *et al*[29] studied the midtrimester uterine artery screening as a predictor of adverse pregnancy outcome in high risk women , concluded that in high risk women ,uterine artery Doppler waveforms analysis, performed best in prediction of severe adverse outcome and was better than clinical risk assessment in the prediction of preeclampsia and SGA babies.

7) Fy Chan et al[29] analysed which criterion performed best in the pregnancy screening by uterine artery Doppler – concluded that the study is better performed at 20 weeks in combination with RI measurement and the assessment of presence of diastolic notch.

Numerous studies with varying results have been published. The controversy is partly explained by the small number of patients enrolled, varying sampling sites, and techniques as well as different criteria used to define the adverse outcome. In addition some of the studies were performed in high risk and some in low risk population.

OUTCOMES OF THE STUDY

Primary outcome measures in our study were preeclampsia, small for gestational age fetus, IUGR, preterm birth.

PREECLAPMSIA:

Preeclampsia is one of the five types of hypertensive disorders of pregnancy.

THE FIVE HYPERTENSIVE DISEASES OF PREGNANCY [1] ARE

1. **GESTATIONAL HYPERTENSION**

   - Blood pressure ≥ 140/90 mm of Hg for the first time in pregnancy
   - No proteinuria.
   - Blood pressure returns to normal <12 weeks postpartum.
   - Final diagnosis made only postpartum.(not used as end point in our study)

2. **PREECLAMPSIA**

   - Blood pressure ≥ 140/90 mm of Hg after 20 weeks of gestation.
   - Proteinuria ≥ 300 mm of Hg /24 hours or > 1 + dipstick.

3. **ECLAMPSIA**

   Seizures that cannot be attributed to other causes in a women with preeclampsia.

4. **SUPERIMPOSED PREECLAMSIA**

- New onset proteinuria ≥ 300mg / 24 hours in a known hypertensive women. but no proteinuria before 20 weeks of gestation .
- A sudden increase in proteinuria or blood pressure in women with hypertension and proteinuria before 20 weeks of gestation.

5. **CHRONIC HYPERTENSION**

- Blood pressure ≥140/ 90 mm of Hg before pregnancy or diagnosed before 20 weeks not attributable to gestational trophoblastic disease.

DIAGNOSIS OF PREECLAMPSIA[1]

Resting blood pressure of 140/90mmHg or greater on two occasions at least 4-6 hours apart or a single diastolic reading of 110mm of Hg .

Proteinuria – urinary excretion of ≥ 300mg of protein in a 24 hours period or persistant 30 mg/dl (1+ dipstick) in random urine samples.

PREDICTION OF PREECLAMPSIA[1]

Measurement in early pregnancy of a variety of biological, biochemical and biophysical markers implicated in the pathophysiology of preeclampsia has been proposed to predict its development. Investigators have attempted to identify early markers of faulty placentation, reduced placental perfusion, endothelial cell activation and dysfunction and activation of coagulation. They are

1. Rollover test- a hypertensive response induced by having a women at 28-32 weeks assume supine position after lying laterally predicted gestational hypertension rather than preeclampsia.
2. Elevated serum uric acid.
3. Elevated serum cellular fibronectin levels.
4. Activation of coagulation.
5. Oxidative stress-increased level of lipid peroxides, and decreased activity of antioxidants.
6. Placental peptides like Activin 4 / Inhibin 4 .
7. Fetal DNA- identification of cellfree fetal DNA in maternal serum.
8. Uterine artery Doppler velocimetry

In preeclampsia ,deficient implantation results in a reduction of maternal placental blood flow[29,36]. It is believed that uteroplacental ischemia is responsible for preeclampsia .The maternal systemic changes seen in preeclampsia may be in response to factors released secondary to placental ischemia.[40,42,43]

Impaired placental perfusion is thought to stimulate the release of pre-eclamptic factors that enter the maternal circulation and cause vascular endothelial dysfunction. Free oxygen radicals are possible promoters of maternal vascular dysfunction. It was, therefore, hypothesized that early supplementation with antioxidants may be effective in decreasing oxidative stress and improving vascular endothelial function, thereby preventing, or ameliorating, the course of preeclampsia

The fetus will grow normally , until it outgrows this maximum placental function at

which time IUGR occurs. These placental blood flow abnormalities give rise to interference with fetal oxygenation and growth.[32] This reduced blood flow can be demonstrated by uterine artery Doppler velocity waveforms abnormalities in patients who are destined to develop preeclampsia and SGA as early as 24 weeks.[23,24,37]

SMALL FOR GESTATIONAL AGE (SGA) / INTRAUTERINE GROWTH RESTRICTION (IUGR)

- Intrauterine growth restriction is best defined as a failure of a fetus to reach its genetic growth potential.
- SGA infants are those whose birth weights are below the tenth percentile for their gestational age[1].
- Low birth weight on the other hand is defined by World health organisation simply as birth weight less than 2.5 kg[3]. Thus these three terms are not synonymous but there is considerable overlap. Some fetus may meet the criteria for just one of their definition whereas others may meet all three. Fetal size is largely determined in the first trimester. Sub optimal first trimester growth restriction was associated with IUGR as well as preterm delivery between 24 and 32 weeks.

SCREENING FOR GROWTH RESTRICTION[1]

1. Clinical- Uterine Fundal Height Monitoring

It is simple, safe, inexpensive and reasonably accurate screening method to detect SGA fetus (Gardon and Frances 1999) .The maternal uterine fundus is objectively measured and

charted during each antenatal visit. Between 18 -30 weeks the normal symphysiofundal height in centimeters approximates the number of weeks of gestation. As a screening tool , its principle drawback is imprecision.

2. Biochemical

Four hormone / protein markers measured in maternal sera early in the second trimester are associated with subsequent IUGR. These include estriol, human placental lactogen ,HCG, and alfa fetaprotein.

3. Ultrasonic Measurements

Routine screening incorporates an initial ultrasound examination at 16-20 weeks to establish gestational age and identify anamolies .This is repeated at 32-34 weeks to evaluate fetal growth. Unfortunately the use of ultrasound for detection of fetal growth restriction does not preclude missed diagnosis.

4. **Uterine Artery Doppler Studies**

GENERAL CONSIDERATIONS - DOPPLER VELOCIMETRY

DOPPLER ULTRASOUND

Doppler velocimetry is a noninvasive technique using high frequency sound waves for evaluation of blood flow. A fairly recent development in antenatal assessment is the application of ultrasound. Doppler ultrasound would indicate the state of uteroplacental vascular bed from which implication about the fetal condition and the probability of developing PIH can be made[19]. Cumulative clinical experience indicate a significant association between abnormal Doppler finding and occurrence of pregnancy complications/adverse outcome in the fetus[37].

This study is being done to prove this point and explore the value of uterine artery Doppler in its efficacy to predict PIH and adverse fetal outcome.

HISTORY OF DOPPLER[4]

Johan Christian Doppler was an Austrian physicist who taught in Prague during the mid -1800. He suggested that when a sound source (for example – red blood cell in fetal umbilical circulation) is moving relative to an observer (for example-an ultrasound transducer), the perceived pitch is different from the true pitch. This is described as Doppler effect and is proportional to the velocity of moving structure.

The Doppler effect has been used widely in astronomy, RADAR and navigation. In 1957, Satomura used it to investigate blood circulation. In 1977 ,Fitz Gerald and Drumm described the first application of Doppler ultrasound in obstetrics. Recent years have witnessed a surge of interest in the application of Doppler ultrasound velocimetry. Doppler devices have been employed for detecting fetal heart activity and continuous external monitoring of FHR activity for over three decades. However these applications only utilize audio output of the Doppler signals generated by cardiac activity or by blood flow whereas the advanced technology of the Doppler velocimetry provides an immense amount of hemodynamic information from the circulation. The capability of the Doppler ultrasound has been clinically utilized in non-invasive cardiac diagnosis and in investigating peripheral vascular disease.

In recent years, the capabilities of ultrasound flow imaging have increased enormously. Color flow imaging is now commonplace and facilities such as ‘power’ or ‘energy’ Doppler provide new ways of imaging flow. With such versatility, it is tempting to employ the technique for ever more demanding applications and to try to measure increasingly subtle changes in the maternal and fetal circulations. To avoid misinterpretation of results, however, it is essential for

the user of Doppler ultrasound to be aware of the factors that affect the Doppler signal, be it a color flow image or a Doppler sonogram.

Competent use of Doppler ultrasound techniques requires an understanding of three key components:

(1) The capabilities and limitations of Doppler ultrasound;

(2) The different parameters which contribute to the flow display;

(3) Blood flow in arteries and veins.

PRINCIPLES OF DOPPLER[20]

Ultrasound images of flow, whether color flow or spectral Doppler, are essentially obtained from measurements of movement. In ultrasound scanners, a series of pulses is transmitted to detect movement of blood. Echoes from stationary tissue are the same from pulse to pulse. Echoes from moving scatterers exhibit slight differences in the time for the signal to be returned to the receiver . These differences can be measured as a direct time difference or, more usually, in terms of a phase shift from which the 'Doppler frequency' is obtained . They are then processed to produce either a color flow display or a Doppler sonogram.

There has to be motion in the direction of the beam; if the flow is perpendicular to the beam, there is no relative motion from pulse to pulse. The size of the Doppler signal is dependent on:

- Blood velocity: as velocity increases, so does the Doppler frequency; Ultrasound frequency: higher ultrasound frequencies give increased Doppler frequency. As in B-mode, lower ultrasound frequencies have better penetration. The choice of frequency is a compromise between better sensitivity to flow or better penetration;

- The angle of insonation: the Doppler frequency increases as the Doppler ultrasound beam becomes more aligned to the flow direction (the angle *q* between the beam and the direction of flow becomes smaller). This is of the utmost importance in the use of Doppler ultrasound.

Doppler shift is a phenomenon that occurs when a source of light or sound waves is moving relative to an observer, the observer detects a shift in the wave frequency .Similarly when sound waves strike a moving object , the frequency of the sound wave reflected back is shifted proportionate to the velocity and direction of the moving object. Because of the magnitude and direction of the frequency shift depends on the relative motion of the moving target, the velocity and direction of the target can be determined.

This relation is defined by the formula

$f_D = 2f_o \, v \cos \theta / c$

where,

f_D is the Doppler shift ,

fo is the frequency of the transmitted ultrasound ,

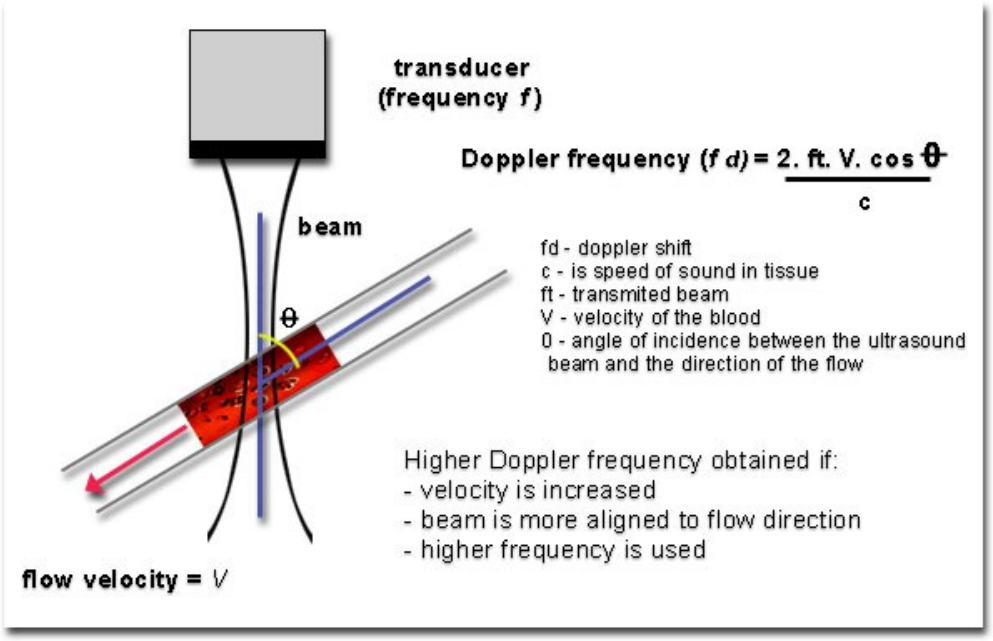
v is the velocity of the relative movement,

θ is the insonation angle and

c is the velocity of the sound within the tissue.

The following figure shows the angle of insonation.

ANGLE OF INSONATION



Doppler ultrasound measures the movement of the scatterers through the beam as a phase change in the received signal. The resulting Doppler frequency can be used to measure velocity if the beam/flow angle is known.

DOPPLER MODES[1,4]

1. CONTINUOUS WAVE DOPPLER (CWD)

As the name suggests, continuous wave systems use continuous transmission and reception of ultrasound. Doppler signals are obtained from all vessels in the path of the ultrasound beam (until the ultrasound beam becomes sufficiently attenuated due to depth). Continuous wave Doppler ultrasound is unable to determine the specific location of velocities within the beam and cannot be used to produce color flow images. Relatively inexpensive Doppler ultrasound systems are available which employ continuous wave probes to give Doppler output without the addition of B-mode images. Continuous wave Doppler is also used in adult cardiac scanners to investigate the high velocities in the aorta.

Continuous wave Doppler has two crystals , one that transmits a high frequency sound wave and another that continuously receives signals. It can record high frequency using low power and it is easy to use. However it is nonselective recognizing all signals and it does not allow visualization of blood vessels.

2. PULSE WAVE DOPPLER

Doppler ultrasound in general and obstetric ultrasound scanners uses pulsed wave ultrasound. This allows measurement of the depth (or range) of the flow site. Additionally, the size of the sample volume (or range gate) can be changed. Pulsed wave ultrasound is used to provide data for Doppler sonograms and color flow images.

Pulsed wave systems suffer from a fundamental limitation. When pulses are transmitted at a given sampling frequency (known as the pulse repetition frequency), the maximum Doppler frequency f_D that can be measured unambiguously is half the pulse repetition frequency. If the blood velocity and beam/flow angle being measured combine to give a f_D value greater than half of the pulse repetition frequency, ambiguity in the Doppler signal occurs. This ambiguity is known as aliasing. A similar effect is seen in films where wagon wheels can appear to be going backwards due to the low frame rate of the film causing misinterpretation of the movement of the wheel spokes.

Pulse wave Doppler uses only one crystal which transmits the signal and then waits until the returning signal is received before transmitting another signal. It can also have colour flow mapping incorporated in it .Blood flowing away from the transducer looks blue and blood

flowing towards the transducer looks red. It is more expensive, requires high power but allows precise targeting and visualization of the vessel of interest.

3. DUPLEX SYSTEM[4,7]

Combination of pulsed Doppler and real time B mode ultrasound is known as duplex system .Here a particular vessel is identified by real time B mode and then characteristic waveforms are obtained with the help of pulsed waves.

4. DOPPLER COLOUR FLOW MAPPING (DCFM)[4,7]

In the DCFM mode, two dimensional flow patterns are superimposed on anatomic images in a real time . The flow patterns are derived from the mean frequency shift using signal processing techniques . Flow towards the transducer is red and flow away from it is blue.

Since color flow imaging provides a limited amount of information over a large region, and spectral Doppler provides more detailed information about a small region, the two modes are complementary and, in practice, are used as such. Color flow imaging can be used to identify vessels requiring examination, to identify the presence and direction of flow, to highlight gross circulation anomalies, throughout the entire color flow image, and to provide beam/vessel angle correction for velocity measurements. Pulsed wave Doppler is used to provide analysis of the flow at specific sites in the vessel under investigation. When using color flow imaging with pulsed wave Doppler, the color flow/B-mode image is frozen while the pulsed wave Doppler is activated. Recently, some manufacturers have produced concurrent

color flow imaging and pulsed wave Doppler, sometimes referred to as *triplex* scanning.

When these modes are used simultaneously, the performance of each is decreased. Because transducer elements are employed in three modes (B-mode, color flow and pulsed wave Doppler), the frame rate is decreased, the color flow box is reduced in size and the available pulse repetition frequency is reduced, leading to increased susceptibility to aliasing.

Power Doppler is also referred to as energy Doppler, amplitude Doppler and Doppler angiography. The magnitude of the color flow output is displayed rather than the Doppler frequency signal. Power Doppler does not display flow direction.

DOPPLER SIGNAL PROCESSING[4]

The total Doppler frequency shift signal is the summation of multiple Doppler frequency shifts back scattered by millions of red cells .The Doppler frequency is therefore composed of a range of frequencies of varying amplitudes. This is subjected to Doppler signal processing which consists of amplification, demodulation, special processing and display.

FILTERS

The Doppler signal consists not only blood flow generated frequency signal but also consists of signals from other sources. These include high amplitude , low frequency signals known as clutter produced by movement of tissue structure and high frequency noise generated by instrumentation. These additional sounds are removed by electronic digital filtering. A low pass filter is used for high frequency noise and high pass for clutter .

All types of Doppler ultrasound equipment employ filters to cut out the high amplitude, low-frequency Doppler signals resulting from tissue movement, for instance due to vessel wall motion. Filter frequency can usually be altered by the user, for example, to exclude frequencies below 50, 100 or 200 Hz. This filter frequency limits the minimum flow velocities that can be measured.

Doppler is generally used in two ways to estimate circulatory hemodynamics

1) Direct measurement of volume of blood flow

2) Indirect measurement of flow velocity using wave form analysis.

ASSESSMENT OF DOPPLER VELOCIMETRY

1. QUALITATIVE ASSESSMENT

The characteristics of flow velocity waveforms (FVW) reflect the flow profile within a vessel[14]. The simplest qualitative method used in interpreting the Doppler data is to decide whether flow is present or not .This can be achieved either visually or by listening to the Doppler signals. The colour flow data can also be regarded in the sense as a qualitative method. Finally the shape of the flow velocity waveforms can be examined .The presence of forward flow during diastole is seen in arteries supplying low resistant vascular beds[27]. Diastolic component disappears or reverses as the peripheral impedance increases[46]. Another example of qualitative assessment of an flow velocity waveforms (FVW) is identification of presence of an early diastolic notch in uterine velocimetry[48].

2. QUANTITATIVE ASSESSMENT

The measurement of the velocity, acceleration and volume of blood flow can be achieved by Doppler data. When the angle between the ultrasound beam and the longitudinal axis of the vessel is known, the Doppler frequency shift can be changed into velocity by applying the Doppler equation.

3. SEMIQUANTITATIVE ASSESSMENT

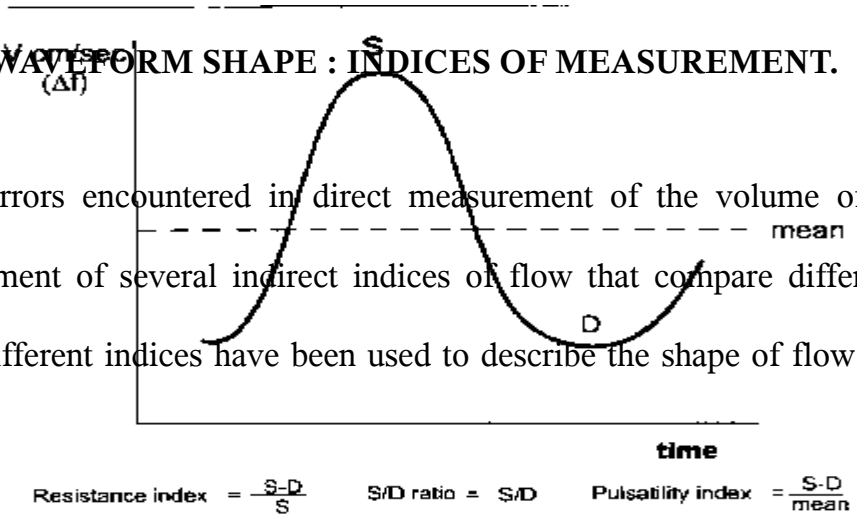
Here the relation between the systolic and diastolic components of the wave form is evaluated as described below and various indices like pulsatality /resistance indices can be arrived at.

DOPPLER VELOCITY WAVEFORM ANALYSIS[4,12,45]

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.

Changes in flow waveform shape have been used to investigate both proximal disease (e.g. in the adult peripheral arterial circulation) and distal changes (in the fetal circulation and uterine arteries). While the breadth of possible uses shows the technique to be versatile, it also serves as a reminder of the range of factors which cause changes to the local Doppler spectrum. If waveform analysis is to be used to observe changes in one component of the proximal or distal vasculature, consideration must be given to what effects other components may have on the waveform.

FLOWWAVEFORM SHAPE : INDICES OF MEASUREMENT.



Errors encountered in direct measurement of the volume of blood flow has led to development of several indirect indices of flow that compare different parts of waveforms. Many different indices have been used to describe the shape of flow waveforms . Techniques

range from simple indices of systolic to diastolic flow to feature extraction methods such as principal component analysis. All are designed to describe the waveform in a quantitative way, usually as a guide to some kind of classification. In general, they are a compromise between simplicity and the amount of information obtained.

Maximum frequency envelope of Doppler flow velocity waveform showing peak systolic frequency shift (S) and end-diastolic frequency shift (D).

S-D/S =Resistant index (RI)

S-D/A =Pulsatility Index (PI)

Where S =maximum peak systolic frequency

D =maximum peak end –diastolic frequency

A =mean Doppler shift frequency during a cardiac cycle

1. S/D RATIO

Stuart and Drumm in 1980 described a simple index of pulsatility called the S/D ratio. This is the simplest and evaluates downstream impedance to flow.

2. RESISTANCE INDEX(RI)

Pourcelot (1974) reported an index called Pourcelot or Resistance index.

RI =S-D/S

R I is the easiest to interpret. RI values approach to zero if resistance decrease and approach to one if resistance increases.

3. PULSATILITY INDEX

Gosling and King(1979) were first to develop the pulsatality index as a measure of systolic –diastolic differential of a pulse velocity waveform.

PI =S-D/A, where A represents temporal mean frequency shift over atleast three cardiac cycles.

PI is only index making evaluation of blood flow possible if end diastolic flow is absent , because in this situation S/D=infinite and RI =1.

4. D/A

End diastolic frequency shift appears to be the most relevant component of the wave form. Maulik at al (1982) therefore suggested direct use of this parameter and developed an index.

These indices are all based on the maximum Doppler shift waveform and their calculation is described as above. 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.

Generally, a low pulsatility waveform is indicative of low distal resistance and high pulsatility waveforms occur in high-resistance vascular beds although the presence of proximal stenosis, vascular steal or arteriovenous fistulas can modify waveform shape. Care should be taken when trying to interpret indices as absolute measurements of either upstream or downstream factors. For example, alterations in heart rate can alter the flow waveform shape and cause significant changes in the value of indices.

WHICH IS THE RIGHT TIME FOR DOPPLER EXAMINATION ?

There is a progressive fall in the impedance with advancing gestation in the fetoplacental circulation especially after 20 weeks . There is continuous increase in end diastolic velocity and concomitant decrease in the indices that predominantly reflect flow

pulsatality. These include S/D ratio , PI and RI. In contrast ,the D/A ratio which reflects the normalized end diastolic velocity continues to increase . Thus gestational age is one of the sources of variance in Doppler indices[14,19]. In general ,the accepted time for starting Doppler sonographic examinations is the beginning of second trimester. This is the right time that allows modification in antenatal care in high risk pregnancy[5].

CLINICAL APPLICATION OF DOPPLER ULTRASONOGRAPHY IN OBSTETRICS[4,19]

I. Placental Doppler ultrasonography examination

   a. Uterine arteries

   b. Umbilical arteries

II. Fetal Doppler ultrasound examination

   1. Arterial

      Middle cerebral artery

      Renal, splenic, hepatic arteries

   2. Venous

      Umbilical vein

      Ductus venoses etc.,

DOPPLER ULTRASONOGRAPHY OF UTERINE ARTERIES-

FUNCTIONAL ANATOMY OF UTERINE ARTERIES[4]

The major arterial supply to the uterus is derived from uterine arteries. The uterine arteries originate from internal iliac arteries. The uterine artery is a branch of anterior division of internal iliac arteries. The uterine artery gives off branches to the cervix and vagina and it

continues upwards on the lateral side of the uterus between the leaves of the broad ligament.

The uterine artery divides into arcuate arteries that encircle the surface of the uterus and form anastomosis with collateral vessels. These arcuate arteries supply the centripetal radial arteries which in turn penetrate the middle third of myometrium. These radial arteries gives rise to spiral arteries. The spiral arteries continue a convoluted course into the endometrium or decidua before breaking into a network of capillaries from which blood is subsequently collected by endometrial veins.

TROPHOBLASTIC INVASION[9,13]

The uterine arteries dilate during pregnancy. There is hypertrophy and hyperplasia of vessel wall. The walls of the terminal ends of these spiral arteries are invaded by trophoblasts (Robertson and Khong 1987). The first change is disintegration of internal elastic lamina so that only thin layer of basement membrane remains between the endothelium and smooth muscle. The trophoblasts penetrate the spiral arteries and media is replaced by matrix containing cytotrophoblast and fibrin fibres. These changes are confined to the decidua of the first trimester (primary invasion) and extends into the myometrial segment of the spiral arterioles in early second trimester (14-16 weeks secondary invasion)

This process converts the spiral arteries to uteroplacental arteries which are maximally dilated vascular channels of low resistance. This is considered as a hallmark of normal placentation (Brosen and Dixon,1966)[5]. These structurally altered spiral arteries are probably

unable to respond to vasoactive stimuli which further supports high volume flow to uteroplacental bed under varying physiological condition.

Trophoblastic invasion results in ten to twelve fold increase in blood flow and progressive decrease in impedance. Continuous forward flow is typical of such impedance vessels.

PLACENTAL CHANGES COMMON TO PREECLAMPSIA AND ADVERSE FETAL OUTCOME

Deficient placentation is highly associated with gestational hypertensive disorders, IUGR and fetal demise[28]. Compromised uteroplacental perfusion from vasospasm is almost certainly a major culprit in the genesis of increased perinatal morbidity and mortality associated with preeclampsia. In preeclampsia, only about half to two thirds of the decidual spiral arteries undergo the physiological changes described already (Khong et al 1986).

The restriction of normal physiological changes results in restricted placental blood flow which becomes more critical with advancing gestation as the demands of the conception increases. These changes are not specific to preeclampsia, but also occurs in, small for gestational age fetus and diabetes mellitus[5]. This transition , programmed to provide an adequate perfusion of the intervillous space through the maternal spiral arteries is fundamental for the growing embryo.

DOPPLER VELOCIMETRY OF UTERINE ARTERIES

The notable changes in the uterine artery hemodynamics occur between 10 and 12 weeks both in terms of flow impedance and volume . The vascular impedance in the uterine arteries decreases with increased peak systolic velocity. The uterine artery flow volume increases very gradually from 77ml/mt at week five to 159ml/mt at week ten and thereafter more rapidly to a level of 665ml/mt at week sixteen. In contrast to uterine arteries , these changes can be detected as early as weeks four to seven in spiral arteries. These changes are attributed to the trophoblastic invasion[8,9].

Apart from the changes of vascular impedance, and flow volume ,a very important change seen in the uterine flow velocity waveforms (FVW) is the disappearance of early diastolic notch during early second trimester[14,17]. The uterine artery Flow velocity waveform (FVW) in non pregnant women has relatively high pulsatality as well as early diastolic notch. The presence of a notch and elevated RI or PI with advancing gestation are indicators of increased uterine vascular resistance and uterine blood flow[15]. Dicey, Schulman H, Farmakides et al have shown that the most significant outcome are in those with diastolic notch[10].

DIASTOLIC NOTCH

Diastolic notch is an important characteristic of vessels having resistance. These notches are seen in the peripheral vessels and is a manifestation of forward and reversed waves caused by the reflection at distant branches and blockage points[11,18] . The diastolic notch represents the

elasticity of the vessel which is generally lost at the end of second trimester[15,18]. Persistence of the notch is said to be the pointer towards PIH and SGA[35]. This reliability of detection of an early notch was studied by Farrell, Chien, Mires et al[34].

TYPES OF ABNORMAL UTERINE ARTERY WAVEFORMS ARE BASED ON FOLLOWING CRITERIA[35,37,46]

1. High resistant index – RI>95th percentile

2. Presence of early diastolic notch (EDN) either unilateral/bilateral in second trimester

3. Presence of early diastolic notch and high Resistance Index

4. High Pulsatality Index (P.I)

TYPES OF ABNORMAL UTERINE ARTERY DOPPLER

TYPE I.

ABNORMAL RESISTANCE INDEX

Once the waveforms are obtained and measured, the results are plotted on a graphs to determine if blood flow during diastole is normal or abnormal. If resistant index increases to a

value above the range of normal , this identifies a fetus at risk or who may be undergrown (too small). To determine the resistance index the peak of systole is divided by the sum of systolic is dived by sum of systolic and diastolic measurements. One of the problem with this measurement is high false positive rate than one uses the presence or absence of notching. For this reason , Devore et al prefers using the presence or absence of a notch to determine if the wave is normal or abnormal.

TYPE II

MILD NOTCHING OF THE UTERINE ARTERY

This is a more serious form than Type I because there is a notch at the beginning of diastole. The notch is the result of an increase in resistance to blood flowing into the placenta .The reason for this is because the blood vessels in the placenta are not enlarging or dilating as they should . When this occurs notching is present in the wave form. The presence of notch, even with normal resistance index , places the patient at high risk for fetal outcome.

TYPE III.

SEVERE NOTCHING WITH AN ABNORMAL RESISTANCE INDEX

When resistance index is abnormal (low diastolic flow) and a notch is present ,this places the patient at the highest risk for adverse pregnancy outcome.

MATERIALS AND METHODS

STUDY DESIGN

- Prospective study

PERIOD OF STUDY

- June 2006-July 2007

PLACE OF STUDY

- Government RSRM lying in hospital, Stanley medical college, Chennai.

- Doppler studies at Mediscan systems ,Royapettah, Chennai.

CASE SELECTION

200 pregnant women who attended obstetric service at the Government RSRM lying in hospital ,Royapuram were recruited into the study.

Only patients who could be followed up to term were included in the study.

INCLUSION CRITERIA

- Any pregnant women irrespective of age and parity

EXCUSION CRITERIA

1. Congenital anomalies

2. Multiple pregnancy

3. Pregnancies complicated by placenta previa

METHODS OF STUDY

The patients, after being recruited into the study were categorised as high risk and low risk depending on presence or absence of any high risk factor for developing PIH and SGA, IUGR, preterm.

In all patients, detailed history, followed by complete general and obstetric examination were done . Routine biochemical investigations were done. Ultrasound and Doppler study were done between 22-24 weeks of gestation. Those patients without notching or increased Resistance Index were given routine antenatal care. Those cases with increased resistance index (R.I) or diastolic notching were asked to attend antenatal clinic once in 15 days. Neverthless, all patients were followed with antenatal checkup with specific references to the variables

indicating development of PIH and small for age gestational fetus.

- Edema legs ,weight
- Blood pressure
- Urine protein
- Uterinefundal height, Fetal heart rate counted.

HISTORY

History to elicit the presence of high risk factor in the mother such as history of hypertension, diabetes, chronic renal failure , SLE. History regarding previous pregnancy outcome was obtained. Patients were asked to complete a questionnaire depending on the history i.e presence of any high risk as described already-patients categorized as high risk or low risk

PHYSICAL EXAMINATION

A note was made on the height, weight, pulse, blood pressure , presence of anemia, oedema legs. Cardiovascular system, respiratory system, and central nervous systems were examined at the entry of the study.

All patients during their visits were examined for

- edema legs
- weight

- blood pressure
- symphysiofundal height.

PREECLAMPSIA diagnosed when there was an absolute increase in pressure > 140/90 –on two occasions at least 4-6 hours apart or a single diastolic reading of 110 mm of Hg in a previously normotensive women - along with protienuria of 300 mgs or more in 24 hrs or two readings of atleast 1+ on dipstick analysis.

IUGR diagnosed when there was a suspicion of small for gestation- clinically and confirmed by ultrasound assessment. The fetal biometry being serially measured obtained atleast 4 weeks apart and severity determined by fetal arterial and venous Doppler studies.

SMALL FOR GESTATIONAL AGE is diagnosed if birth weight $<10^{th}$ percentile for that gestational age.

LAB INVESTIGATIONS

- Baseline urine examination(albumin, sugar, deposit)
- Haematological investigations
- Relavent biochemical investigation if they developed PIH

METHODS OF DOPPLER STUDY

Doppler ultrasound was done between 22-24 weeks. First a basic ultrasound examination of the fetus which included determination of gestational age, anatomical survey was done. Then Doppler examination of the right and left uterine arteries were done.

PROCEDURE

Patients were placed in supine position with left lateral tilt of 15 degrees to avoid caval compression. Uterine artery was examined with probe kept 3 cm medial to anterior superior iliac spine and directed towards lateral wall of the uterus. The crossover of uterine artery and external iliac vessels was seen and sample site was chosen. Waveforms were recorded in both uterine arteries.

ABNORMAL UTEROPLACENTAL WAVEFORMS

- High resistance wave forms -The peak systolic flow and end diastolic flow were measured and the resistance index calculated.Resistance index above 95th percentile (0.6) taken as abnormal.

- Presence of diastolic notch - unilateral or bilateral

- High resistance index > 95 th percentile + End diastolic notch unilateral or bilateral.

FOLLOWUP OF CASES

All patients were followed till delivery . All patients without notching or increased resistant index were given routine antenatal care. Those patients with diastolic notching or increased RI were followed every 15 days in antenatal O.P. Those patients who developed Preeclampsia- categorized as mild /severe Preeclampsia were investigated and managed. In patients with IUGR –growth of fetus monitored and Doppler study of fetal vessels done, and managed accordingly.

FOLLOWING DETAILS OF PREGNANCY OUTCOME STUDIED

- Gestational age at delivery.
- Mode of delivery- labour natural /cesarean section
- Birth weight of the baby.
- APGAR < 7 at 5 min.
- Admission to NICU

CRITERIA TAKEN AS ADVERSE OUTCOME

1. Elevation of blood pressure >140/90 on two occasions six hours apart with proteinuria – greater than 300mg for 24 hrs are persistent 1+ on dipstick analysis - Preeclampsia.

2. Small for gestational age –birth weight less than tenth percentile for that gestational

age.

3. Fetal death

4. Intrauterine growth retardation as diagnosed by serial ultrasounds.

5. Spontaneous birth before 37 completed weeks of gestation.

RESULTS AND DISCUSSION

In this study out of two hundred randomly selected patients,

- 157 patients had no risk factors (low risk group).
- 43 patients were at high risk for developing PIH, SGA, IUGR, Preterm (high risk group).

Among the 43 patients in high risk group, the various risk factors present were

TABLE - 1

HIGH RISK FACTORS

Serial number	Risk factors	Number of patients
1.	Previous h/o PIH	16
2.	Previous h/o SGA / IUGR	7
3.	Previous h/o PRETERM	8
4.	BOH	6
5.	ELDERLY PRIMI	5
6.	CHRONIC HYPERTENSION	1
Total		43

During the course of follow up 3 patients developed glucose intolerance –gestational diabetes mellitus and they were included in high risk group. So 154 were under low risk group (77%) and 46 were under high risk group (23%) as shown in figure 1. This is similar to the study by Harrington et al[17] where study among unselected population showed low risk (73%) and high risk (27%). Among 154, low risk cases 13 were lost in follow up, 4 cases among the high risk group could not be followed up to delivery.

The final number of patients in the study being 141 –low risk group and 42 in high risk group.

TABLE - 2

DOPPLER FINDINGS IN UNSELECTED POPULATION.

	Abnormal Doppler	**Normal Doppler**	**Total**
HIGH RISK	15	27	42
LOW RISK	11	130	141
TOTAL	26	157	183

In our unselected population 26 had abnormal Doppler finding constituting 14.2% (Figure 4) of the total, whereas the study by Kurdew et al[23] showed 23% abnormal Doppler finding among the unselected group. This variation is mainly due to the difference in criteria used to define adverse outcome.

Discrepant results between the studies may be the consequence of differences in Doppler technique for sampling and the definition of abnormal flow velocity waveform, differences in the populations examined (for example, the prevalence of pre-eclampsia varied from as low as 2% to as high as 24%), the gestational age at which women were studied, and different criteria for the diagnosis of pre-eclampsia and intrauterine growth restriction.

Among the high risk patients alone 35% (15/42) had abnormal Doppler findings (Figure 2). This correlates with the study by Coleman et al[29] showing 40% abnormal Doppler finding among high risk while Zimmerman et al[30] showed only 24.1%

7.8% of the low risk patients had abnormal Doppler finding in contrast to the study by

Falk Gurhan et al showing 16.8% (Figure 3). The studies by Albaiges[32] and Harrington et al[15] on the other hand showed 4.4% and 3.9% respectively.

TABLE - 3

RISK FACTOR AND ADVERSE OUTCOME –PREECLAMPSIA

Risk group	Number of cases	Developed Preeclampsia	Percentage
Low risk	141	6	4.2%
High risk	42	9	21.4%

P=0.0339 p<.05 Significant.

In our study ,7.6% of the total patients developed PIH. The prevalence of PIH in our study is 5.8%.,while comparing the prevalence of PIH at RSRM in 2006 which was 8.3% Preeclampsia developed in 21.4% of the high risk cases. The prevalence of preeclampsia among the high risk in various studies being Arduine et al[21] 37%, Jacobson et al[26] 29% , Zimmerman et al[30] 18%. In low risk cases, 4.2% developed preeclampsia. This correlates with the study by Irion et al[25] which showed a prevalence of 4% for preeclampsia in low risk women.

TABLE - 4

RISK FACTOR AND ADVERSE FETAL OUTCOME

Risk group Number of patients	SGA	Preterm	Fetal death	Total	Percentage
LOW RISK (n=141)	3	0	1	4	2.8%
HIGH RISK (n=42)	4	3	1	8	19%

P= 0.028 P<05.Significant

Adverse fetal outcome occurred in 6.5% of the total patients. This is in par with the study by North et al[22] which showed prevalence of 6.6%.

When considering the high risk population alone, the prevalence of adverse fetal outcome was 19%, whereas it was 2.8% among the low risk cases in contrast to the study by Irion et al[25] which showed a prevalence of 11% (Figure 5).

TABLE – 5

CORRELATION BETWEEN DOPPLER FINDING AND ADVERSE OUTCOME IN LOW RISK POPULATION

Doppler findings Number of patients	Number of patients With Preeclampsia	Number of patients With adverse fetal outcome	Total
Normal (n=130)	5 (3.8%)	2 (1.5%)	7
Abnormal (n=11)	1 (9.09)	2 (18.8%)	3
Total	6	4	10

P 0.1588 P> 0.05 Not significant.

Among the low risk patients having normal Doppler, 3.8% developed preeclampsia correlating the study by Falk Gurhan et al[31] 3.4%. 1.5% developed adverse fetal outcome inpar with Falk Gurhan et al[31] showing 3%.

Among the low risk patients 11 had abnormal Doppler findings. Out of which 9.09% developed preeclampsia in par with the study by Fark Gurhan et al[31] showing 12.9% and 18.8% developed adverse fetal outcome in contrast to the above study showing 9.8 %.

TABLE – 6

CORRELATION BETWEEN DOPPLER FINDING AND ADVERSE FETAL OUTCOME IN HIGH RISK POPULATION

Doppler findings Number of patients	Number of patients With Preeclampsia	Number of patients With adverse fetal outcome	Total
Normal (n=27)	2 (7.4%)	1 (3.7%)	3
Abnormal (n=15)	7 (46.6%)	7 (46.6%)	14
Total	9	8	17

P = 1.6 P< 0.05 Significant.

Among the high risk patients , 15 had abnormal Doppler findings .Out of which 46.6% developed preeclampsia and 46.6% developed adverse fetal outcome. In the study by Harrington et al[17] the high risk group with abnormal Doppler findings , 47% developed preeclampsia and 53%developed adverse fetal outcome.

Among the 27 high risk patients with normal Doppler, 11% developed adverse fetal outcome in contrast to the study by Harrington[17] et al showing 6.6% .

TABLE - 7

DISTRIBUTION OF CASES DEVELOPING PREECLAMPSIA ACCORDING TO AGE.

Age of the patient	Low risk group(n=6)	High risk group (n=9)
16-20	5	5
21-25	1	1
26-30	0	1
31-35	0	2

In the present study, 62.5% of patients were in the age group of 16-20 years (Figure 6). In our hospital statistics , we found that most of antenatal patients who developed PIH were in this age group of 18-30 years in both high and low risk pregnancies.

According to Macgillivray et al, the relationship of maternal age and incidence of PIH gives a J- shaped curve with increased incidence among young primigravida and marked increased incidence among older primigravida.

TABLE - 8

ASSOCIATION OF PREECLAMPSIA WITH PARITY

Parity	Low risk (n=6)	High risk (n=9)
Nullipara	6	3
Para I	0	5
Para II	0	1

The effect of parity on development of preeclampsia is striking. Macgillivray et al has shown that primigravida are 10-15 times more likely to develop preeclampsia than multigravida. In our study the prevalence of PIH in primigravida is 57.4% among the low risk pregnancies, while in high risk it is 33.3% (Figure 7).

TABLE - 9

GESTATIONAL AGE AT DEVELOPMENT OF PREECLAMPSIA

Gestational age(weeks)	High risk	Low risk
28 to 32	1	1
32 to 36	5	1
36 to 40	3	4

42.8% of the patients with preeclampsia were detected clinically in 32-36 gestational age. Early onset cases had significant Doppler finding and associated with higher perinatal mortality and morbidity then compared to late onset preeclampsia (Figure 8) .

TABLE :10

ADVERSE FETAL OUTCOME IN HIGH RISK GROUP

	Normal	Abnormal

	Doppler	Doppler
Good Outcome	26	8
Adverse Outcome	1	7
- Preterm	1	2
- SGA	-	4
- Fetal death	-	1

P 0.0011 P<0.05 Significant.

TABLE - 11

ADVERSE FETAL OUTCOME IN LOW RISK GROUP

	Normal Doppler	Abnormal Doppler
Good Outcome	128	9
Adverse Outcome	2	2
- Preterm	-	-
- SGA/IUGR	1	2
- Fetal death	1	-

P 0.0880 P >0.05 Not significant.

Most of the adversely affected babies had low APGARS (<7 in 5mts) and needed admission in NICU for one or the other reason. Among the low risk group two patients developed IUGR and babies were admitted in NICU .

Table - 12

ABNORMAL UTERINE ARTERY DOPPLER FINDINGS (Figure 9)

Adverse Outcome	Resistance index >95th percentile (0.6)	Notching Unilateral / bilateral	Resistance index >95th percentile + Notching	Total
PIH	2	6	2	10
Adverse fetal outcome	2	4	1	7
PIH + Adverse Fetal Outcome	0	3	2	5
Total	4	13	5	22

TABLE - 13

UTERINE ARTERY DOPPLER R. I DISRIBUTION IN ADVERSE OUTCOME

Adverse Outcome	0.38-0.47 series 1	0.48-0.57 series 2	0.58-0.67 series 3	0.68-0.77 series 4	0.78-0.87 series5
PIH (n=10)	0	4	2	3	1
Adverse Fetal outcome (n=7)	0	2	2	2	1
PIH + Adverse Fetal outcome (n=5)	0	0	0	3	2

The sensitivity, specificity, positive predictive value and negative predictive value of Uterine artery Doppler study in detecting preeclampsia /Adverse fetal outcome in UNSELECTED POPULATION in our study.

TABLE - 14

PREECLAMPSIA

S. No.		**Results Of Our Study**
1.	Sensitivity	53.33%
2.	Specificity	95.54%
3.	Positive predictive value	53.33%
4.	Negative predictive value	95.54%

TABLE - 15

ADVERSE FETAL OUTCOME.

S.No.		**Results of Our Study**
1.	Sensitivity	75.00%
2.	Specificity	91.12%
3.	Positive predictive value	37.50%
4.	Negative predictive value	98.09%

The sensitivity, specificity ,positive and negative predictive values for detecting preeclampsia and adverse fetal outcome in HIGH RISK POPULATION in our study in

comparison with other studies is given below

TABLE - 16

PREECLAMPSIA

	Arduniet et al	**Jacobson et al**	**Zimmerman et al**	**Our study**
Sensitivity	64%	44%	56%	77.78%
Specificity	94%	73%	83%	75.76%
Positive predictive value	70%	33%	43%	46.67%
Negative predictive value	80%	81%	89%	92.59%

TABLE - 17

ADVERSE FETAL OUTCOME

	Coleman et al	**Results of our study**
Sensitivity	84%	87.50%
Specificity	39%	76.47%
Positive predictive value	33%	46.67%
Negative predictive value	86%	96.30%

The results of uterine artery Doppler study for prediction of preeclampsia / adverse fetal outcome in LOW RISK POPULATION of study in comparison with other studies

TABLE - 18

PREECLAMPSIA

	Kurdew et al	Irion et al	North et al	Our Study
Sensitivity	62%	26%	27%	16.67%
Specificity	89%	85%	90%	92.59%
Positve predictive value	11%	7%	8%	10.00%
Negative predictive value	99%	---	97%	96%

TABLE - 19

ADVERSE FETAL OUTCOME

	Kurdew et al	Irion et al	North et al	Our study
Sensitivity	37%	29%	47%	50%
Specificity	89%	89%	91%	93.43%
Positive predictve value	22%	25%	27%	18.18%
Negative predictive value	96%	---	96%	98.46%

SUMMARY

Out of 200 recruited cases, 154 – Low risk, 46 - high risk for developing preeclampsia / IUGR / SGA / Preterm.

17 low risk and 4 high risk lost in followup.

Final number of patients in study, 141- low risk, 41 – high risk.

1) Out of 141 low risk cases, 130 are normal doppler, 11 had abnormal doppler. out of 42 high risk cases, 27 had normal doppler, 15 had abnormal doppler.

2) Among the patients having abnormal uterine artery doppler study (including high and low risk patients) 8 developed preeclampsia and 9 developed adverse fetal outcome.

3) Out of 42 high risk cases

Abnormal Doppler	**15**	**Normal Doppler**	**27**
Developed preeclampsia	7	Developed preeclampsia	2
No preeclampsia	8	No preeclampsia	25
Had adverse fetal outcome	7	Had adverse fetal outcome	1
Normal fetal outcome	8	Normal fetal outcome	26

4) Out of the 141 low risk cases

Abnormal Doppler	**11**	**Normal Doppler**	**130**
Developed preeclampsia	1	Developed preeclampsia	5
No preeclampsia	10	No preeclampsia	125
Had adverse fetal outcome	2	Had adverse fetal outcome	2
Normal fetal outcome	9	Normal fetal outcome	128

CONCLUSION

Uterine artery Doppler study was done in two hundred randomly selected cases between 22-24 weeks . R I >95th percentile and / or presence of early diastolic notch in the FVW was used to interpret the Doppler flow velocity waveform.

Abnormal Doppler indices were early predictors of fetal compromise and preeclampsia and correlated with adverse perinatal outcome in patients at high risk of developing PIH, SGA, IUGR when compared to low risk patients. Observation of the outcome in patients with normal Doppler is strongly linked with good neonatal outcome.

Once an abnormal Doppler finding is identified then the obstetrician is made well aware of the possible complication that can set in and delivery should be planned in a tertiary care centre with good neonatal care facilities.

Further the risk as determined by the Doppler flow would allow ultrasound resources and clinical follow up to be tailored to the pregnant women for the most appropriate use of antenatal care.

Normal uterine artery Doppler studies at 22-24 weeks constitute a group that have a low risk of developing obstetric complications related to uteroplacental insufficiency. Women with abnormal uterine artery Doppler finding have a increased risk of developing complications. Uterine artery Doppler velocimetry was able to detect 53.3% of cases who subsequently developed preeclampsia and 75% of the patients who had adverse fetal outcome among high risk patients.

This study demonstrates the feasibility of defining with some precision an individuals risk of severe outcome relating to impaired trophoblastic invasion .This requires a philosophical shift away from the concept of categorizing women simply as high or low risk pregnancies to a level of risk that can instead be quantified. Individualized risk would allow a more accurate assessment of the effectiveness of intervention in reducing adverse pregnancy outcome.

Of particular clinical potential is using uterine artery risk assessment as a basis to determine a plan of antenatal care for each women allowing clinicians to make rational choices in deciding the use and frequency of fetal and maternal monitoring services and minimize unnecessary interventions.

This study demonstrates that addition of uterine artery Doppler waveform analysis to monitoring profile of women at risk of developing PIH, SGA, preterm , perinatal death can further define those in a high risk group and of use in determining the type and level of antenatal care offered to them.

The availability of treatment or prevention of this target disorder is an important prerequisite for establishing a screening test. In the case of preeclampsia, this has not been achieved . A considerable amount of research is going on in preventing preclampsia based on underlying pathophysiology. This scenario may change in future.

At the present time, the consensus on the effectiveness of uterine artery screening has resulted in only limited number of centers, using this test to identify high risk pregnancy. This is regrettable because the test is quick and immediate and will identify a cohort of women at

risk of preeclampsia and other conditions associated with impaired trophoblastic invasion such as SGA / IUGR . All three contribute significantly, perinatal morbidity and mortality.

In the future, uterine artery screening will probably be combined with biochemical markers of platelet activation or endothelial damage to further improve the screening results.

Further studies are still necessary to determine how information from uterine artery Doppler studies should modify current practice in high risk women.

BIBLIOGRAPHY

1) F.GARY CUNNINGHAM, KENNATH J. LEVENO, STEVEN L. BLOOM et al Ultasonography and Doppler, Hypertensive disease of pregnancy. Williams Obstetrics , 22 nd edition Mc Graw Hill 2005.

2) D.K. JAMES, D. J. STEER., CP WEINER et al. Fetal growth disorders. High risk pregnancy –manage. option 3 rd edition.

3) GEOFFRAY CHAMBERLIN , PHILIP T. STEER et al. Fetal growth restriction, pregnancy induced hypertension. Turnbull' s obstetrics .3 rd edition- Churchill Livingston.

4) CALLEN PW, Ultrasonography in obstetrics and gynaecology, 4th edition.

5) ROBERTSON W B, BROSONS I , DIXON HG. Uteroplacental vascular pathology . Eur J. Obstetr. Gynaecol 86; 93 ,1049-1059.

6) A KUBILAY ERTIAN ,H ALPER TANRIVERDI, WERNER SCHIMIDT Doppler Sonography in Obstetrics. Donald School- Text Book of USG IN obst and gynaec-First edition

7) CAMPBELL S, DIAZ, RECASENS,GRIFFIN DR et al. New Doppler techniques for assessing uteroplacental blood flow. Lancet 1:675; 1983.

8) DICKEY RP. Doppler ultrasound investigation of uterine and ovarian blood flow in early pregnancy. Hum report update 3; 467,1977.

9) VALTIN L , SLADE VICIUS , LAURIN R et al. Uteroplacental and luteal circulation in normal first trimester pregnancies. Am J. Gynaecol.174;768,1996.

10) SCHULMAN H, DICEY Y, FARMAKIDES G. et al. Uterine artery

Doppler velocimetry- the significance of divergent systolic/diastolic ratios. Am .J. Obstetr.and Gynaecol. 1987,157;1539-1542.

11) THALER et al. Systolic and diastolic notch in uterine artery Doppler velocimetry in hypertensive pregnant patients-relationship to outcome. Obstet. Gynaecol. 1992 Aug 80(2) 277-82 .

12) THOMON RS, TRUDINGER BJ,COOK CM. Doppler ultrasound wave form indices ;A/B ratio, pulsatality index and Pourcelet ratio. Br.J. OBS.GYNAECOL 1988; 95; 581-588.

13) PIJENBORG R ,BLAND. J M . ROBERTON W B. Uteroplacental arterial changes related to interstitial trophoblast migration in early pregnancy placenta 1983-4 (387-414)

14) PEARCE J M F , MACPARLAND. Doppler uteroplacental waveforms Lancet 1988 9 ;1278.

15) HARRINGTON K, COOPER D, LEEC C et al. Doppler ultrasound of uterine arteries; The importance of bilateral notching in the prediction of preeclampsia , placental abruption or delivery of small for gestational age baby. Ultrasound Obs. and Gynaecol 7 ; 182 1996.

16) HARRINGTON K, CARPENTER RG, GOLDFRAD C, CAMPBELLS. Transvaginal Doppler ultrasound in the early prediction of preeclamsia and IUGR.

17) HARRINGTON et al. The value of uterine artery Doppler in the prediction of uteroplacental complication in multiparous women. Ultrasound and Gynaecol 2004. Jan 23 (1).

18) NIPPON SANKA FUJUNKA GAKKAI ZASSHI et al. A study of predicting toxemia of pregnancy by diastolic notch in pulsed Doppler

flow velocity waveform of the uterine arteries-Quantitative analysis of diastolic notch as uterine arterial index . SATOH 1995 oct 47 (10) 1055-62.

19) HENRETTY K P, PRIMEROSE MH, NEILSON J P , WHITTLE MJ. Pregnancy screening by Doppler uteroplacental and umbilical artery waveforms . OBSTET.GYNAECOL 1989 ,96. 1163-7.

20) LOWE TW, PETERS MT, TWICKER D et al. Obstet.sonography update, Williams obstet. 18th edition.

21) ARDUINI D, RIZZO G, ROMANINI C et al. Uteroplacental bloodflow velocitywaveforms as predictors of pregnancy induced hypertension. Eur J. Obs. Gyn.Reprod Biol.26;335;1987.

22) NORTH RA , FERRIER C, LOND O et al, Uterine artery Doppler flowvelocity waveform in the second trimester for the prediction of preeclampsia and growth retardation .Obst.Gynae. 83 ,378,1994.

23) BEWLEY S, COOPER D, CAMPBELL S. Investigation of uteroplacental blood flow resistance in the second trimester . A screening study for preeclampsia and IUGR. Br.J . OBS .GYNAE. 98;871 ,1991.

24) BOWLERS S , BEWLEY S ,CAMPBELL, Improved prediction of preeclampsia by two stage screening of uterine arteries using the early diastolic notch and colour Doppler imaging. OBS. GYNAECOL 82; 78, 1993.

25) IRION O, MASSE J , FOREST J C et al. Prediction of preeclamsia , low birth weight gestation by uterine artery blood flow velocity waveforms analysis in the low risk nulliparous women . Br.J OBST.GYNAECOL. 105, 422, 1998.

26) JACABSON SL. IMHOF R, MANNING N et al. The value of uterine artery Doppler in the prediction of uteroplacental circulation in predicting preeclampsia and IUGR. Am. J. OBS. GYNAECOL. 162; 110; 1992.

27) BOWLER S KINGDOM J, CAMPBELL S .Objective and subjective analysis of abnormal uterine artery blood flow velocity waveforms. Ultra. OBS.GYNAECOL 1998;12;260-264.

28) PAPAGEORGHIOU AT, YU CK, CICERO S et al. Second trimester uterine artery Doppler screening in unselected population ; A review J . Maternal fetal neonatal medi.2002;12 78-88.

29) COLEMAN MA, MC COWEN LM, NORTH RA . Midtrimester uterine artery screening as predictor of adverse pregnancy outcome in high risk women .Ultrasound OBST. GYNAECOL 2000, 15 ,7-12.

30) ZIMMERMANN ,RANTA et al. Doppler assessment of uterine and uteroplacental circulation in the second trimester in pregnancies at high risk for preeclampsia and IUGR. Ultra. OGS. GYNAECOL 1997, 9,330-8.

31) FACK GURKHAN YAZKI et al .Relation of early diastolic notch in uterine artery Doppler measurement with pregnancy complications in low risk pregnancies . Perinatal journal. 2005 13 (3) 152-157.

32) ALBAIGES G, MISSFELDER LOBOS H, PARRA M,NICOLAIDES KH. Comparison of colour Doppler –uterine artery indices in a population at high risk for adverse outcome at 24 weeks gestation . Ultra. OBS. GYNAECOL 2003 ,21; 170-3.

33) KURDEW, CAMPBELL S, AQUILINA , ENGLAND .Role of colour Doppler imaging at 20 weeks of gestation in staratyfying antenatal care.

34) FARREL T, CHIEN PF , MIRES GJ. The reliability of detection of an EDN in uterine artery Doppler velocimetry. Br. J .OBS. GYNAECOL 105 1308,1998.

35) OHKUCHIA, MINIKAMI H, SATO I , NAKANO T. Predicting the risk of preeclampsia and small for gestational age infants by quantitative assessment of the diastolic notch in the artery flow velocity waveforms in unselected women . Ultrasound OBST. GYNAECOL 2000, 16; 171-78.

36) VALENSISE H, BEZZECCHERI V, RIZZO G.Doppler velocimetry of uterine artery as a screening test for gestational hypertension . Ultrasound OBST. GYNAECOL1993 3; 18-22.

37) SIEROZEWSKI P, GUROWSKI G, SOSNOWSKI et al The usefulness of U.A.doppler in the high risk pregnancy diagnostics (PIH and IUGR). GINEKOL; POL 2005 may 76 (5-342-7).

38) LOW J A. The current status of maternal and fetal blood flow velocimetry. Am. J . OBS. GYNAE. 164; 1049, 1991.

39) AUDIBERT F, BENCHIMOL Y, BENATTOR C et al. Prediction of preeclampsia and IUGR by second trimester screening and uterine artery velocimetry. Fetal diagnostics and therapy 20; 48 . 2005.

40) CHAPPLE L, BEWLEY S,. Preeclamptic toxemia – the role of uterine artery Doppler . Br .J . OBS. GYNAECOL 105, 379 , 1998.

41) CONDE AGUDELO, VILLER J , LINDHEIMER M, WHO Systematic Review Of screening test for preeclampsia. OBS. GYNAECOL 104;1367, 2004.

42) AARDEMO MW , OSTERHOF H , TIMMERA et al .Uterine artery

Doppler flow and uteroplacental vascular pathology in normal pregnancies and pregnancies complicated by preeclampsia and small for gestational fetus.

43) FERRAZZI E, BULFAMANE G , MEZZOPANE R et al. Uterine artery Doppler velocimetry and placental hypoxic ischemic lesion in pregnancies with fetal IUGR. Placenta 1999, 20;389-394.

44) AQULINA J ,BARNETT A, THOMPSON O, HARRINGTON K. Comprehensive analysis of uterine artery flowvelocity wave forms for the prediction of preeclampsia ultra. OBS. GYNAECOL 2000;16.163-170.

45) PETER MC , PARLAND J, MACCOLM PEARCE. Doppler studies in pregnancy Recent advances in OBS. AND GYNAECOLOGY 16 p 44.

46) KOFFINOS et al . Interrelationship and clinical significance of increased resistance in the uterine artery in patients in PIH . Am . J .OBS . GYNAECOL 1992 ; 166; 601- 606.

47) CHRISTOPH LEE, MAURO PARRA , HANNAH, ANNE MORGAN S et al Individualised risk assessment for adverse pregnancy assessment by uterine artery Doppler at 23 weeks. OBST. GYNAECOL 1995 , 85; 596-602.

48) LEIBERMAN J R, MEIZMER I, FRASER D. The association between increased mean arterial pressure and abnormal uterine artery resistance to blood flow during pregnancy. OBST. GYNAECOL 1993; 965-969.

49) YU CK , PAPAGEORGHIOU AT, PARRAM et al. Fetal medicine foundation second trimester screening group. Randomized controlled trial using low dose asprin in the prevention of preeclampsia in women with abnormal uterine artery Doppler at 23 weeks gestation. Ultraso.

OBSTET. GYNAECOL, 2003;22,233-239.

50) FY CHAN et al, Pregnancy screening by uterine artery Doppler velocimetry which criteria performs best. OBSTET. GYNAECOL 1995;85,596-602.

GLOSSARY

PIH	:	Pregnancy induced hypertension
SGA	:	Small for Gestational Age
IUGR	:	Intrauterine Growth Retardation
PT	:	Preterm
FVW	:	Flow Velocity Wave Form
FD	:	Fetal Death
p/h	:	Previous History

PROFORMA

Name Age O P no Unit
Address
SE Education
Obst.Code
LMP EDD
Medical history - DM / Chronic hypertension /Chronic renal failure
Other illness
Personal history
Marietal history
Consanguinity I II III
Obst H/o
General examination:
Height Weight
Anemia PR
Edema BP
Breast / Thyroid
CVS
RS
Obst.Examination :Fundal height

Investigations:
Hb%
Urine – albumin
-sugar
Blood group
VDRL

DOPPLER

UTERINE ARTERY	RESISTANT INDEX	DIASTOLIC NOTCH
RIGHT		
LEFT		

FOLLOWUP

DATE	GA weeks	WEIGHT	EDEMA LEGS	BLOOD PRESSURE	URINE PROTEIN

DELIVERY
Date of delivery
Spontaneous / induced
Mode of delivery
APGAR
Birth weight
Admission to NICU