"STUDY OF UMBILICAL ARTERY,MIDDLE CEREBRAL ARTERY AND FETAL AORTIC ISTHMUS DOPPLER IN INTRAUTERINE GROWTH RESTRICTION AND ITS PERINATAL OUTCOME AT A TERTIARY CARE HOSPITAL IN CHENNAI-A PROSPECTIVE STUDY"

A dissertation submitted to

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY
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In Partial fulfilment of the Regulations for the Award of the Degree of

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CERTIFICATE BY THE INSTITUTION

This is to certify that dissertation entitled "**STUDY OF UMBILICAL ARTERY, MIDDLE CEREBRAL ARTERY AND FETAL AORTIC ISTHMUS DOPPLER IN INTRAUTERINE GROWTH RESTRICTION AND ITS PERINATAL OUTCOME AT A TERTIARY CARE HOSPITAL IN CHENNAI-A PROSPECTIVE STUDY "**is a bonafide work done by **Dr K.MONISHA** at R.S.R.M Lying in Hospital, Stanley Medical College, Chennai. This dissertation is submitted to Tamilnadu Dr. M.G.R. Medical University in partial fulfilment of university rules and regulations for the award of M.S. Degree in

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DECLARATION

I, Dr.K.MONISHA solemnly declare that the dissertation titled, "**STUDY OF UMBILICAL ARTERY, MIDDLE CEREBRAL ARTERY AND FETAL AORTIC ISTHMUS DOPPLER IN INTRAUTERINE GROWTH RESTRICTION AND ITS PERINATAL OUTCOME AT A TERTIARY CARE HOSPITAL IN CHENNAI-A PROSPECTIVE STUDY"** is a bonafide work done by me at R.S.R.M. Lying in Hospital. Stanley Medical College, Chennai – during November 2020–to December 2021 under the guidance and supervision of **Prof. Dr.V.RAJALAKSHMI M.D DGO.,** Professor and Head of the Department , Obstetrics and Gynaecology. The dissertation is submitted to the Tamilnadu Dr. M.G.R. Medical University, in partial fulfilment of University rules and regulations for the award of M.S. Degree in obstetrics and Gynaecology.

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LIST OF ABBREVIATIONS

AEDF - ABSENT END DIASTOLIC FLOW

REDF REVERSE END DIASTOLIC FLOW

AIEDF ABSENT END DIASTOLIC FLOW

BS - BORDERLINE SIGNIFICANT

CPR - CEREBRO PLACENTAL RATIO

CTG - CARDIOTOCOGRAPHY

DV - DUCTUS VENOSUS

IUGR - INTRA UTERINE GROWTH RESTRICTION

LSCS - LOWER SEGMENT CAESAREAN SECTION

MCA - MIDDLE CEREBRAL ARTERY

NICU - NEONATAL INTENSIVE CARE UNIT

NS - NOT SIGNIFICANT

NST - NON STRESS TEST

PE - PRE ECLAMPSIA

PI - PULSATALITY INDEX

REDF - REVERSED END DIASTOLIC FLOW

DA DUCTUS ARTERIOSUS

RI - RESISTANCE INDEX

S/D RATIO - SYSTOLIC/DIASTOLIC RATIO

SGA - SMALL FOR GESTATIONAL AGE

UA - UMBILICAL ARTERY

AI/AOI AORTIC ISTHMUS

INTRODUCTION

Pre eclampsia and IUGR are two conditions that are felt to be the result of abnormal placenta formation involving defective trophoblastic invasion of spiral arteries and a reduction in the vascular resistance in the uteroplacental circulation.

Hypertensive disorders remain the most common medical complications during pregnancy, leading to a majority of adverse perinatal and maternal outcome, despite numerous efforts have been made at early diagnosis, prevention and treatment. It accounts for a total of 7-10% of perinatal mortality in developed countries and 20% in developing countries. Early detection of preeclampsia may allow vigilant antenatal surveillance and appropriate timing of fetal delivery in order to avoid serious sequelae.

The decreased uteroplacental perfusion can result in fetal growth restriction, reduced amniotic fluid volume and an inability to tolerate the in utero environment leading to intrauterine death.

The timely diagnosis of fetal compromise is very important so that delivery can be affected before fetus suffers irreversible damage and dies in utero.

Doppler sonography offers an unique tool for the non invasive evaluation of physiologic, hemodynamic fetoplacental blood flow information. Doppler does correlate well with fetal compromise giving earlier warning sign of fetal distress than other tests.

REVIEW OF LITERATURE

Pre-eclampsia is a major cause of maternal and perinatal mortality and morbidity worldwide causing 24% of all maternal deaths in India.[1,2]

Human placentation relies on the trophoblastic invasion of the maternal decidua, myometrium and their blood vessels. Cytotrophoblastic cells invade and partially replace the endothelium of the maternal spiral arteries, leading to progressive dilatation of these vessels. This process begins as early as 10th day post conception and continues all through pregnancy.[3,4]

Defective placentation is considered to be the major etiological factor in the development of pre-eclampsia and IUGR, both of which are major causes of perinatal mortality and morbidity worldwide.[5,6]

The growth of the fetus and the ultimate outcome of pregnancy depends to a large extent on a continuous flow of oxygen and nutrients from mother. The exchange of gas and nutrients in the placenta occurs partly through passive diffusion and partly through active transport.

The oxygen and nutrient enriched blood enters fetal circulation via umbilical vein. Fetal circulation varies from that of adult circulation by the presence of three major shunts, ductus venosus, foramen ovale and ductus arteriosus, and by a parallel functional arrangement of pulmonary and systemic circulations.

Fetal sheep experiments show that approximately 55% of oxygen enriched blood from placenta enters directly into the inferior venacava via the ductus venosus. About 27% of the stream that enters the right atrium passes directly to left atrium via foramen ovale. Additionally deoxygenated blood from pulmonary veins flows into left atrium accounting for 8% of total output.

Around 8% of left ventricular output in fetus is distributed to coronary arteries, 63% enters cerebral circulation, remaining 29% pumped into descending aorta ensuring optimum blood supply to the brain and myocardium.

The deoxygenated blood from superior venacava, inferior venacava and coronary sinus enters right atrium and passes into right ventricle through tricuspid valve. Due to high vascular resistance in the pulmonary circulation, only about 13% enters pulmonary arteries, while 87% enters descending aorta through ductus arteriosus. 60% of deoxygenated right ventricular output and 19% of oxygenated left ventricular output are returned to placenta for renewed exchange of gas and nutrients.

The steady supply to the fetus is ensured by continuous adjustments of the umbilico placental circulation throughout pregnancy. The distribution of fetal cardiac output to the placenta is regulated by the balance between the resistance in that organ relative to that elsewhere in the fetus. The umbilical circulation has no autonomic control. Variation in the cardiac output by the fetus will alter flow. The fetus does not need to regulate the placental blood flow precisely because there is a wide range over which oxygen extraction can be achieved. The balance between fetal umbilical and maternal uterine placental circulations is important for optimal oxygen transfer across the placenta.[7]

The cardiac output of the fetus increases with advancing gestation from 250ml/min at midgestation to over 1500ml/min at term. The umbilical circulation which represents almost 50% of fetal cardiac output, also increases throughout gestation. These changes are due to a progressive decrease in the placental vascular resistance.

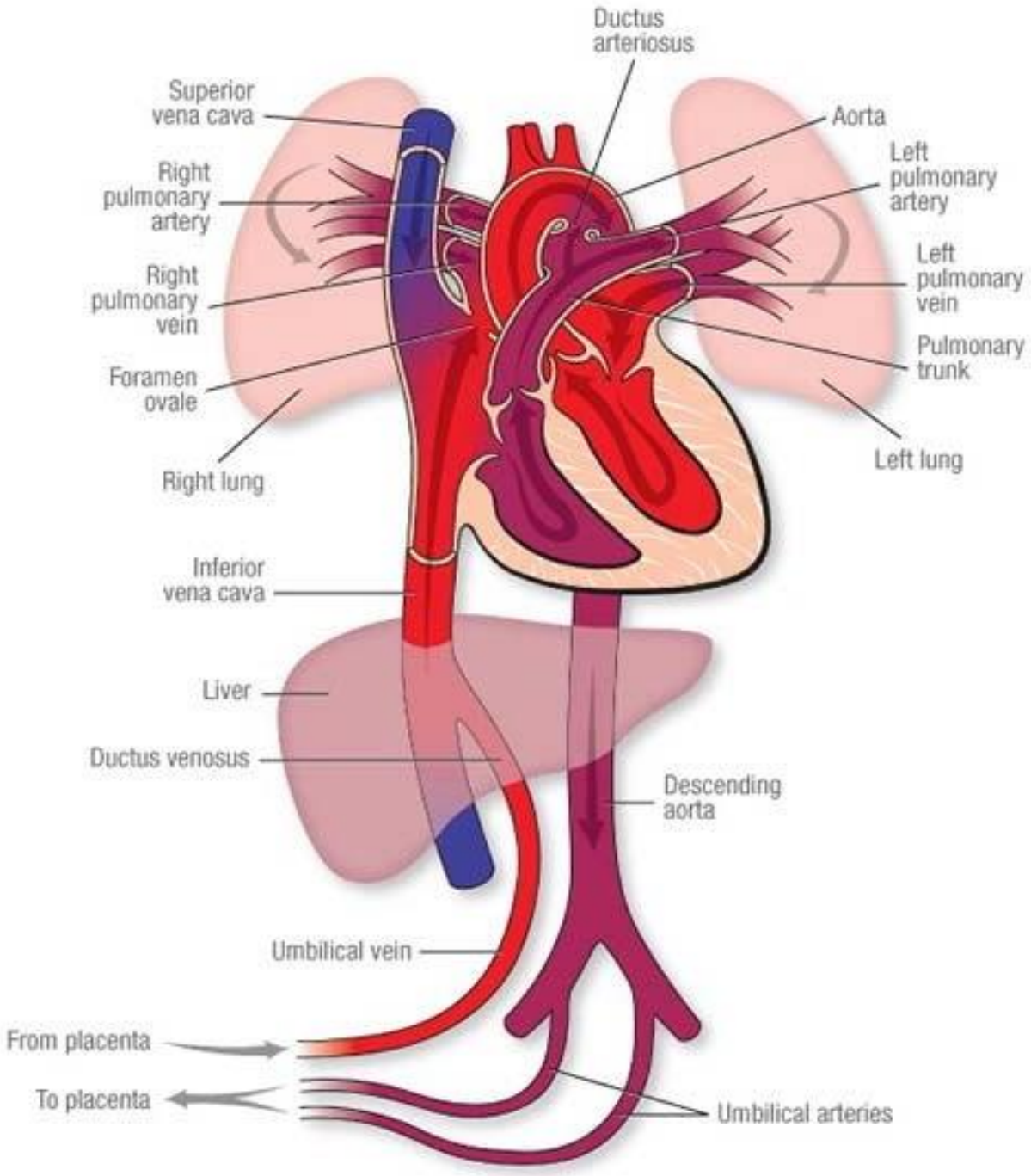


Figure 1: Fetal hemodynamics

DOPPLER ULTRASONOGRAPHY

HISTORY

Christian Johann Doppler described the Doppler effects in 1842. The principles applied to Doppler technology include the physical property described by Christian Doppler that the frequency of waves (sound) produced by objects (moving RBC) approaching the observer (transducer) is higher than that of objects moving away from the observer.

When the source and observer move closer, the frequency increases, when they move apart, the frequency decreases. This is known as “Doppler effect”, the change in frequency is known as Doppler frequency shift or just the Doppler shift.

Doppler effect is also observed in relation to reflected ultrasound. This basic principle provides the foundation for constructing Doppler ultrasound devices to measure blood flow velocity.[8]

The magnitude and direction of the frequency shift depends on the relative motion of the moving target, their velocity and direction can be determined.[9]

The first pulsed wave Doppler equipment was developed by the Seattle Research team Donald Baker, Dennis Watkins and John Reid began working on this project in 1966 and produced one of the first pulsed Doppler devices.[10]

The Seattle team also pioneered the construction of Duplex Doppler instrumentation. Based on mechanical sector scanning head in which a single transducer crystal performs both imaging and Doppler functions on a time-sharing basis.

The Duplex Doppler technique allowed the ultrasound operator to determine for the first time the target of Doppler insonation. This development is of critical importance in Obstetrics and Gynaecological applications, as such range discrimination allows reliable Doppler interrogation of a deep lying circulation, such as that of fetus and maternal pelvic organs

The use of Doppler ultrasonography to study the flow velocity wave forms in fetal umbilical artery was reported for the first time by Fitzerald and Drumm in 1977[11] and McCallum et al.[12]

The former are recognised as the first group to publish a peer- reviewed article in this field. These publications were followed by an era of impressive research productivity during which investigators[13-21] extended the use of Doppler velocimetry for assessing various components of fetal and maternal circulations. These studies utilized continuous wave and duplex pulsed-wave Doppler technology.

PHYSICAL PRINCIPLES

DOPPLER EFFECT

The Doppler effect is the phenomenon of observed changes in the frequency of energy wave transmission when relative motion occurs between source of wave transmission and the observer. The change in frequency is known as the Doppler frequency shift or simply the Doppler shift.

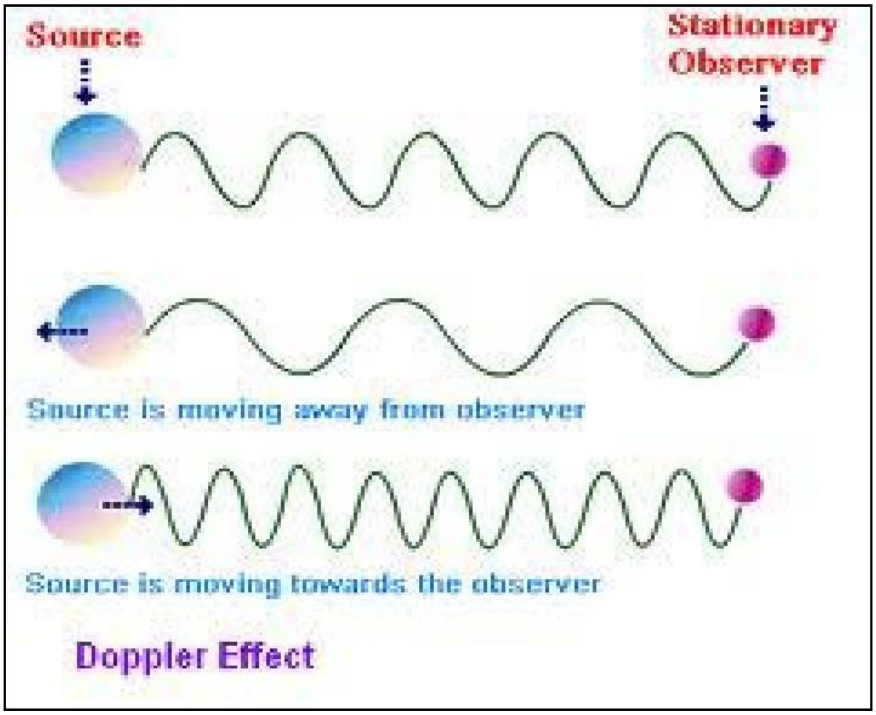


Figure 2: Doppler effect

$$Fd = Ft - Fr$$

Where,

Fd = Doppler shift

frequency Ft =

Transmitted frequency Fr

= Received frequency

When the source and the observer move closer, the wavelength decreases and the frequency increases. Conversely, when the source and the observer move apart, the wavelength increases and the frequency decreases. The utility of the Doppler effect originates from the fact that the shift in frequency is proportional to the speed of movement between the source and the receiver and therefore can be used to assess this speed.

DOPPLER UTRASOUND

The phenomenon of Doppler effect is also observed when an ultrasound beam encounters blood flow. With blood circulation millions of RBC'S act as moving scatterers of the incident ultrasound. In this circumstance the erythrocytes act first as moving receiver and then as moving sources forming the basis for the Doppler equation.

$$Fd = 2Ft\ V/C$$

Fd = Doppler frequency shift

Ft = Frequency of incident beam (transducers frequency) V = Velocity of the scatterer in a given direction

C = Propagation frequency of sound in the medium

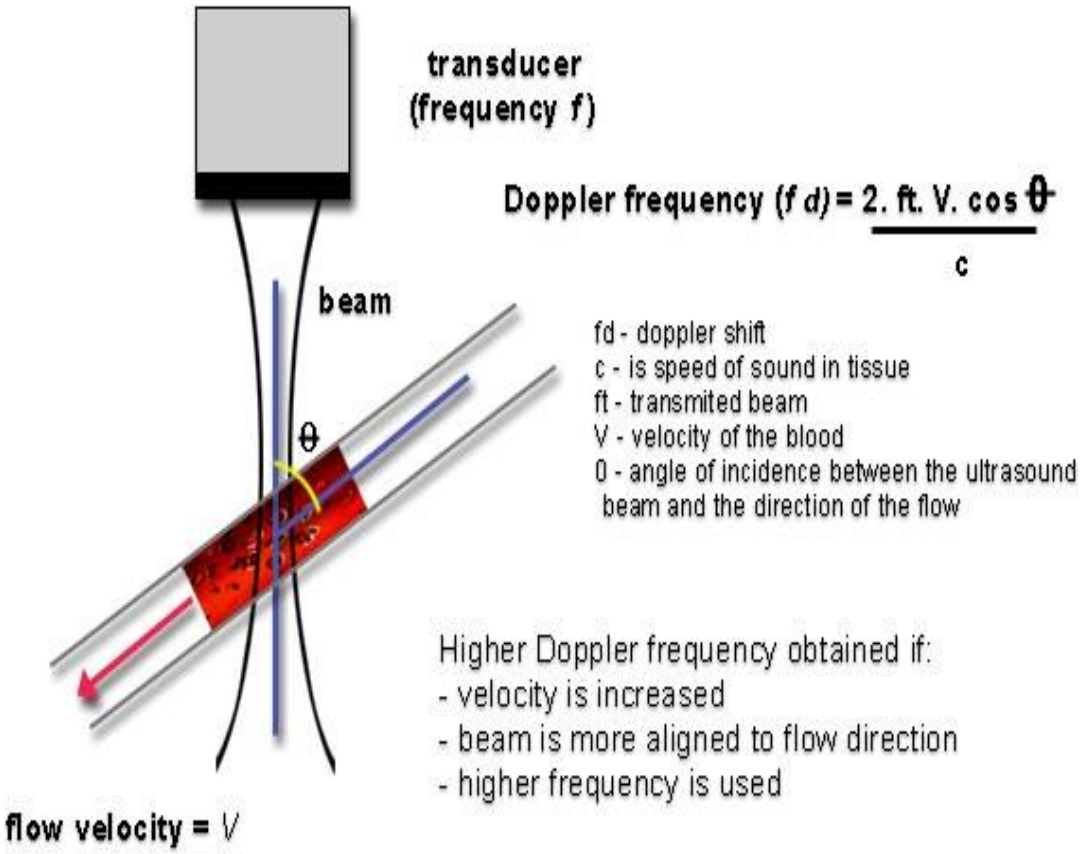


Figure 3: Doppler frequency equation

If the direction of the incident beam is at an angle to the direction of blood flow, the v in the Doppler equation is replaced by the component of the velocity in the direction of the flow (obtained by the cosine of angle $\cos\theta$)

$$Fd = 2Ft \cos V/\cos\theta$$

To determine the velocity of the scatterer the equation can be rewritten as follows

$$V = Fd\ C/2Ft \cos\theta$$

Thus, if the angle of the beam incidence and the Doppler shift are known, the velocity of the blood shift are also known, assuming that the transducer frequency and the velocity of sound in tissue remain relatively constant. The above principle forms the basis for clinical application of the Doppler principle.

High pass and Low pass filtering: The total signal input of Doppler system is comprised of not only Doppler frequency shift signals from the target vessel but also low frequency/high amplitude signals originating from moving adjacent structures such as vessel wall and cardiac valves. It also contains high frequency noise contribution from within the instrumentation. Electronic digital filters are used to eliminate the errors that arise from frequency from the external sources.

Two types of filters are used:

1) High pass filters
2) Low pass filters

High pass filters eliminates the extrinsic low frequency Doppler signals, which arise predominantly from the vessel wall or adjacent slow moving structures. This should be used with caution as a high setting eliminates end diastolic frequency shifts from

umbilical or uteroplacenatal circulation.

Low pass filter is used for high frequency noise.

Three types of devices can obtain Doppler signals

1. Continuous wave Doppler
2. Pulsed wave Doppler
3. Doppler colour flow mapping

Continuous wave Doppler: machine has two crystals one that transmits high frequency sound wave another that continuously receives signals. It can record high frequencies using low power output and is easy to use. Unfortunately it is non selective and recognises all signals along its path and does not allow visualisation of blood vessels of interests. It is used to detect fetal heart movements of even umbilical artery pulsations

Pulse wave Doppler: It has equipment that uses only one crystal which transmits the signal and then waits until the returning signal is received before transmitting another one. It is more expensive and requires higher power, but allows precise targeting and visualisation of the vessels of interest. One shortcoming of pulse wave Doppler is that a new pulse cannot be emitted before the last echo of the preceding pulse has arrived at the transducer.

Colour flow imaging: The earlier two dimensional flow imaging were based on continuous wave Doppler and non real time scanning.[22] In early 1980, a real time two-dimensional, flow imaging technique that utilized an auto correlation processor for the

detection of a moving target was introduced.[23]

Power Doppler has the greatest sensitivity and is used to detect low flow and low intensity signals such as those characteristic of venous circulation. It is not capable of determining direction of flow.

High definition Doppler is the newest addition to Doppler technology in obstetrics.

It combines the sensitivity of power Doppler with the ability to demonstrate direction of flow of colour Doppler and is useful in the interrogation of fetal venous circulation.

Various combinations of continuous wave Doppler, pulse wave Doppler, colour-flow Doppler and real-time ultrasound are commercially available and are loosely referred to as duplex Doppler.[24]

Doppler is generally used in two ways to estimate circulatory hemodynamics.

- Direct measurement of volume of blood flow
- Indirect estimation of flow velocity using waveform analysis

Blood flow measurements

Doppler shifted sound frequencies depend upon a number of factors. Pragmatic concerns include the angle of insonation(. The cosine of the angle remains close to 1 as long as the angle is kept low, but at higher angles of insonation, especially more than 60°, considerable error in measurement is introduced. Large angles between the ultrasound beam and the vessel result in a weak Doppler signal because the frequency shift is small. This phenomenon can have significant clinical importance because diastolic blood flow in a vessel can be missed because of large incident angle of the beam. Hence measurements are better, if flow is directed “head on” to the

transducer, a feat sometimes difficult to accomplish.

Blood velocity waveform analysis

Errors in direct measurement of the volume of blood flow have led to the development of several indirect indices of flow that compare different parts of the waveform, these indices are independent of the angle of insonation and do not require measurement of the diameter of the vessel.

All calculated indices are based upon the relationship between systole and diastole. Because these parameters are taken from the same cardiac cycle, these parameters are virtually independent of the angle of insonation.

Doppler indices

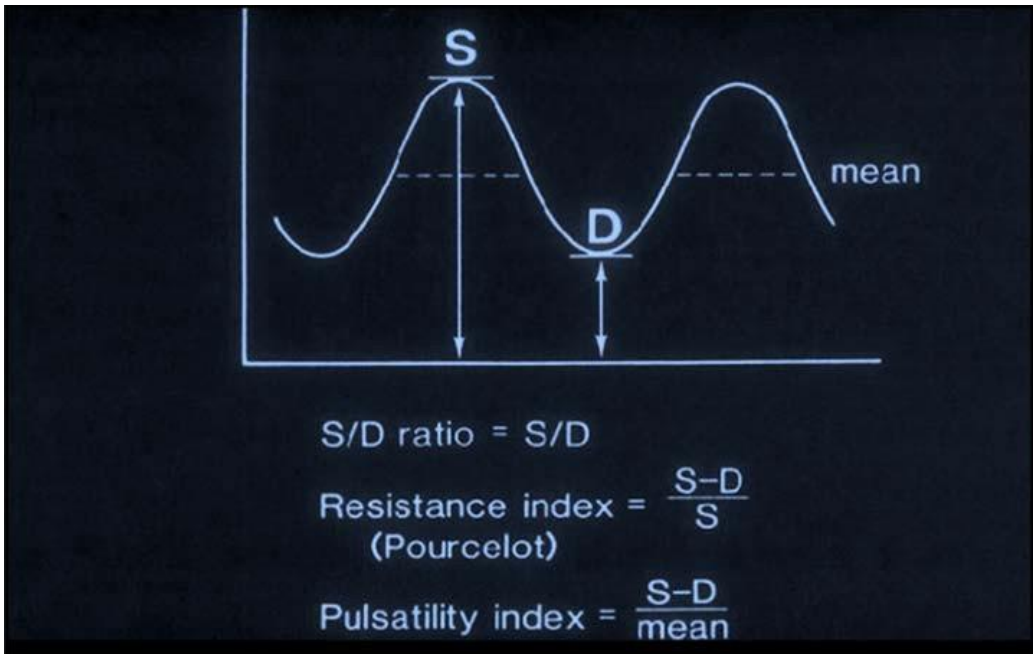


Figure 4: Doppler indices

S/D ratio gives a simple evaluation of blood flow during diastole and provides estimation of downstream resistance.[25] The pourcelot index or RI is useful when the

diastolic flow is absent or reversed and the S/D cannot be calculated.[26] Hence it helps in comparing any waveform irrespective of its diastolic flow.

The pulsatality index considers the mean velocity as diameter i.e. the whole of the flow is given consideration not just the diastolic flow and hence can be used to analyse data from various vessels without encountering the excessive variation that can be caused by division by small numbers as with the other two indices.[25]

Sources of discrepancy of Doppler indices

The configuration of an arterial Doppler waveform is modulated by hemodynamic and non-hemodynamic factors. or long term. Short term being any change in the impedance or heart rate. Long term changes in the impedance include changes in umbilical circulation with progression of pregnancy.

As gestation advances the fetoplacental circulation undergoes a consistent increase in the end-diastolic velocity and concomitant decrease in the pulsatality. The S/D ratio, RI, PI decrease throughout pregnancy. The most likely reason is the circulation experiences a progressive fall in the impedance with advancing gestation especially after 20^{th} week

The indices are also affected by:

1.fetal breathing movements: affect the fetal circulation and thus effect the peak systolic and diastolic frequencies, in addition altering the cardiac cycle. Because of this variation, Doppler waveforms from umbilical artery should be recorded only during fetal apnoea.

2)fetal heart rate: If heart rate slows, end-diatolic frequency is likely to fall, with a corresponding increase in the S/D ratio, RI and PI and vice versa. However most authors do not make corrections for heart rate as the marked changes in the umbilical artery waveform that occur due to increased placental vascular resistance over shadow the small variations due to heart rate changes.

1) location of measurement.

Non hemodynamic modalities: Inter observer and intra observer variations are the main illustrators of such errors.[27]

FDA guidelines for doing Doppler in pregnancy

1. Doppler study to be done only in clinically indicated cases for benefit of mother/fetus.
2. Equipment should be sufficiently sensitive to detect Doppler signals at low output intensity ($\leq$94mv/cm^2).
3. Operator must know the power output of machine before use.

Qualitative flow assessment

The arterial flow velocity waveforms recognised by the Doppler studies correspond to the qualitative assessment of hemodynamic status of the fetus. The ascending limb of the waveform represents the systolic blood flow that in turn represents the cardiac pump; the systolic portion of the waveform in the uterine artery represents the maternal cardiac pump and the systolic peak in umbilical artery the fetal cardiac pump.

The descending limb is the diastolic portion of the waveform that represents the status of the vascular bed. The vascular bed of uterine artery is the intervillous space and that of the umbilical arteries is the tertiary villous arteries. The early diastolic portion of the waveform represents the elasticity of the vessel wall and helps to identify whether secondary trophoblastic invasion has happened in the spiral arteries.

If the peripheral resistance falls, the slope of the descending limb decrease and the end diastolic velocity increases. In situations of high peripheral resistance, the fall in diastolic velocity will be abrupt, and the end diastolic velocity, low or absent altogether.

When flow velocities are higher than a set threshold, a phenomenon known as ‘aliasing’ occurs, which signifies high velocity flow. Ductus venosus always shows aliasing due to very high velocity flow.

Umbilical artery

Umbilical artery blood flow is an index of fetal peripheral vasoconstriction.

Umbilical artery evolves continuously during pregnancy.

Umbilical circulation:

- Twelve weeks gestation- 8.5 ml/min
- 26 weeks gestation- 80ml/min
- 37 weeks- 300 ml/min

Umbilical circulation is completed by 12^{th} week of gestation. After this the size of the cotyledon increases from 0.28 to 0.5 mm. By 20^{th} week all foetuses should have end diastolic flow. Doppler umbilical flow waveforms are early predictors of vascular disease (relative to other tests) however it is until 50% or more of the resistance vessels are obliterated that S/D ratio increases significantly. For reversal of flow more than 70% of the placental arteries must be obliterated. In the absence of any acute incident, a normal study of waveform do not develop loss of end diastolic flow within 7 days.

During normal pregnancy the UA's have low resistance with abundant diastolic flow and resultant low S/D ratios. During normal pregnancy there is a slow and continuous decline in the S/D ratio reaching lowest after 36 weeks of gestation.[28] Thus the S/D ratio decreases, from about 4 at 20 weeks to 2 at term.

Brar et al. Noted that patients with umbilical artery S/D ratio above 3 had significantly greater incidence of SGA infants, fetal distress in labour, presence of meconium at delivery, caesarean section and 5 minute APGAR<7.[29]

In placental vascular insufficiency: Placental growth continues throughout pregnancy, as demonstrated by the increasing weight. The overall increase in placental size with the resulting increase in numbers of tertiary villi and total numbers of small arterial channels results in continuing expansion of the umbilical placental vascular tree and the decreasing vascular resistance. The small arterioles of the tertiary villi are known as the resistance vessels.

The resistance vessel number per high power field is around 7 to 8 in normal as contrasted against 1-2 in subjects with abnormal umbilical artery waveforms. Placental lesion of vascular sclerosis with obliteration of tertiary villous arterioles could be expected to cause an increase in flow resistance in the umbilical flow, and could be described as the umbilical placental insufficiency.

The umbilical artery Doppler is an index of resistance to flow in the fetal- placental circulation and has a strong correlation with the presence or absence of fetal hypoxia and acidosis.

In cases of placental vascular insufficiency diastolic flow decreases causing the umbilical artery S/D ratio to increase to values 2SD or higher above the mean for the gestational age. With progression of placental vascular insufficiency there will be absent diastolic flow (AEDF) thereon reverse diastolic flow (REDF) which is an ominous sign indicating the presence of fetal hypoxia and need to deliver the fetus.[28]

Umbilical artery Doppler is considered abnormal if the S/D ratio is above the 95th percentile for the gestational age. Absent diastolic flow necessitates a complete fetal evaluation as almost 50% of cases may be due to fetal aneuploidy or a major congenital abnormality (Wenstrom and associates, 1991).

In the absence of fetal anomaly or a reversible maternal medical complication, reversed end diastolic flow suggests severe fetal circulatory compromise usually prompts immediate delivery.[30] Time gap between loss of end diastolic flow and fetal death varies for each fetus.[31]

To obtain consistent results, the umbilical artery should be studied in a free loop of cord midway between the placental insertion, the site of less resistance, and the fetal insertion, the site of maximal resistance to flow. The measurements should be taken when the fetus is not moving.[28]

A decrease in the umbilical artery end diastolic velocity and increase in the resistance index or pulsatility index can be witnessed once 30% or more of the placental vasculature is abnormal.[32] Once 60-70% of the villous tree has occurred absent or reversed end diastolic flow results.[33]

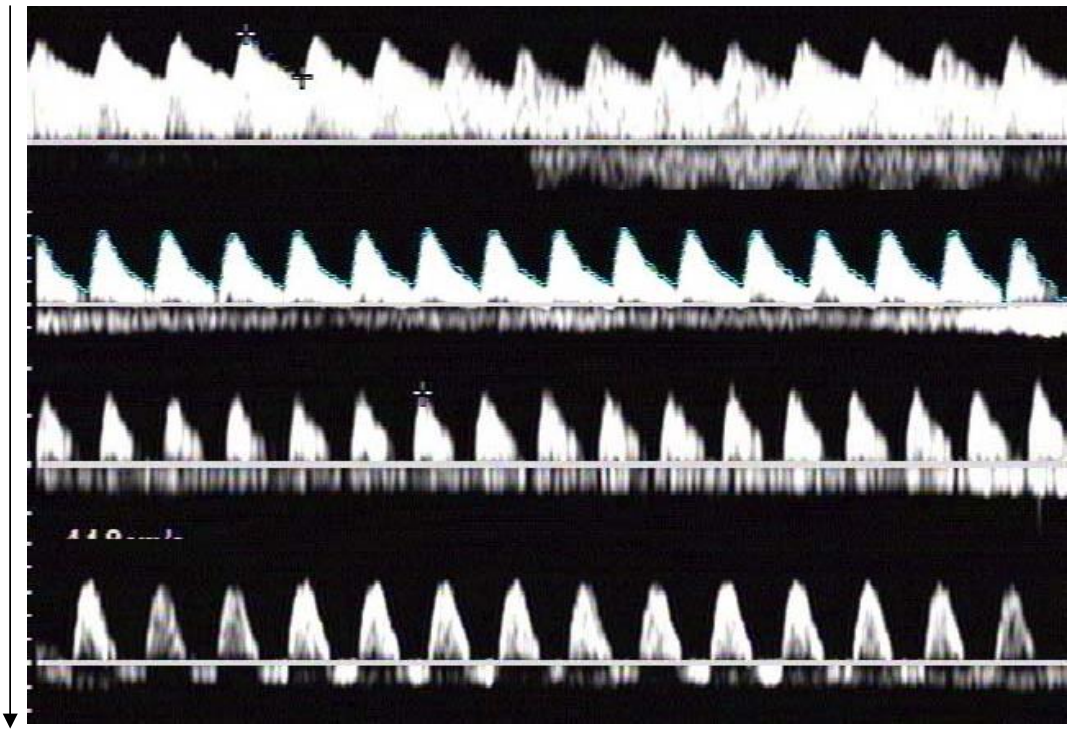


Figure 5: Increasing fetoplacental impedance and subsequent changes in umbilical artery Doppler waveforms

Absent end diastolic flow velocity

Foetuses with AEDV weighed less, were born earlier, and spent more days in ICU than other foetuses. APGAR scores were significantly low at 1 and 5 min. The perinatal mortality has been 40% (Rochelson, 1989).[34] Acidosis commonly occurs in upto 50% of foetuses with AEDV. AEDV may precede clinical stress by long period of time. It could manifest even one month before clinical signs of PIH and abnormal heart rate.

The Doppler finding with the greatest impact on pregnancy management is absent or reverse end diastolic flow in umbilical artery. REDV is an ominous finding and is associated with a high mortality rate within 1-7days if fetus is left in utero.[35]

Absent flow suggests a poor prognosis as well although outcome in these foetuses is not as poor as in those with reversed flow. With either of these findings, prompt delivery must be considered.

Uterine arteries

The majority of blood flow to the uterus is supplied by the uterine arteries. Throughout gestation, uterine blood flow increases 10-12 fold as a result of combination of physiological modification and trophoblastic invasion of spiral arteries within the myometrium and deciduas, and 50% increase in maternal blood volume.

As trophoblasts invade the walls of terminal ends of spiral arteries, there is disintegration of the internal elastic lamina. Trophoblasts penetrate the spiral arteries, media is replaced by the matrix containing cytotrophoblast and fibrin fibres. These changes are confined to the deciduas during first trimester that is primary invasion. Penetration extends into the myometrium in the early second trimester that is secondary invasion. The coiling of spiral arteries disappears by 19 weeks. By third trimester the number of spiral arteries correlates with the number of placental cotyledon. Uteroplacental circulation evolves from 14 weeks and relatively fixed by the 26th week of pregnancy.

Failure of trophoblastic invasion in spiral arteries in early weeks of pregnancy prevents the normal development of maternal placental arteries into low resistance

vessels.This leads to reduced oxygen and nutrient supply to the intervillous space.[36] The uterine blood flow increase from 50ml/min in early gestation to 500 to 750ml/min by term.

Uterine artery Doppler waveform is unique characterised by high diastolic velocities similar to systole and highly turbulent flow, with many different velocities apparent. Diastolic velocity increases and thus the indices decreases as term approaches (Hendricks 1989).[37]

Failure of the pattern to appear or the presence of a notch in the waveform at end systole has been reported with fetal growth restriction (Schulman 1986).[38] External iliac arteries can be distinguished from the uterine arteries because they normally do not have diastolic flow.

Fleischer et al. showed that when mean uterine artery S/D ratio was ≤ 2.6, there was a normal pregnancy outcome. When this level exceeded or when there was a notching in the waveforms, the pregnancy was complicated by stillbirth, premature birth, IUGR and preeclampsia.[39]

Umbilical vein

Intra abdominal portion of the umbilical vein is relatively straight and the flow tends to be constant rather than pulsating. Blood flow ranges from 108 to 153 ml/kg/min, with decreasing flow as gestation advances (Gerson 1987).[40]

Middle cerebral artery

It has high impedance low flow circulation and is a more sensitive parameter of fetal oxygenation status than umbilical blood flow. As gestation advances the fetal cerebral arterial Doppler indices show a progressive decline in the pulsatality consequent to progressive increase in the end diastolic velocity. However the normal S/D ratio of MCA is very high, compared to that of UA. The fetal MCA blood flow is a high resistance circulation throughout pregnancy and probably accounts for 7% of fetal cardiac output.[19]

In animal studies the fetal response to hypoxia is seen as a redistribution of the cardiac output in favour of the brain, myocardium and the adrenal glands at the expense of the visceral organs. This is called the "brain sparing effect".[41]

Similar changes have been documented in Doppler studies of MCA of the human fetus.[42,43,44] It is shown that the pulsatility index of the MCA was significantly lower and the mean systolic velocity was higher in the foetuses with IUGR when compared to the reference ranges for the normal foetuses.

In the growth retarded fetus, the PI of internal carotid artery and MCA were reduced and the PI of the descending thoracic aorta and umbilical artery were raised

suggesting an increased peripheral vascular resistance in the fetal body and placenta and a compensatory reduction in peripheral vascular resistance in the fetal cerebrum i.e., a brain sparing effect, in the presence of fetal hypoxia.[45]

Cerebro placental ratio is the ratio of the MCA to UA Doppler systolic to diastolic ratios. CPR compare the resistance to blood flow in the umbilical artery and the MCA.

It measures the proportion of flow supplying the brain and the placenta. It is heart rate independent and has a significant single cutoff value of 1 (CPR is normal if it >1). In redistribution of blood flow to the brain CPR becomes < 1.

The CPR ratio is a possibly better predictor of adverse outcome than the ratio in either of the vessels on their own.[46]

CPR ratio varies from 1.41 at 21 weeks to peek of 2.36 at 33 weeks. Subsequently there is a fall in the CPR to 1.97 at 39 weeks. It is important to note that in normal foetuses, the CPR is always >1, irrespective of the gestational age.[47]

The overstressed fetus can lose the brain sparing effect. It is reported that the MCA PI is below the normal range when the fetal po2 is reduced. Maximum reduction in PI is reached when the po2 is two to four standard deviations below

normal for gestation. When the oxygen deficit is greater than these levels, there is a tendency for the PI to rise again, reflecting the development of brain edema.[45]

MCA Doppler index is frequently normal during the early stages of placental dysfunction. Demonstration of cephalisation enhances the PPV of an elevated UA Doppler index for hypoxemia. It further predates the appearance of late decelerations on the CTG strip by an average of two weeks.[48]

Fetal hypoxia

Hypovolemia and hypoxia causes reduced perfusion of the liver and intensified shunting of oxygenated blood through ductus venosus. Impaired venous return from the placenta induces redistribution of umbilical venous blood.

One of the fetal adaptive responses to hypoxemia is decreased cerebral resistance.[19,45] Cephalisation of flow is associated with redistribution of cardiac output in favour of the left ventricle perfusing the brain and myocardium preferentially with oxygenated blood.[49,50]

Middle cerebral Doppler index is frequently normal during the early stages of placental dysfunction. A decrease in its Doppler measured resistance coupled with an increase in the umbilical artery Doppler index is consistent with fetal hypoxemia. Demonstration of cephalisation enhances the positive predictive value of an elevated umbilical artery Doppler index for hypoxemia. Further it predates the appearance of late decelerations on the CTG strip of IUGR fetus by an average of two weeks.[48]

Cardiac deterioration is associated with acidemia. Here venous studies are informative.[51] Venous studies reflect ventricular function and to a certain extent cardiac overload. Prolonged hypoxemia leads to hypoxemic cardiomyopathy, ventricular dysfunction, and a fall in cardiac output. As cardiac output declines,

central venous pressure raises causing increased reversal flow during atrial systole. As the severity intensifies, direction of blood flow in the ductus venosus reverses during atrial contraction causing pulsatile umbilical venous flow.

Hence the typical progression begins with increased resistance in the umbilical artery that is followed by decreased resistance in the middle cerebral artery .

AORTIC ISTHMUS DOPPLER

The aortic isthmus (AoI) is anatomically located between the origin of the left subclavian artery and the aortic end of the ductus arteriosus (DA) . There are three points in the fetal circulation that have been described as ‘watersheds’, suggesting they represent a meeting point between two vascular systems . These are the left portal vein, the foramen ovale with its crista dividens, and the AoI . Watersheds are of particular interest as their velocity waveform reflects both ventricular contributions to flow and/or the difference in downstream vascular impedance between circulations . In particular they provide significant information about fetal haemodynamic compromise and structural pathology. Because of the location of the AoI, it may also be described as the only ‘arterial shunt’ in the fetal circulation with the pos sibility for blood to be directed from its original destination towards a circuit with lesser resistance . These circuits include the brachiocephalic or the placental and subdiaphragmatic circulation, depending on the downstream impedance of each

Physiology

The fetal circulation comprises two parallel circuits with two ventricular pumps perfusing the one systemic circulation . The left ventricle (LV) perfuses the coronary and brachiocephalic circulations, while the right ventricle (RV) perfuses the subdiaphragmatic circulation and placenta . Due to this parallel arrangement, it is important to have tools to assess the LV and the RV separately . In normal fetal development the RV is predominant, with a mean cardiac output (CO) 13– 25% greater than that of the LV . In certain pathological conditions where the fetus is haemodynamically compromised, such as in intrauterine growth restriction (IUGR), it is thought that the RV is affected earlier

and to a greater degree . This RV strain is demonstrated.

by earlier dilation, hypertrophy, and dysfunction compared to changes in the LV . The anatomical location of the AoI means the LV and RV contribute to AoI flow in opposing directions . LV ejection is responsible for systolic anterograde flow through the AoI, whereas the RV is responsible for systolic retrograde flow . The direction of systolic AoI blood flow is thus determined by the comparative LV and RV stroke volumes along with the downstream vascular impedances . In diastole, when the two semilunar valves are closed, the direction of AoI blood flow is determined purely by the balance of downstream vascular impedance in the brachiocephalic and placental and subdiaphragmatic circulation . The AoI waveform can therefore be seen as the product of a complex interaction between (a) LV and RV ejection and (b) brachiocephalic plus placental and subdiaphragmatic vascular impedance. The numerous inputs that shape the AoI waveform distinguish it as a vessel of interest whilst making its interpretation difficult. The AoI has a characteristic Doppler velocity waveform. Firstly, there is a quick systolic upstroke ranging between 30 and 100 cm/s from 11 weeks' gestation to term that gradually decelerates during gestation . By 25 weeks a narrow incisura then appears which suggests a progressive reduction in AoI antegrade flow . A brief reversal of systolic flow is visible from 28 weeks' gestation that has been identified as the nadir of systole . A previous study questioned whether this could be an artefact , but the systolic nadir is now thought to be physiologically accurate. The AoI waveform changes slightly throughout gestation, reflecting both the physiological evolution of fetal ventricular function and changes in peripheral vascular impedance with gestation. In normal fetuses antegrade flow is present in the first half of pregnancy in both systole and diastole of the AoI waveform due to low placental vascular impedance. The gradual deceleration of the

systolic upstroke with a brief reversal of flow may be due to increasing RV dominance, coupled with the rise in placental impedance that occurs with gestation . However, a large cross-sectional study (458 fetuses) found no correlation between AoI PI and umbilical artery (UA) PI, suggesting rather that they could be considered independent factors for fetal surveillance . The reduction in cerebrovascular resistance that occurs during normal gestation, as evidenced by the progressive decrease in the middle cerebral artery (MCA) resistance indices, may also contribute to these changes that occur later in gestation, due to the rise in RV preload and output being directed via the DA .

AORTIC ISTHMUS DOPPLER IN IUGR

Intrauterine Growth Restriction IUGR complicates approximately 3–10% of all pregnancies , and may be characterised by 'brain sparing', where the fetus compensates for chronic hypoxia by redistributing blood flow to vital organs including the brain and myocardium, particularly in early-onset disease . This haemodynamic compensation can cause sequential right cardiac failure, followed by left cardiac failure being observed just prior to intrauterine demise . As there is no effective in utero therapy , obstetric management involves timing delivery before decompensated heart failure but preferably after sufficient fetal lung maturation to minimise neonatal complications . In current clinical practice, fetal heart rate analysis, biophysical parameters, and ultrasound indices such as UA, MCA, and ductus venosus (DV) Doppler can only guide clinicians, as the usual sequence of recognised changes do not occur in all fetal demise cases . Other Doppler indices or vessels of interest published in the literature in relation to IUGR monitoring include the cerebroplacental ratio [CPR, which combines two of the above parameters (MCA PI/UA PI)], MPI, hepatic artery, umbilical vein, E/A ratios, and

outflow tracts . The direction of oxygenated blood to the brachiocephalic circulation with uteroplacental insufficiency has led the AoI to be studied in IUGR fetuses . Placental insufficiency causes a reduction in RV CO, while LV CO is usually preserved . Alterations in the diastolic component of the AoI therefore reflect comparative impedance of the cerebral and peripheral vascular beds. To date most studies involving AoI Doppler have focused on diastole, attempting to assist in the timing of delivery of IUGR fetuses . Reversed diastolic AoI flow suggests significant fetal hypoxic deterioration, usually occurring after the UA, MCA, and CPR Doppler parameters become abnormal, but preceding DV Doppler abnormalities by an average of 1 week . In a fetal sheep model with stepwise compression of umbilical veins, as well as in a computer based fetal circulation model, the appearance of net retrograde flow in the AoI physiologically demonstrates cerebral hypoxia despite local vasodilation and preservation of cerebral blood flow. This is due to poorly oxygenated preplacental blood coming from the RV contaminating the ascending aortic blood (coming from the LV) destined for the brain, resulting in a reduction in mean oxygen tension in the cerebral vascular bed . Additionally, these fetuses cannot shift their RV CO from the pulmonary circulation through the foramen ovale. IUGR fetuses that maintain antegrade AoI net blood flow increase the flow across the foramen ovale to ensure highly oxygenated blood flow reaches the coronary and cerebral vascular beds.

This has led to questioning whether the cerebral hypoxia detected by reverse net diastolic AoI blood flow causes cerebral damage. Retrograde diastolic AoI waveforms have been shown to be associated with poor neurodevelopmental outcome , although despite being highly specific, sensitivity was low . Similarly, it was suggested abnormal AoI PI and/or IFI could predict adverse perinatal outcomes including perinatal mortality in early-onset

IUGR and may be a complementary measure in timing delivery, although gestational age at delivery was a significant cofounding factor in these studies . A prospective multicentre study of 157 early-onset IUGR fetuses aimed to validate these results. While abnormal AoI IFI was significantly associated with perinatal mortality, on decision tree analysis and multivariate models it was not clinically useful for predicting mortality, suggesting it is instead a surrogate marker of brain sparing . The large PORTO study also investigated the sensitivity and clinical utility of AoI PI and RI (among other Doppler measures) in monitoring small for gestational age fetuses and did not find the AoI to be of benefit. However, a sizeable portion of their cases were of late-onset IUGR. Hence their findings cannot be applied to early-onset cases, and the AoI may yet prove to have a clinical role in the early-onset subgroup . AoI IFI, PI, and RI are therefore still largely research tools for the assessment and management of placental insufficiency and are yet to be incorporated into clinical practice. Studies thus far have identified the specificity of AoI diastolic indices to detect IUGR and have made some significant research associations with neurological sequelae; yet the AoI lacks the sensitivity to detect all IUGR fetuses at risk . Until longitudinal follow-up studies or randomised study protocols indicate a benefit from AoI use in clinical practice, it will continue to remain a research tool. As AoI ISI is a new index, only two abstracts exploring the ISI in IUGR fetuses exist in the literature. One study found that the ISI was significantly lower in 62 IUGR fetuses compared to controls until 32 weeks' gestation. It also found that the systolic nadir of the AoI became retrograde at 26 weeks in IUGR fetuses compared to 31 weeks in their normal population ; yet the established ISI normal range study found that the systolic nadir appeared at 28 weeks' gestation in a normal population . The other abstract on 113 IUGR fetuses also found statistically different systolic nadir values when

comparing IUGR fetuses with balanced haemodynamic status to those with poor circulatory status (CPR<1)

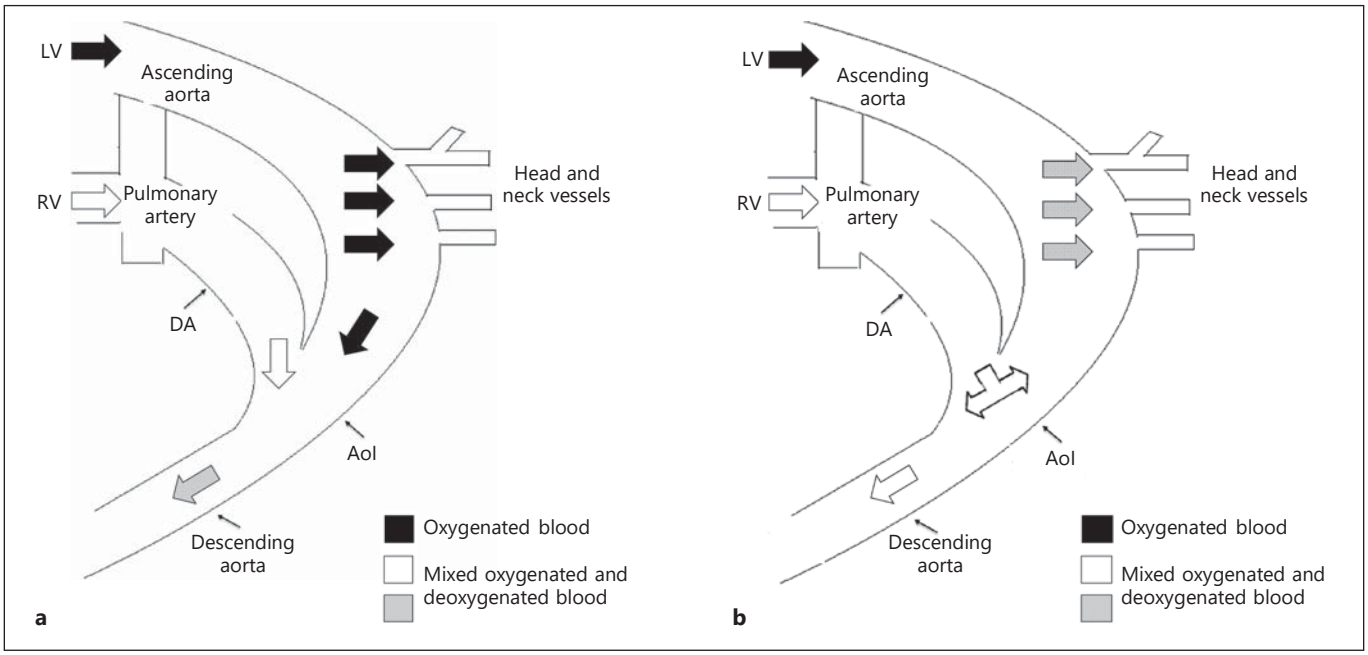


Fig 6 schematic representation of blood flow in aortic isthmus in normal and IUGR fetus

Doppler in the management of Growth restricted foetuses

Management depends upon the gestational age. In mature foetus, little is gained by continuing pregnancy, and they tend to decompensate early, hence delivery is recommended. Induction of labour would be reasonable with a reassuring fetal heart rate. In immature foetus close surveillance is needed. Once there is AEDF in the UA, twice weekly BPP and repeat of Doppler indices, daily fetal kick counts, and growth scans every 2-3 weeks should be done. With flow reversal in UA or cephalisation in MCA, daily BPP and Doppler studies are indicated. Pulsatile pattern in ductus venosus Doppler indicates fetal acedemia and necessitates delivery. A fetus with either REDF/DV pulsations has little reserve and will not likely tolerate labour.[55]

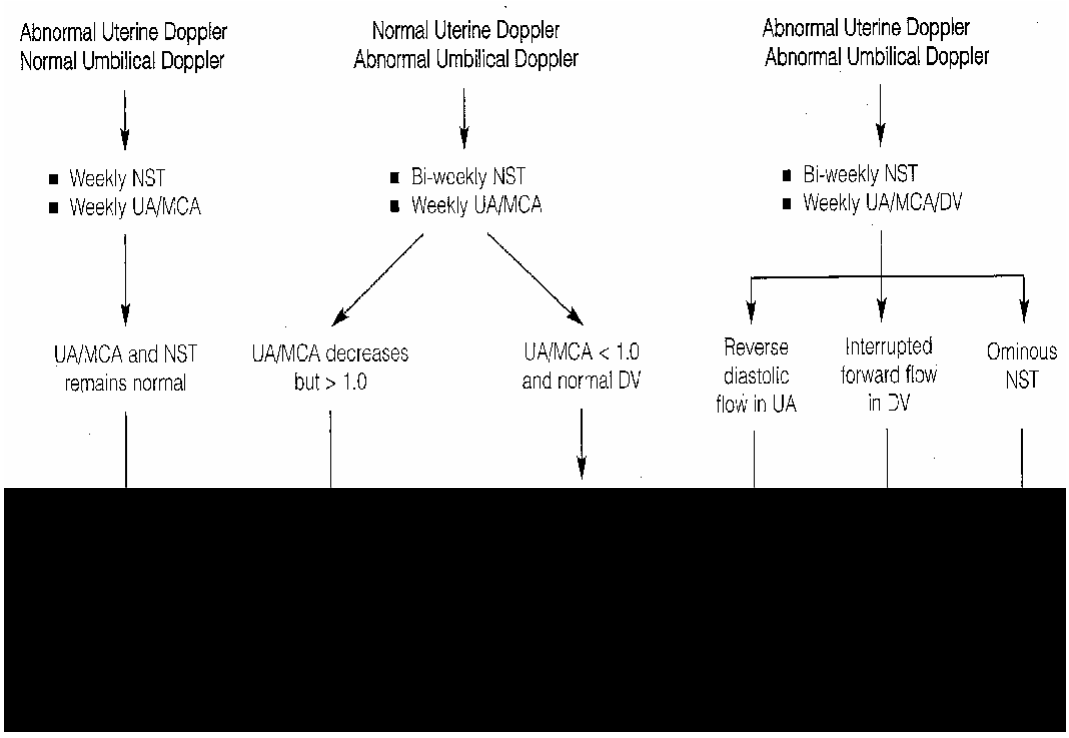


Figure 7: Management of fetal growth restriction secondary to placental insufficiency

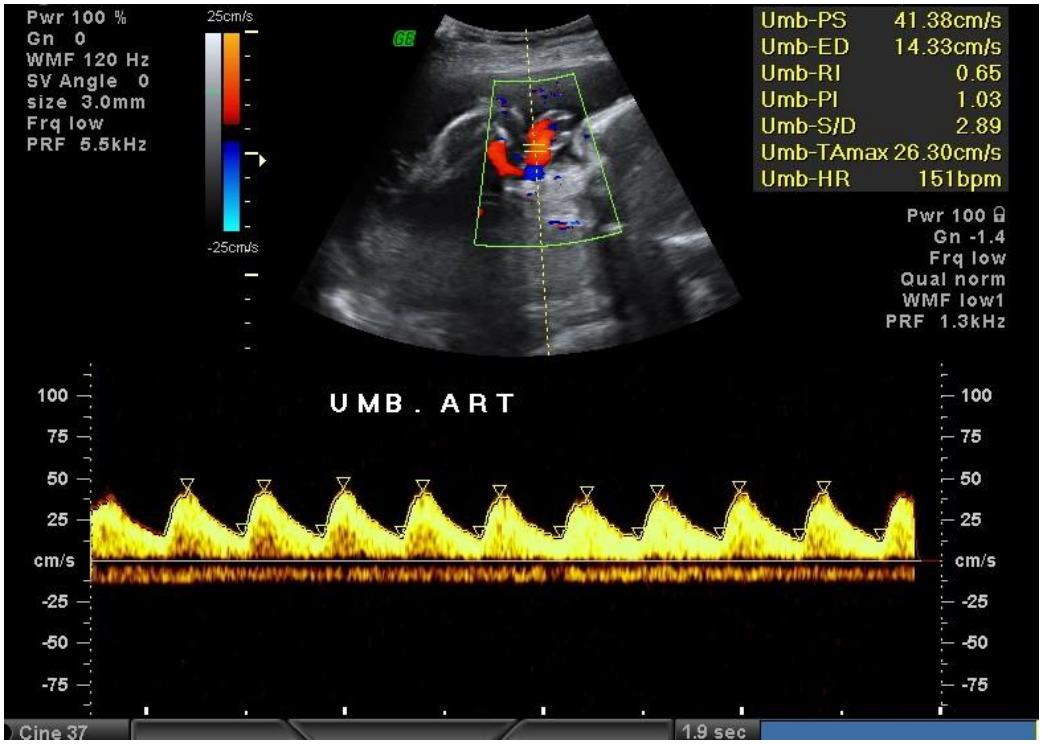


Figure 8: Normal umbilical artery wave form

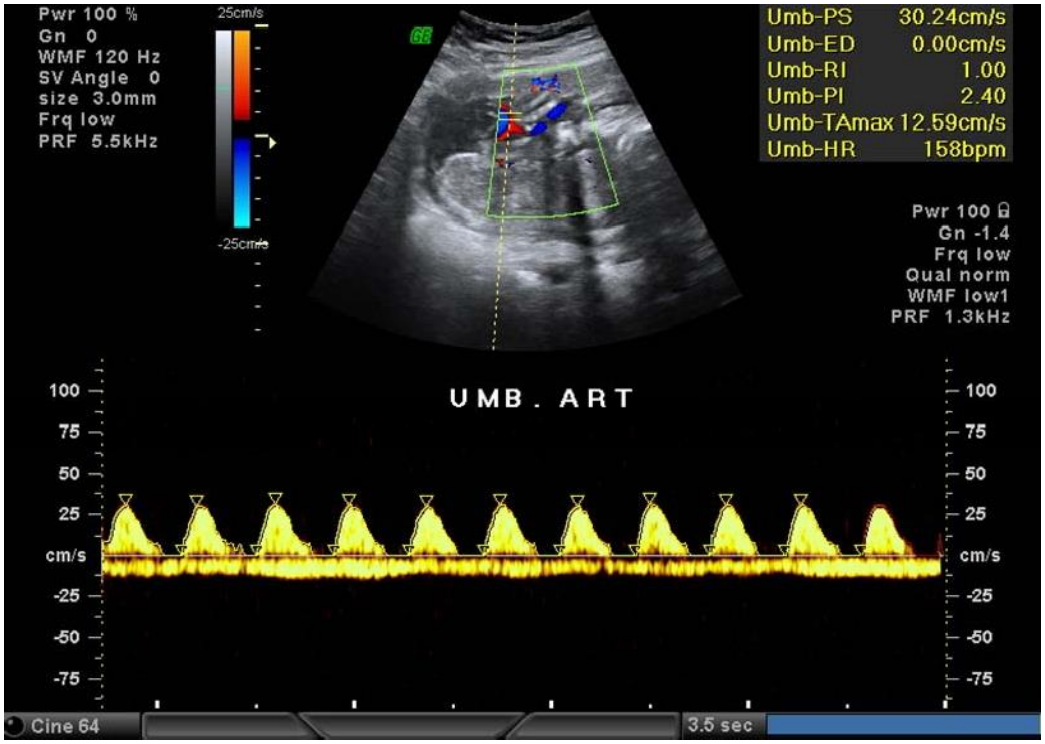


Figure 9: AEDF in umbilical artery

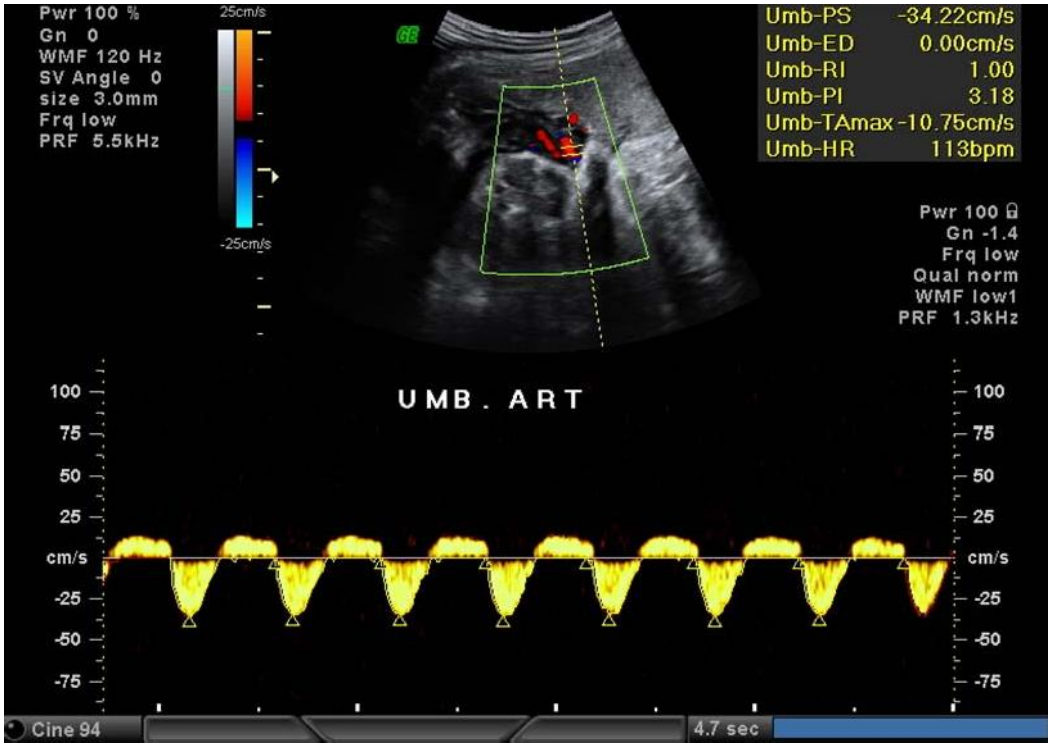


Figure 10: REDF in umbilical artery

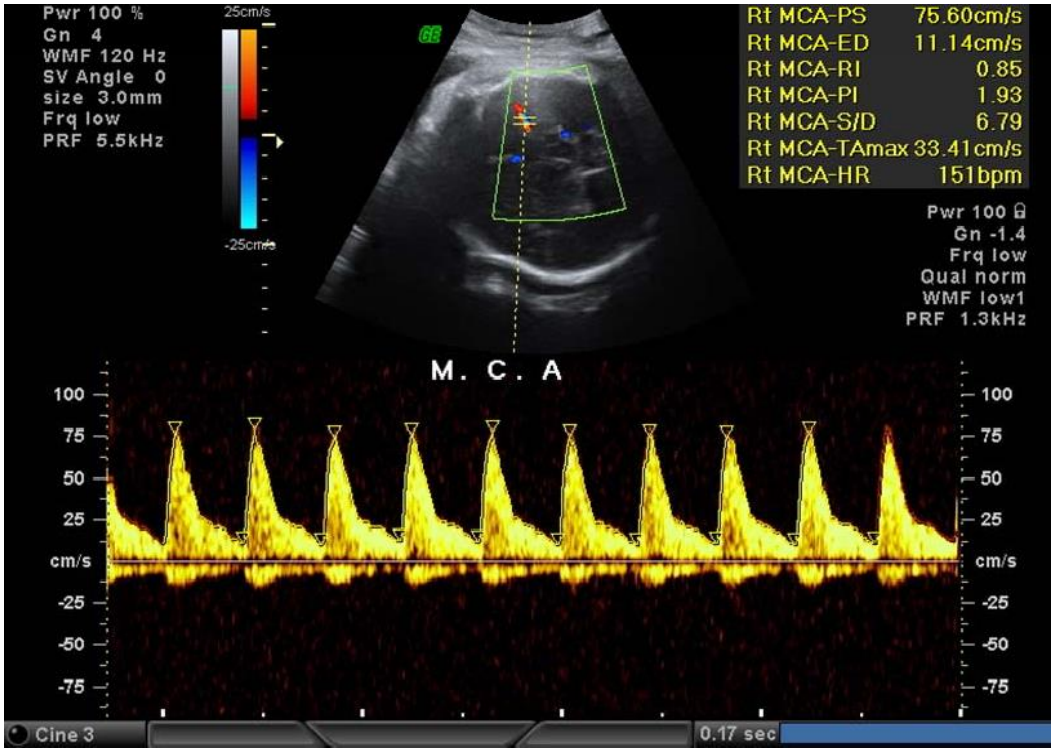


Figure 11: MCA normal flow

Figure 12: Redistribution of flow in MCA

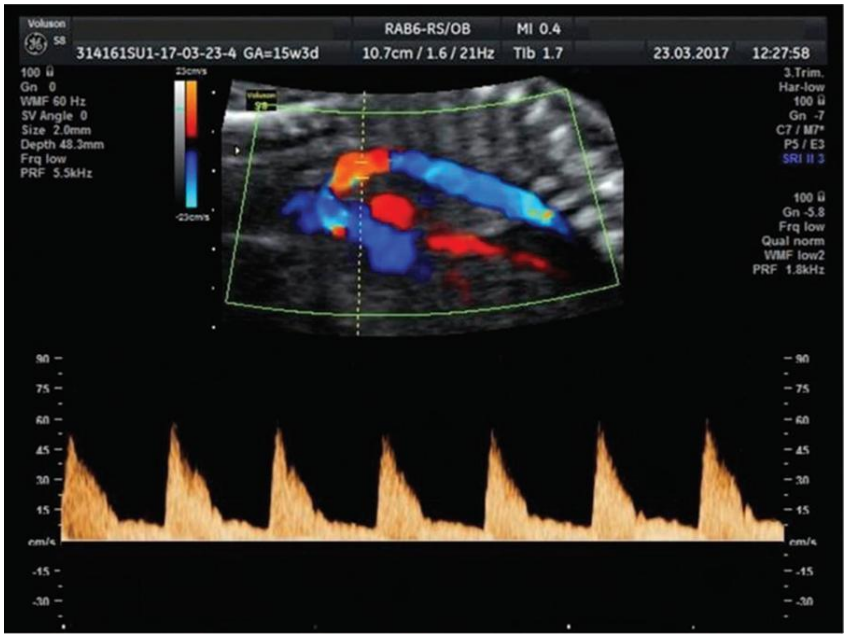


Fig 13 Anterograde flow in aortic isthmus

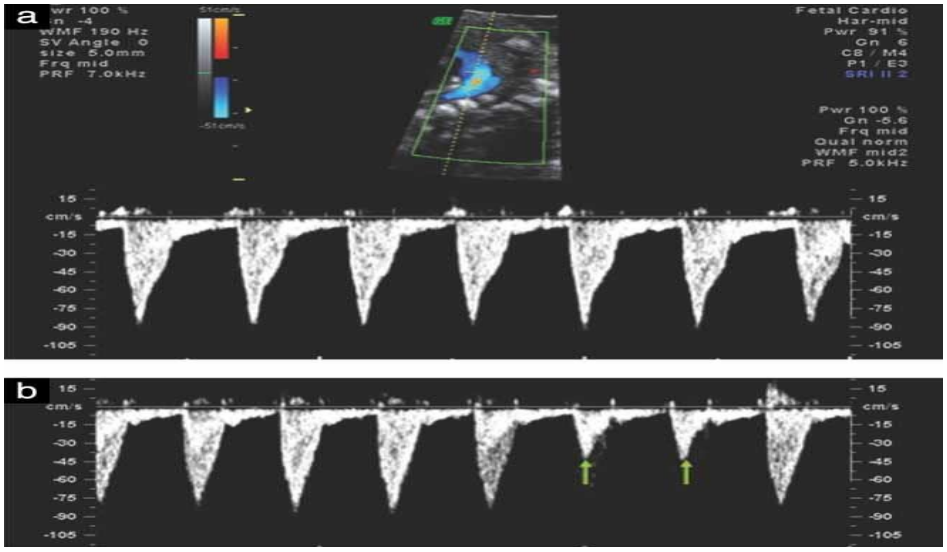
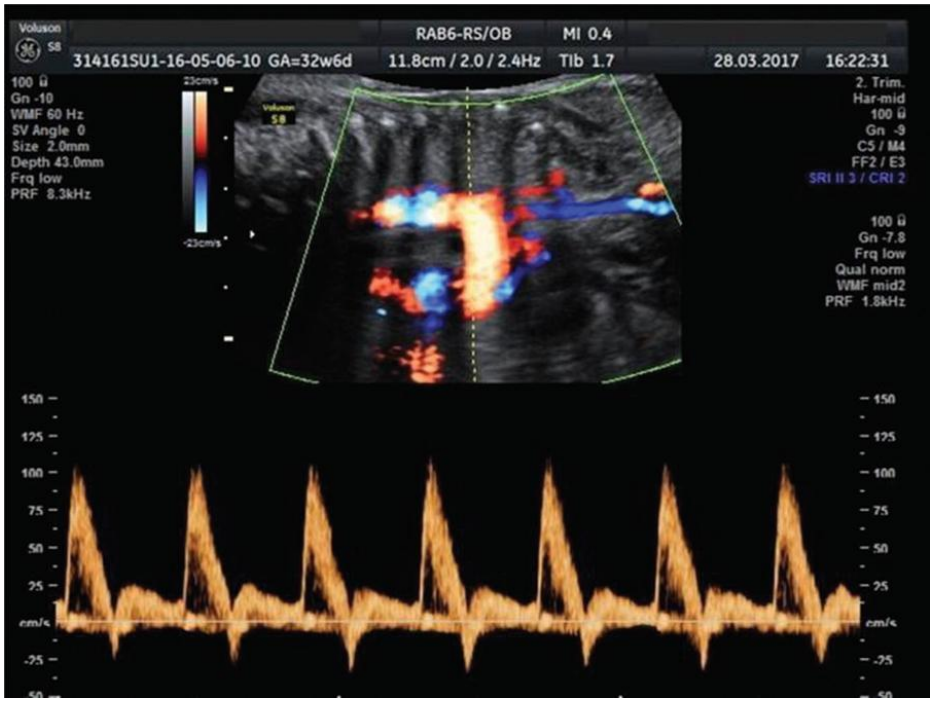


fig 14 retrograde flow in aortic isthmus



Literatures:

Maulik D, Yarlagadda AP, et al.[56] investigated the diagnostic efficiency of umbilical artery S/D ratio as a screening tool in 350 consecutive singleton pregnancies at 34-36 weeks. Abnormal S/D ratios resulted in abnormal perinatal outcomes which included SGA, APGAR<7 at 5 minutes, umbilical artery PH at birth <7.2, presence of thick meconium, fetal distress in labour, NICU admissions.

Brar et al. 1989[29] noted that when umbilical artery S/D ratio is >3 than there is a greater chance of SGA, APGAR score<7 at 5 minutes, caesarean section for fetal distress and thick meconium in labour.

Yoon, Lee, Kim[57] reported that an abnormal umbilical artery velocimetry had a significantly higher rate of complications like caesarean section for fetal distress, preterm delivery, low APGAR score, neonatal morbidity and perinatal death. He concluded that an abnormal Doppler umbilical artery waveform is a strong and independent predictor of adverse perinatal outcome in patients with preeclampsia.

Karsdorp VH, Van Vugt JM, et al.[58] classified high risk pregnancy according to the degree of waveform abnormality. The study concluded that reversed diastolic flow velocities had the most unfavourable outcome. Abnormal umbilical Doppler study alerts the possibility or probability of fetal compromise associated with placental pathology.

Thakur Sita, Negi PC, et al.[59] studied Doppler waveform analysis of umbilical artery of 53 normal pregnant women, of which 29 were primigravida and 24 multigravidas. From the study it was concluded that Doppler evaluation of the umbilical artery flow velocity waveform can be used as an additional diagnostic tool in identifying foetuses at risk in complicated pregnancies and their management.

Kusum Saxena, Sofia H, et al.[60] conducted blood flow study of arteries on 58 antenatal patients with known gestational age through last menstrual period. This study concluded that colour Doppler study of various arteries, indicating their flow pattern during pregnancy is important for obstetricians when dealing with complicated pregnancies such as those with PIH and IUGR. The blood flow indices directly correlates with the neonatal outcome in the form of baby weight, APGAR score and neonatal morbidity. In hypertensive group 66.66% were AGA and 33.33% were SGA. Among AGA abnormality of uterine arteries were seen in 31 patients, 66.66% in right uterine arteries and 62.5% in left uterine artery. 17 patients(70.83%) in umbilical artery, 22 patients (91.66%) showed brain sparing effect while 2 patients(8.33%) had abnormality in MCA. In the group of SGA, out of 12 patients all (100%) had abnormalities in uterine arteries, umbilical artery, 50% showed brain sparing effects and 50% showed abnormal MCA.

Chauhan R, Samiksha T[61] studied 23 pregnant patients who had high risk factors. Patients were subjected to Doppler study of umbilical artery beyond 30 weeks of gestation. S/D ratio>3 were taken as abnormal (13 cases showed normal Doppler and 9 cases showed increased S/D ratio in umbilical artery and 1 case had absent flow during diastole). 90% of patients with abnormal umbilical artery Doppler study had adverse perinatal outcome and the perinatal outcome with normal Doppler was good.

Lakhkar BN, Rajagopal KV, Gourisankar PT[62] studied fifty eight singleton pregnancies beyond 30 weeks of gestation complicated by IUGR and severe preeclampsia or both using Doppler ultrasonography of the umbilical artery, middle cerebral artery, descending abdominal aorta, umbilical vein and inferior venacava. 36 patients of the 58 included included in the study population had atleast one major or minor adverse outcome. Major adverse outcome criteria incuded perinatal deaths. Minor outcomes included caesarean delivery for fetal distress, APGAR score below 7 at 5 minutes, admission to NICU for treatment. S/D ratio of MCA/UA is the most sensitive and specific index in predicting major perinatal adverse outcome(83% and 75%) while umbilical artery S/D ratio is the most sensitive index (66.6%) in predicting any adverse perinatal outcome. They concluded that the sensitivity of Doppler studies can be significantly increased by studying multiple vessels (91.6%) and can help in the monitoring of compromised fetus and can help predicting neonatal mortality.

Padmagirison Radhika, Rai Lavanya[63] compared the efficacy of Doppler vascular technique over non stress test (NST). There were 55 women with preeclampsia or IUGR, 29 cases with abnormal Doppler and 20 with abnormal NST. Doppler abnormalities preceded NST changes; lead time was 4-14 days. There were

10 perinatal deaths, 5 of which occurred in the group were both tests were abnormal. Doppler identifies fetal compromise earlier than NST.

Shah Nehal[64] studied 70 women with high risk pregnancy, patients were subjected to serial ultrasonography Doppler studies of umbilical and middle cerebral artery, 16 neonates (22.85%) required neonatal intensive care unit admission. Caesarean section was required in 25 (35.71%), 36 subjects (51.42%) had SGA fetus, 5 still births and 2 early neonatal death. Umbilical artery AEDF was observed in 10 subjects, of whom 4 declined still birth. The umbilical artery PI<5th centile in 3 women, all of whom had a still birth.

Ghosh GS, Gudmundsson S[65] studied 353 singleton pregnancies complicated by foetal growth restriction. The women underwent Doppler examination of the umbilical and uterine arteries. Abnormal uterine artery Doppler velocimetry was seen in 120 (33.4%) pregnancies and abnormal umbilical artery Doppler in 102 (28.4%). There was a statistically significant correlation between abnormal Doppler of both the umbilical and uterine arteries and adverse outcome of pregnancy in the form of small for gestational age newborns, caesarean delivery, premature delivery (<37 weeks of gestation) and admission of the newborn to a neonatal intensive care unit. Women with normal umbilical artery Doppler (251) were analysed separately. Abnormal uterine artery Doppler, seen in 61 (24.3%) of those women, showed a statistically significant correlation for adverse outcome of pregnancy. They concluded Doppler examinations of the uterine and/or the umbilical arteries are comparable as predictors of outcome in pregnancies complicated by fetal growth restriction. Including uterine artery Doppler in the surveillance of growth-restricted fetuses might detect a group of pregnancies at high risk, even though the umbilical artery Doppler was normal.

Rozeta Shahinaj, Nikita Manoku et al.[66] studied the Doppler velocity waveforms in 738 patients with preeclampsia and gestational hypertension. The study population was divided into two groups depending on the normal or abnormal values of MCA/UA pulsatility index ratio. Neonates of mothers with abnormal values of MCA/UA pulsatility index ratio(314 patients) had significantly lower gestational age at delivery (34.8 versus 38.4), lower birth weight (2174.6 g versus 3215.0g), significantly greater risk for perinatal death (30.8% versus 0.23%) significantly greater risk of admission to intensive care unit (77.8% versus 47.4%), longer duration of treatment in NICU (10.6 days versus 6.5 days), greater rate of caesarean delivery for fetal distress (76.7% versus 62.5%), a great number of neonates with low APGAR score at 5 minute (61.9% versus 22.4%), a great number of foetuses with IUGR (7.18% versus 1.76%). They concluded that MCA/UA pulsatility index ratio is a very good predictor of adverse outcome in the fetuses of women with preeclampsia and gestational hypertension.

Shahina Bano, Vikas Chaudhary, Sanjay Pande, Mehta VL, Sharma AK[67] Studied 90 pregnancies of 30-41 weeks of gestation diagnosed clinically with IUGR. The UA PI and the MCA PI as well as the cerebro/umbilical(C/U) ratio were calculated. Of the 90 pregnancies in the study, 24 showed abnormal UA PI. Among these, 21 (87.5%) were SGA and 19 (79.2%) had adverse perinatal outcome. Of the four of the 90 pregnancies that showed abnormal MCA PI, all were SGA and had adverse perinatal outcome. Similarly, of the 20 out of 90 pregnancies that showed abnormal C/U ratio (<1.08), all 20 (100%) were SGA and had adverse perinatal outcome. They concluded that (1) The C/U ratio is a better predictor of SGA fetuses and adverse perinatal outcome than the MCA PI or the UA PI used alone, (2) The UA

PI can be used to identify IUGR per se and (3) The MCA PI alone is not a reliable indicator for predicting fetal distress.

Yelikar Kanan A, Prabhu Akahata, et al.[68] conducted a prospective study on 189 pregnant women beyond 32 weeks of gestation with preeclampsia or growth restricted foetuses who were evaluated with Doppler velocimetry of umbilical and middle cerebral artery and NST. Accordingly both Doppler and NST had a better specificity and negative predictive value, indicating that these tests were more predictive of a healthy fetus. The fetal compromise in terms of APGAR scores, NICU admissions, birth weight, etc., was greater when both Doppler and NST were abnormal. Doppler detected changes earlier in the disease cascade than NST as evidenced by the lead time of 5.86 days.

Varsha Deshmukh, Yelikas KA, Priyanka Deshmukh[69] studied 150 preeclamptic and gestational hypertension patients and stratified them into two groups based on the MC/UA PI ratio. 110 women were in group A (ratio>1.08) and 40 women in group B (<1.08). Rate of LSCS was significantly high (P<0.001) in group B than group A. There was a statistically significant increase in perinatal morbidity in group B. APGAR scores were found to be lower in group B than group A. In group A 35 (31.8%) were IUGR babies and 37 (92.5%) in group B. Stillbirth were 2(1.8%) in group A and 3(7.5%) in group B. ratio<1.08). They concluded that MCA/UA PI ratio is a valuable predictor of perinatal outcome in pregnancies complicated by preeclampsia and hypertension.

AIM:

- Role of umbilical artery, middle cerebral artery, and fetal aortic isthumus waveforms in predicting adverse pregnancy outcomes in clinically suspected IUGR and the role of doppler velocimetry in clinical management of such pregnancies

OBJECTIVES :

- To analyse the blood flow in fetal aortic isthumus, Umbilical artery Middle cerebral artery, in a group of patients with clinically suspected high risk pregnancies
- To assess the value of Doppler ultrasound in analyzing PERINATAL OUTCOME in patients with clinically suspected high risk pregnancies

Study center Govt. RSRM Lying in Hospital

Duration of Study NOVEMBER 2020 TO DECEMBER 2021

Study design Prospective study

Methodology

This study was conducted on 200 women with high risk pregnancies within inclusion criteria admitted to Govt RSRM Lying in hospital, Chennai

A routine History taking ,General examination, Obstetric examination was done

Patients were explained about the atraumatic nature of the investigation and Informed written consent will be obtained

Synthetic ultrasound gel was applied over the abdomen to get good accoustic coupling

The instrument used was a Mindray colour Doppler ultrasound machine with a convex transducer 2 to 5 mhz frequency.

Doppler wave form was obtained after localising the vessels by B mode real time scanner

Pulsed Doppler was used to get the Doppler signals after localising the vessels

The maximum Doppler shift frequencies were obtained and various ratios will be calculated from each vessel.Doppler examination will be done when fetus is in apneic state to avoid influence of fetal respiration on doppler signals

The gestational Age was based on the LMP ,Ultrasound biometry performed before 20th week if LMP is uncertain. Follow up Doppler studies were conducted if clinically indicated or in case of worsening Doppler indices.

Identification of various arteries and their criteria

1.Aortic Isthmus: Assessment of fetal aortic isthmus index was performed in the longitudinal aortic arch or the three vessels and trachea view.a quantitative assessment of flow velocity waveform of the aortic isthumus was made

2**. Umbilical Artery**: Flow velocity waveforms from umbilical artery can be easily Obtained, for this colour flow is not usually needed. Doppler signals were acquired from different points in cord, usually from mid portion of cord. Values of S/D ratio, RI and PI>95th percentile as per the Harrington et al Doppler indices, presence of absent end diastolic velocity (AEDV) and reversed end diastolic velocity (REDV) were considered abnormal.

3. **Middle Cerebral Artery (MCA):** MCA was visualized in transverse axial view of fetal head at a Slightly more caudal plane than the one used for BPD. PI and RI < 5^{TH} percentile as per the Harrington et al Doppler indices were considered abnormal

Systolic flow (A) and the diastolic flow (B) for the above mentioned arteries were obtained. Doppler indices were calculated.

Systolic/Diastolic(S/D) ratio= A/B Resistance

index= A-B/A Pulsatality index= A-B/mean

Further management of the cases were decided depending on the clinical status of the patients and the Doppler report, and pregnancies were terminated as and when indicated.Patients who continued pregnancy after the Doppler examination, Doppler was repeated at weekly interval. Doppler study done within 7 days prior to termination of pregnancy was taken into consideration for the study.

INCLUSION CRITERIA

All antenatal cases more than 30 weeks of gestation singleton pregnancies, clinically diagnosed as the following were included

- IUGR(EFW <10TH percentile for gestational age)
- Those who gave consent for the study
- The gestational Age will be based on the LMP, Ultrasound biometry performed before 20th week if LMP is uncertain

EXCLUSION CRITERIA:

The following pregnancies were excluded

- Cardiovascular disease
- Multiple gestation
- Fetus with congenital anomalies
- Renal disease
- Essential hypertension prior to pregnancy
- Intrauterine death at the time of first doppler examination

Sample size : 200

Based on the reference study 200

Formula:

$n = Z^2pq / d^2$

Where Z = 1.96 (statistical significant constant for 95% CI)

p = 95% (Sensitivity of Cerebroplacental ratio in Triple vessel doppler in predicting adverse perinatal complications or death from previous study.)

q = 5% (100-p)

d = 3% absolute precision

On substituting, in the formula

n = 3.84 x 95 x 5 / 9=202 ; Adding 10% non response rate

n = 220 (minimum sample size)(1 GROUP)

OUTCOME CRITERIA

Doppler ultrasound results will be analysed for prediction of perinatal outcome. Outcome variables included are

- Birth weight $<10^{th}$ percentile
- Perinatal death
- Emergency Lscs for fetal distress
- Low Apgar score (5 min score less than 7)
- Admission to NICU for complications of low birth weight ,NICU stay >48 hrs

- Meconium stained liquor

Pregnancy was considered to be adverse if any of the above criteria were present

STATISTICAL METHODS APPLIED

Descriptives: The Descriptives procedure displays univariate summary statistics for several variables in a single table and calculates standardized values (z scores). Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which you select the variables (the default).

Crosstabs (Contingency table analysis): The Crosstabs procedure form two–way and multiway tables and provides variety of tests and measures of association for two–way tables. The structure of the table and whether categories are ordered determine what test or measure to use.

Chi–Square Test: The Chi-Square Test procedure tabulates a variable into categories and computes a Chi-Square statistic. This test compares the observed and expected frequencies in each category to test either that all categories contain the same proportion of values or that each category contains a user-specified proportion of values. The results are considered statistically significant if the p value<0.05.

The sensitivity and specificity of positive test is also computed wherever required for Doppler. All the statistical calculations were done through SPSS for Windows (v 16.0).

RESULTS

The study comprised a total of 200 patients.

Table 1: Age distribution

Age in years	No. of patients	Percentage
<20	75	35
21-25	80	42
26-30	40	21
30-40	4	2
Total	200	100

The age of the patients in this study ranges from 18 years to 36 years of which majority belonged to the age group of 21-25 years with a mean age of 22.8 years (SD 3.6 years).

Figure 15: Age distribution

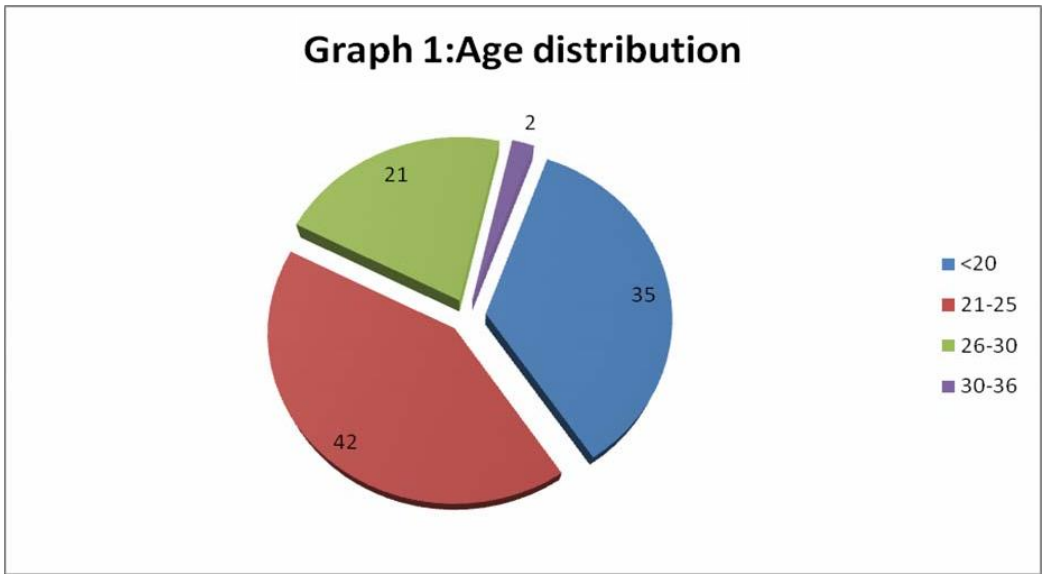


Table 2: Parity of patients

Parity	No. of patients	Percentage
Primi	138	69
Multigravida	62	31
Total	**200**	**100**

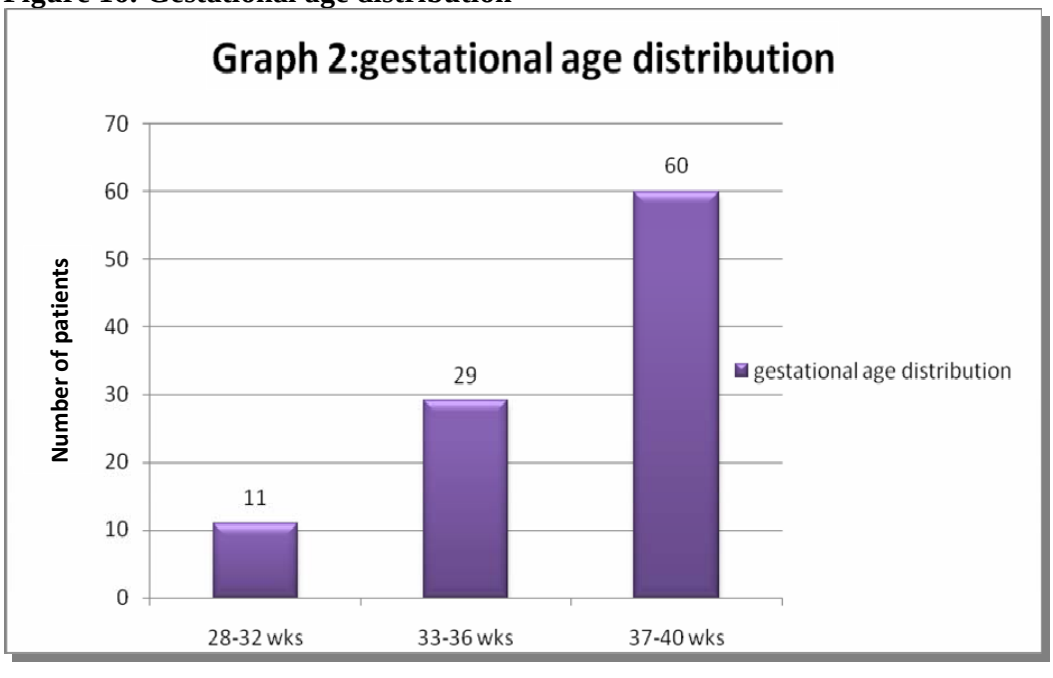
In the present study the incidence of primigravida (69%) was more than that of multigravida (31%).

Table 3: Gestational age distribution

Gestational age(wks)	No. of patients	Percentage
28-32	22	11
33-36	58	29
37-40	120	60
Total	**200**	**100**

The study group included patients whose gestational age ranged from 28-40 weeks. Mean gestational age was Maximum number of patients (60) belonged to 37-40 weeks group.

Figure 16: Gestational age distribution



Umbilical artery Doppler studies

Table 4: Umbilical artery S/D ratio distribution analysis

S/D ratio	No. of patients	Percentage
<3	82	43.5
>3	102	56.5
Total	**184**	**100**

Out of the 200 patients studied 10 patients had AEDF and 6 patients had REDF, hence S/D ratio could not be calculated in them. Amongst the remaining 182 patients 43.5% (82 patients) had a normal umbilical artery S/D ratio(<3) while the rest 56.5% (102 patients) had elevated S/D ratio.

Table 5: Umbilical artery S/D ratio correlation with fetal outcome

Fetal outcome	Increase in S/D ratio		Normal S/D ratio		p-value	Sensitivity	Specificity
	No. (N=102)	%	No. (N=82)	%			
Birth weight <10th percentile	26	57.7	40	25.0	<.05	75%	57.6%
LSCS for fetal distress	22	25.0	2	5.0	<.05		
Meconium stained liquor	25	51.9	16	15.0	<.05	81.8%	61.8%
APGAR<7 (5 min)	28	53.8	1	2.5	<.05	96.5%	66.1%
NICU admission	41	78.8	8	20	<.05	83.6%	74.4%
NICU stay >48hrs	27	51.9	3	7.5	NS	90%	26.3%
Perinatal mortality	13	25	0	-			

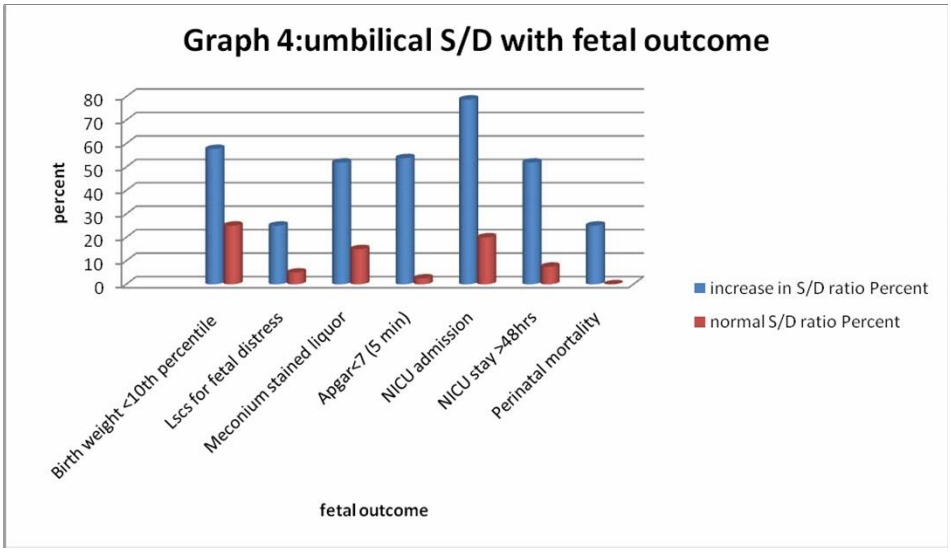


Figure 17: Umbilical artery S/D ratio correlation with fetal outcome

Umbilical artery S/D ratio analysis showed that patients with S/D ratio>3 had a poor perinatal outcome. Perinatal mortality was seen in 13 patients with an elevated S/D ratio, while those with a normal S/D ratio had no perinatal mortality. Birth weight<10th percentile was seen in 57.7% patients in the abnormal S/D group. Thirteen patients with an elevated S/D underwent LSCS for fetal distress, whereas the incidence was only (5%) in the normal S/D ratio group. Meconium stained liquor was present in (51.9%) and (53.8%) had babies with APGAR<7 at 5 minutes in the elevated S/D ratio group. (78.8%) of babies in the elevated S/D group required NICU care of whom (51.9%) had to stay for>48hrs, whereas in the normal S/D group(20%) required NICU care and 3 amongst them had to stay >48hrs.

The above data shows a strong statistical correlation with poor pernital outcome and increased perinatal morbidity and mortality with an increased umbilical artery S/D ratio (<3).

Table 6: Umbilical artery RI ratio

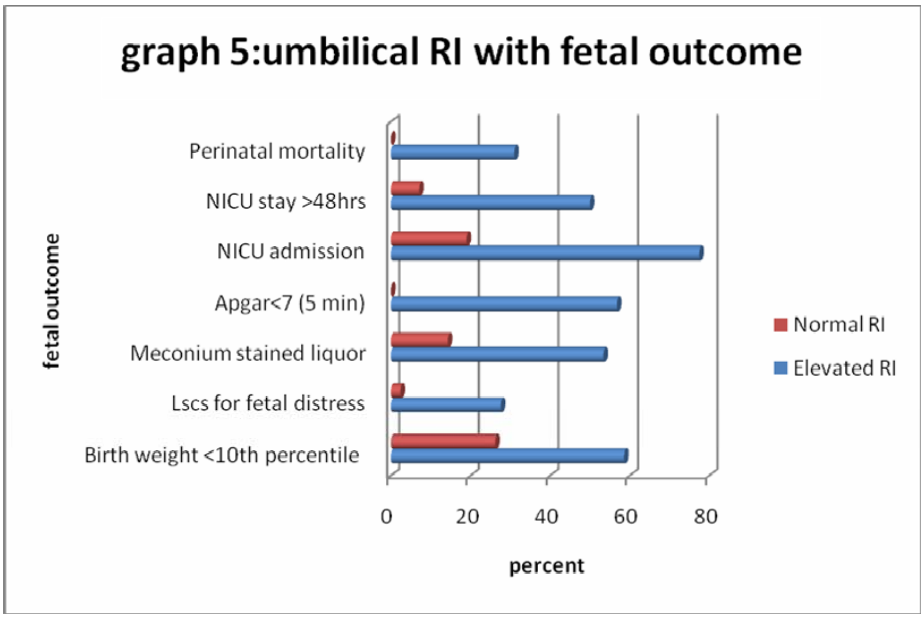
RI	No. of patients	Percentage
Elevated	116	58
Normal	84	42
Total	**100**	**100**

After analysis of umbilical artery RI ratio it was seen that 116 (58%)patients had elevated RI, whereas 84 of the remaining had normal RI.

Table 7: Umbilical RI values correlation with fetal outcome

Fetal outcome	Elevated RI		Normal RI		p-value	Sensitivity	Specificity
	No. (N=116)	%	No. (N=84)	%			
Birth weight <10th percentile	40	58.6	32	26.2	<.05	75%	56.3%
LSCS for fetal distress	16	27.6	4	2.38	<.05		
Meconium stained liquor	31	53.4	20	14.28	<.05	83.7%	64.2%
APGAR<7 (5 min)	33	56.8	0	-	<.05	100%	71.1%
NICU admission	45	77.5	22	19	<.05	84.9%	72.3%
NICU stay >48hrs	29	50	6	7.1	NS	90.6%	23.8%
Perinatal mortality	18	31	0	-			

Figure 18: Umbilical RI values correlation with fetal outcome



Umbilical artery RI value analysis showed 40(58.6%) patients delivered babies weighing<10th percentile compared to 32(26.2%) in those with a normal RI. LSCS for fetal distress had to be done in 16 patients in the elevated RI group while only 4 patient with a normal RI underwent LSCS for the same. 31(53.4%) patients had meconium stained liquor in the elevated RI group compared to 20(14.28%) amongst the normal RI group. All babies in the normal RI group had 5 minute APGAR values>7 while 33(56.8) babies in the elevated RI group had APGAR<7. NICU care was required in 45(77.5%) and NICU>48hrs in 22(50%) in the elevated RI group, compared to 8(19%) and 3(7.1) in the normal RI group. Perinatal mortality rate was 31%(18) in the elevated RI group.

Most of the values were statistically significant ($p<.05$) except NICU stay>48hrs. In this study elevated RI had 100% sensitivity in predicting APGAR<7 at 5 minutes.

Table 8: Umbilical PI values

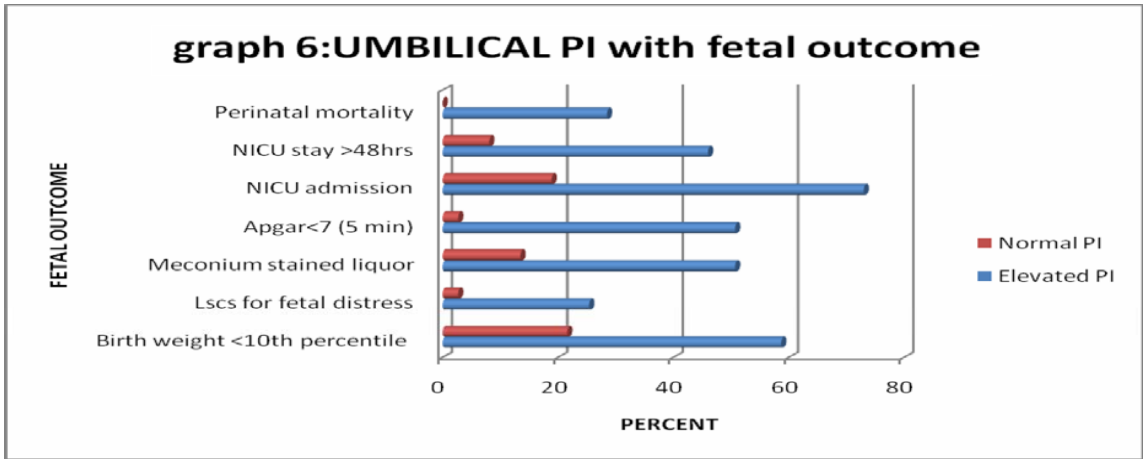
Umbilical PI	No. of patients	Percentage
Elevated	126	63
Normal	74	37
Total	**200**	**100**

126 patients of the 200 had elevated PI values whereas remaining 74 patients had normal PI values.

Table 9: Umbilical PI correlation with fetal outcome

Fetal outcome	Elevated PI		Normal PI		p-value	Sensitivity	Specificity
	No. (N=126)	%	No. (N=74)	%			
Birth weight $<10^{th}$ percentile	66	58.7	26	21.6	<.05	82.2%	52.7%
LSCS for fetal distress	16	25.4	14	2.7	<.05		
Meconium stained liquor	32	50.7	16	13.5	<.05	86.4%	57.1%
APGAR<7 (5 min)	32	50.7	7	2.7	<.05	96.9%	61%
NICU admission	46	73	20	18.9	<.05	86.7%	63.8%
NICU stay >48hrs	29	46	10	8.1	NS	90.6%	19.0%
Perinatal mortality	18	28.5	-				

Figure 19: PI values distribution with fetal outcome



66 (58.7%) patients with an elevated PI values delivered babies weighing <10th percentile and those with normal PI had 21 (21.6%) babies weighing <10th percentile. Sixteen (25.4%) with an elevated PI underwent LSCS for fetal distress while only 7 (2.7%) with a normal PI underwent LSCS for the same. Thirty-two (50.7%) patients with elevated PI had meconium stained liquor and baby APGAR values<7 at 5min. Only 16(13.5%) had meconium stained liquor and 7(2.7%) had APGAR<7 in the normal PI group. NICU admission was needed in 46(73%) in the elevated RI group and 29 of them required care for >48hrs, whereas 7(18.9%) required NICUcare and 3 of them had to stay beyond 48hrs in the normal PI group. Perinatal mortality rate was 28.5%(18) in the abnormal PI group, whereas none of the cases with a normal PI had perinatal mortality.

Statistical correlation was drawn and found to be significant ($p<.05$)in most of the parameters(except NICU stay>48hrs) in predicting poor perinatal outcome. PI values had highest sensitivity(96.9%) for predicting low APGAR values and highest specificity(63.8%) for predicting NICU admission.

Absent end diastolic flow in umbilical arteries

Out of the 100 cases studied 10 patients had AEDF in the umbilical arteries.

AEDF correlation with fetal outcome

Out of the 10 cases with AEDF, 2 delivered a stillborn fetus, 4 babies were deeply asphyxiated and died within 5 hours of birth. One of the 6 perinatal mortalities was 2 preterm baby. 4 out of the 5 live births had meconium stained liquor and all 4 had APGAR<7 at 5 minutes. 3 cases had babies weighing <10th percentile.

REDF in umbilical arteries and fetal outcome

6 cases out of 200 studied had REDF in the umbilical arteries. All 6 delivered stillborn babies. 5 out of 6 cases were preterm.

Table 10: Absent/Reversal of flow velocities

AEDF/REDF in umbilical arteries	No. of patients	Percentage
Present	16	9
Positive diastolic flow	184	91
Total	200	100

Middle cerebral artery Doppler indices MCA S/D

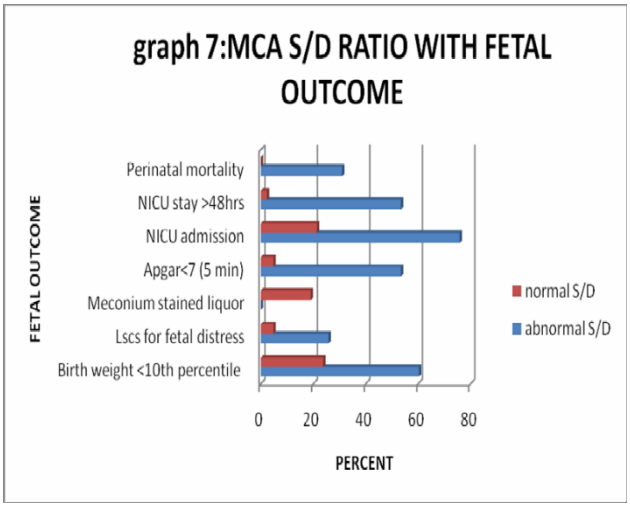
ratio

Amongst the 200 cases 116 had abnormal MCA S/D ratio and the remaining 84 had normal S/D ratio values.

Table 11: MCA S/D ratio with fetal outcome

Fetal outcome	Abnormal S/D ratio		Normal S/D ratio		p-value	Sensitivity	Specificity
	No. (N=116)	%	No. (N=84)	%			
Birth weight <10th percentile	60	60.3	30	23.8	<.05	77.7%	58.1%
LSCS for fetal Distress	15	25.8	10	4.76			
Meconium stained liquor	55	50.0	18	19.0	<.05	78.3%	60.7%
APGAR<7 (5 min)	31	53.4	4	4.76	<.05	93.9%	67.7%
NICU Admission	78	75.8	20	21.4	<.05	83%	70.2%
NICU stay >48hrs	31	53.4	3	2.3	<.05	96.8%	38.0%
Perinatal mortality	18	31	-				

Figure 20: MCA S/D ratio with fetal outcome



In this study it was seen that abnormal MCA S/D ratio was associated with 60(60.3%) babies with birth weight<10^{th} percentile, 15(25.8%) LSCS for fetal distress, 55(50%) patients with meconium stained liquor, 31 babies with APGAR <7(5min), 78 NICU admissions amongst which 31 required stay beyond 48hrs and a perinatal mortality rate of 31%(18). In those cases with a normal S/D ratio, 30(23.8%) had babies weighing<10^{th} percentile, 10 LSCS for fetal distress, 18(19%) patients with meconium stained liquor, 4 babies with APGAR<7(5min), 20(21.4%) NICU admissions. No perinatal mortality was seen amongst the normal MCA S/D ratio group.

All data showed statistical significance(<.05) and MCA S/D had a sensitivity of 96.8% in determining the NICU stay>48hrs and a specificity of 70% in determining NICU admissions.

MCA RI ANALYSIS

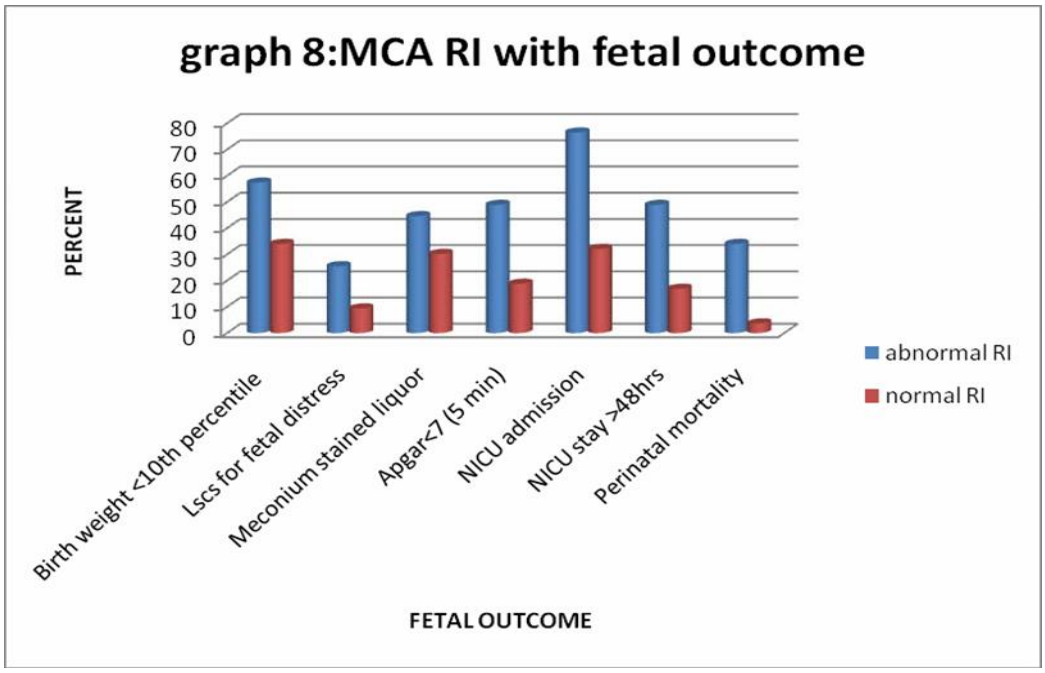
94 patients had decreased RI values in the fetal MCA and the remaining 106 had normal values.

Table 12: MCA RI with fetal outcome

Fetal outcome	Abnormal RI		Normal RI		p-value	Sensitivity	Specificity
	No. (N=94)	%	No. (N=106)	%			
Birth weight <10^{th} percentile	55	57.4	33	34	<.05	60%	63.6%
LSCS for fetal distress	25	25.5	10	9.4	<.05		
Meconium stained liquor	40	44.6	30	30.2	BS	56.7%	66.0%
APGAR<7 (5 min)	48	48.9	19	18.8	<.05	69.6%	72.8%
NICU admission	70	76.5	28	32.1	<.05	67.9%	76.5%

NICU stay >48hrs	36	48.9	18	16.9	NS	71.8%	38.0%
Perinatal mortality	16	34	4	3.7			

Figure 21: MCA RI with fetal outcome



94 cases had abnormal MCA RI and 106 had a normal RI. 55(57.4%) of the abnormal group had SGA babies compared to 18(34%) in the normal group. LSCS for fetal distress rate was 25.5% in the abnormal group and 9.4% in the normal. 40 cases had meconium stained liquor and 48 had APGAR<7 at 5min in abnormal group as against 16 and 10 in the normal group. 36 cases (76.5%) babies of the abnormal group were admitted to NICU and 23 of them hat to stay>48 hrs, while in the babies of the normal group the incidence of NICU admission was 32.1% (17 cases) and NICU>48hrs was 16.9% (9 cases). Perinatal mortality rate in abnormal group was 34% and 3.7% in normal group.

MCA RI had the highest sensitivity (71.8%) for NICU stay >48hrs and highest specificity for predicting NICU admissions (76.5%).

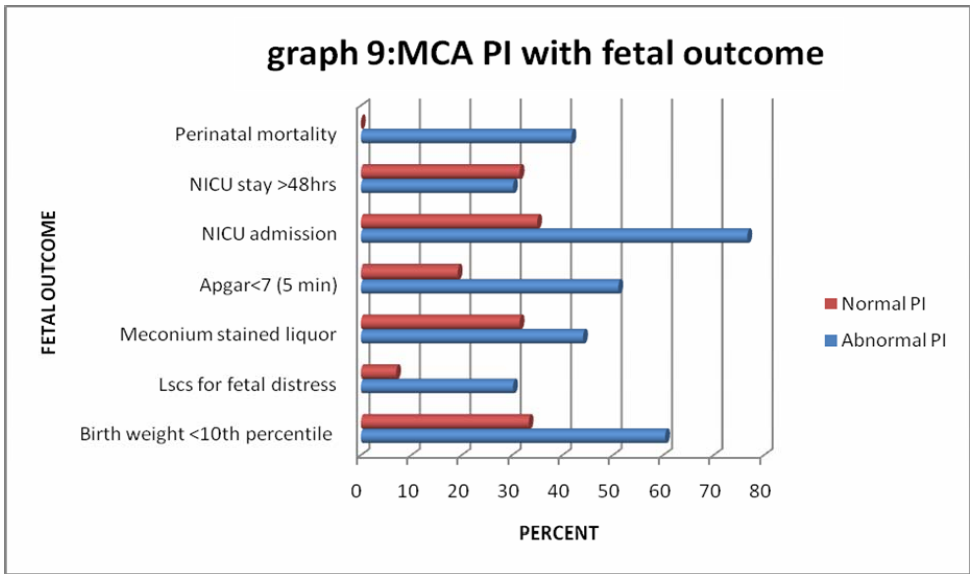


Figure 22: MCA PI with fetal outcome

In this study it was seen that abnormal MCA PI was associated with 66(60.4%) babies with birth weight<10th percentile, 36(30.2%) LSCS for fetal distress, 50(44.1%) patients with meconium stained liquor, 52 babies with APGAR <7(5min), 87 NICU admissions amongst which 34 required stay beyond 48hrs and a perinatal mortality rate of 41.8%(18). In those cases with a normal PI, 35(33.3%) had babies weighing<10th percentile, 4 LSCS for fetal distress, 38(31.5%) patients with meconium stained liquor, 22 babies with APGAR<7 (5min), 30(35%) NICU admissions.

No perinatal mortality was seen amongst the normal MCA PI ratio group. All data except two showed statistical significance(<.05) and MCA PI had a sensitivity of 66.6% in determining APGAR<7 at 5min and a specificity of 78.7% in determining

NICU admissions.

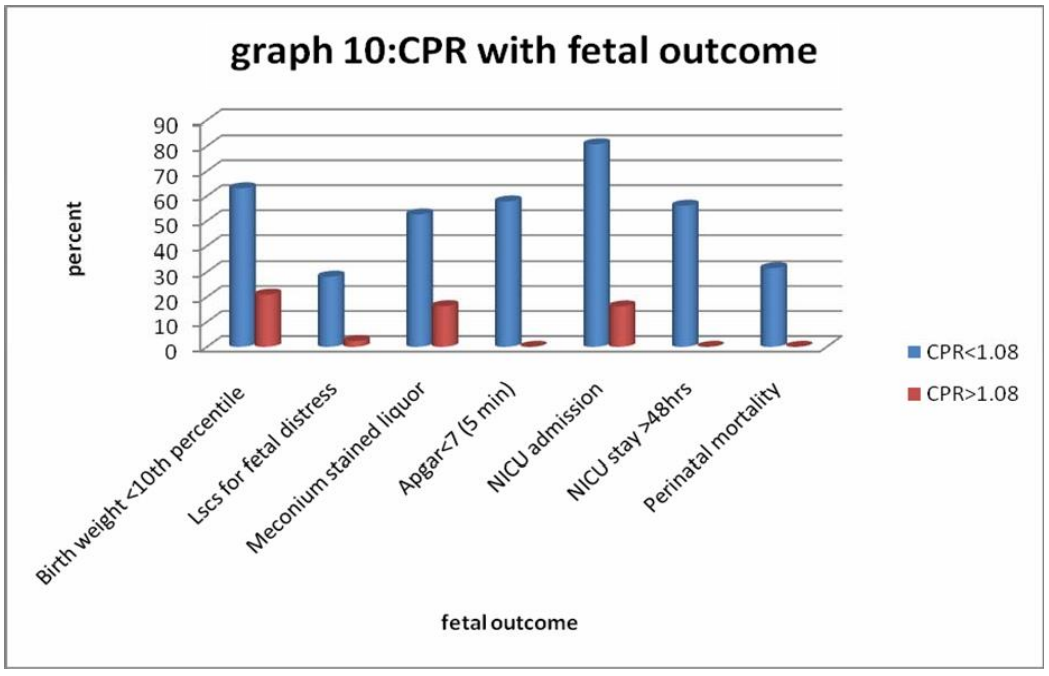
Cerebro placental ratio analysis

Is the ratio of PI of MCA to PI of umbilical artery. 114 cases out of 200 had a CPR <1.08 showing redistribution of blood flow ("BRAIN SPARING EFFECT").

Table 13: CPR correlation with fetal outcome

Fetal outcome	CPR<1.08		CPR>1.08		p-value	Sensitivity	Specificity
	No. (N=114)	%	No. (N=86)	%			
Birth weight <10th percentile	64	63.1	26	20.9	<.05	80%	61.8%
LSCS for fetal distress	30	28.1	10	2.3	<.05		
Meconium stained liquor	57	52.6	28	16.3	<.05	81%	64.2%
APGAR<7 (5 min)	59	57.8	0		<.05	100%	72.8%
NICU admission	91	80.7	28	16.2	<.05	86.7%	76.5%
NICU stay >48hrs	56	56.1	0		<.05	100%	33.3%
Perinatal mortality	18	31.5					

Figure 23: CPR correlation with fetal outcome



AORTIC ISTHMUS DOPPLER ANALYSIS

Of the 200 cases studies 97 had retrograde AIEDF and 103 had anterograde AIEDF

Table 14: aortic isthmus doppler analysis

Fetal outcome	AIEDF RETROGRADE		AIEDF ANTEROGRADE		p-value	Sensitivity	Specificity
	No. (N=97)	%	No. (N=103)	%			
Birth weight <10th percentile	67	73.1	22	20.9	<.05	90%	61.8%
LSCS for fetal distress	55	58.1	13	2.3	<.05	92%	60%
Meconium stained liquor	65	70.6	20	16.3	<.05	88%	64.2%
APGAR<7 (5 min)	78	80.8	0		<.05	100%	72.8%
NICU admission	92	95	17	16.2	<.05	95%	76.5%
NICU stay >48hrs	88	91	2	4	<.05	94%	78%
Perinatal mortality	28	31.5					

In this study it was seen that abnormal AIEDF was associated with 67(73.4%) babies with birth weight<10th percentile, 55(58.2%) LSCS for fetal distress, 65(70.6%) patients with meconium stained liquor, 78 babies with APGAR <7(5min), 92 NICU admissions amongst which 88 required stay beyond 48hrs and a perinatal mortality rate of 28.8%(28). In those cases with a normal PI, 22(20.3%) had babies weighing<10th percentile, 13 LSCS for fetal distress, 20(16.5%) patients with meconium stained liquor, NO babies with APGAR<7 (5min), 17(16%) NICU admissions. No perinatal mortality was seen amongst the normal AIEDF ratio group. All data showed statistical significance(<.05) and AIEDF had a sensitivity of 100 % in determining APGAR<7 at 5min and a specificity of 78.7% in determining NICU

Stay >48 hrs

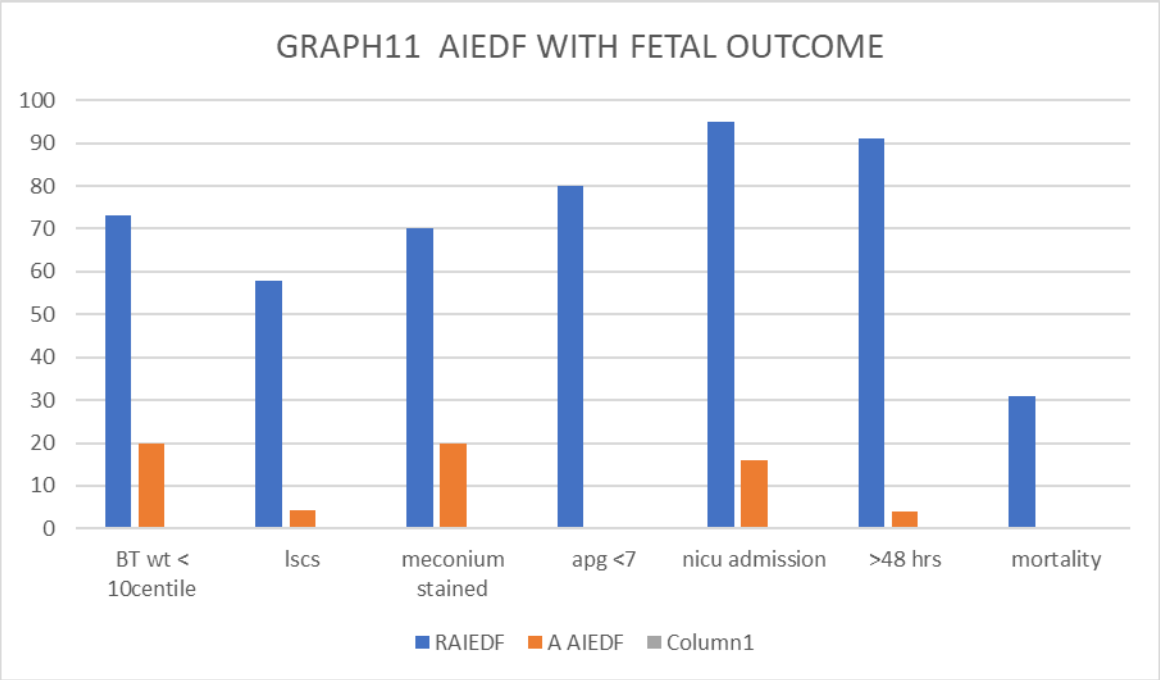


FIG 24 aortic isthmus doppler with fetal outcome corelation

Statistical correlation was drawn and found to be significant ($p<.05$)in all the parameters in predicting poor perinatal outcome. AIEDF followed by CPR had the highest sensitivity (100%) compared to all other indices.

DISCUSSION

The role of Doppler ultrasound in the study of uteroplacental and fetoplacental circulation is well known. It helps in detecting the extent of placental pathology and also predicts the fetal outcome. Numerous studies have been conducted to know the association between Doppler waveforms and perinatal outcome and have had variable results.

The present study showed that abnormal Doppler waveforms was associated with adverse perinatal outcome.

Umbilical artery waveforms

When umbilical artery velocity was correlated to fetal outcome in the present study, it was shown that there was an increase in the perinatal morbidity and mortality in cases with an abnormal umbilical artery S/D ratio.

The present study was compared with study of Yoon et al.[57]

Fetal outcome	Present study	Yoon, Lee, Kim
Mean birth weight	2±0.63	1.32±0.62
APGAR score <7 at 5 minutes	53.8%	57%
NICU admission	78.8%	93%
Perinatal death	25%	35%

When umbilical artery S/D ratios were compared to the study of Trudinger et al.[70] it showed the following results.

	Trudinger et al.	**Present study**
Number of patients with elevated S/D ratio	64%	56.5%
Birth weight <10th percentile	33%	57.7%
Perinatal mortality	16%	25%

Diagnostic performance of UA S/D ratio in detecting birth weight<10th percentile was compared to Adil Fleisher study, and was noted that the sensitivity was comparable with the present study.

	Adil Flesischer et al.[71]	**Present study**
Sensitivity	78%	75%
Specificity	83%	57.6%

Brar et al. noted that when umbilical artery S/D ratio is >3 than there is a greater chance of SGA, APGAR score<7 at 5 minutes, caesarean section for fetal distress and thick meconium in labour that correlated with the present study.[29]

AEDF or REDF in umbilical arteries

When the fetoplacental flow is severely affected there is an increased impedance to flow resulting in end diastolic flow becoming absent. With further hemodynamic compromise there will be reversal of flow in the umbilical arteries.

Such a development is ominous and results in a profoundly adverse perinatal outcome.

In our study it was seen that AEDF or REDF correlated with poor perinatal outcome with an increase in the perinatal mortality and morbidity.

AEDF correlation to perinatal mortality

Authors	Perinatal death
Fairlie et al.[72] 1991	43.7%
Bhat CJ et al.[73] 2003	50%
Neena Malhotra et al.[74] 2006	40%
Present study	60%

The perinatal mortality rate in those with a REDF in our was 100%. Hence from the above correlation and the results of the present study it is evident that in women with AEDF/REDF, if the baby is salvageable and NICU facilities are available, it is safer to deliver the baby for a better perinatal outcome.

Delivery can be delayed by 1-2 weeks if desired, with very intensive fetal surveillance in cases of AEDF, but immediate delivery is advocated when REDF sets in. REDF is a terminal event associated with an extremely high perinatal mortality.

Middle cerebral artery

Redistribution of blood flow occurs as an early stage in fetal adaptation to hypoxemia (brain-sparing reflex), wherein there will be an increased end diastolic flow resulting in decrease in PI and RI.

Our study showed similar findings of decrease in the MCA Doppler indices with an elevated umbilical artery resistance.

Low index of pulsatality in the MCA associated fetal compromise has been described by many authors. In our study it was found that low MCA PI was associated with 60.4% of SGA babies and 41.8% of perinatal mortality.

Diagnostic performance various pulsatality indices in detecting IUGR.

	Present study		**Shahina Bano et al.**[67]	
	Sensitivity	**Specificity**	**Sensitivity**	**Specificity**
UA PI	82.25%	52.7%	46.7%	93.3%
MCA PI	57.7%	65.41%	8.9%	100%
C/U ratio	80%	61.8%	44.4%	100%

Although our values did not correlate with that of Shahina Bano et al. but we also had a relatively higher sensitivity of the UA PI probably because it directly reflects the resistance in the placental vascular bed. Thus in suspected IUGR cases UA PI may be enough to detect IUGR as recommended in the study of Shahina Bano et al.

Cerebroplacental ratio

MCA/UA pulsatality index ratio is potentially more advantageous in predicting perinatal outcome as it not only incorporates data on the placental status but also on fetal response.

Gramellini et al. calculated the C/U ratio and found that it remains constant in the last 10 weeks of pregnancy. They have also shown that it provides a better diagnostic accuracy than either vessels PI considered alone.

	Present study	Gramellini et al. (1992)[75]	Varsha Deshmukh et al. (2013)[69]
Birth weight <10th percentile (%)	63.1	100	92.5
LSCS for fetal distress (%)	28.1	88.8	86.7
APGAR<7 at 5mins	57.8	16	10.8
NICU>48 hours	56.1	77	70

Diagnostic performance of CPR in relation to perinatal death was compared with other studies.

	Sensitivity	Specificity
Gramellini et al.	68.0%	98.4%
Rozeta et al.[66]	98%	66%
Present study	100%	52.4%

Our study was comparable to the study of Rozeta et al., although it varied from that of Gramellini et al.

In our study CPR had the highest sensitivity (100%) when compared to other indices in predicting NICU stay>48 hours and APGAR<7 at 5 minutes.

AORTIC ISTHMUS END DIASTOLIC FLOW

In study group 51.5% and 48.5% patients had antegrade, and retrograde flow respectively. Retrograde diastolic blood flow in the aortic isthmus signifies redistribution of fetal circulation, indicating lower cerebral resistance. Rio and Martinez have conducted a similar study in preterm IUGR patients and found that aortic isthmus Doppler blood flow has an important role in predicting the severity of placental insufficiency and decision making about termination of pregnancy. They

found significant correlation (P < 0.001) between retrograde blood flow in the AoI and adverse perinatal outcome, the overall perinatal mortality being higher in the retrograde group (70% vs. 4.8%, P < 0.001). It was also observed that with increase in severity of abnormality in Doppler parameters of umbilical artery, aortic isthmus wave forms also became abnormal. Patients with absent or reverse end diastolic flow in umbilical artery also showed absent or reverse flow in aortic isthmus. In women with increase S/D ratio in umbilical artery showed a normal antegrade flow in the aortic isthmus.In our studies AIEDF had higher sensitivity in terms of apgar prediction,NICU admission and prolonged NICU stay

Comparitive analysis was done with other studies.

	Present study	**Cecilia et al(2018)**[75]	**Shalaka bansode et al. (2018)**[69]
Birth weight <10th percentile (%)	73.1	65	80.5
LSCS for fetal distress (%)	58.1	38.8	45.2
APGAR<7 at 5mins	80.8	60	85
NICU>48 hours	91	87	100

Diagnostic performance of AIEDF in relation to perinatal outcome was compared with other studies.

	Sensitivity	**Specificity**
Boomika et al.	100.0%	78.4%
hernandez et al.[66]	95%	56%
Present study	100%	52.4%

CONCLUSION

- The present study noted an adverse fetal outcome in cases of severe preeclampsia and or IUGR which showed abnormal Doppler results.
- The finding of REDF is ominous and AEDF also correlated with poor fetal outcome with a perinatal mortality of 60%.
- In our study AIEDF had the highest sensitivity of 100% in predicting adverse fetal outcomes.
- Because CPR incorporates data not only on the placental side but also the fetal response it can be considered potentially more advantageous.
- Doppler patterns follow a longitudinal trend with early changes in the umbilical artery followed by middle cerebral artery.
- Doppler investigation of the fetal circulation plays an important role in monitoring the redistributing fetus and thereby may help to determine the optimal time for delivery.
- Doppler serves as an important yardstick for the obstetricians when dealing with pregnancies complicated with preeclampsia and growth restriction.

SUMMARY

The study comprised of 200 clinically diagnosed cases of Intra uterine growth restriction. Age of the patients ranged from 18 to 36 yrs with a mean age of 22.8 yrs (S.D 3.6 yrs). Of them 69% were primigravida and 31 were multigravida. Gestational age of the patients ranged between 28-40 weeks. Maximum number of patients (60%) belonged to 37-40 wks group. All patients were subjected to Doppler waveform analysis of Umbilical and MCA and Aorthic isthmus and all the indices were noted.

Umbilical artery Doppler studies revealed that 104 patients had elevated S/D ratio, 108 had elevated RI and 126 had elevated PI. The perinatal mortality was highest in the elevated RI(31%) group when compared to elevated S/D(25%) and elevated PI(28.5%) group. Amongst the umbilical artery waveforms highest LSCS for fetal distress was done in those with an elevated RI (27.6%). Meconium stained liquor incidence (53.4%) was also highest amongst the elevated RI group. Number of cases with birth weight<10^{th} percentile was equal (58.6%) in elevated RI and PI group. Umbilical RI also had a 100% sensitivity in predicting APGAR<7 at 5min. The highest specificity (74.4%) was for S/D ratio in predicting NICU admissions.

10 cases of 100 had AEDF and 6 had REDF. Perinatal mortality was worst amongst the REDF group wherein all delivered stillborn foetuses. Perinatal mortality and birth weight <10^{th} percentile in those with AEDF was 60%. 80% had APGAR<7 at 5 mins and meconium stained liquor.

MCA Doppler studies revealed that when there was an increase in the umbilical

artery resistance there was a decrease in the values of MCA indices showing a brain sparing effect. 116 cases had an abnormal MCA S/D ratio,

84 had abnormal RI and had 86 abnormal PI. Amongst the MCA indices perinatal mortality was highest for abnormal PI (41.8%) when compared to 34% (abnormal RI) and 31% (abnormal S/D). Both abnormal S/D and PI correlated with 60.3% of birth weights $<10^{th}$ percentile. LSCS for fetal distress was highest, 30.2% amongst the abnormal PI group. Meconium stained liquor incidence was highest in the abnormal S/D group (50%) and was equal in the other two abnormal indices groups (44%).

Incidence of APGAR<7 at 5 mins also was highest amongst abnormal S/D group (53.4%). NICU admissions was comparable amongst the three groups (~76%). However abnormal S/D ratio had the highest specificity of 96.8% for predicting NICU stay>48 hrs.

In all the foetuses with a brain sparing effect the CPR was <1.08(114 cases). Perinatal mortality rate was 31.5% in those with a CPR <1.08, 80.7% needed NICU admissions and 57.8% babies had APGAR<7 at 5mins. 30 (28.1) with CPR<1.08 underwent LSCS for fetal distress and 64(63.1%) had birth weight $<10^{th}$ percentile. CPR had 100% sensitivity in predicting NICU stay >48hrs and APGAR<7 at 5mins. Specificity of CPR was 76.5% in determining NICU admissions. Overall highest CPR had the highest sensitivity (100%) and MCA PI had the highest specificity (78.7%).

A total of 97 fetuses had retrograde flow in the aortic isthmus end diastolic flow

Perinatal mortality was 31 % in those with retrograde AIEDF.73 % of the babies were of birth weight less than 10^{th} centile. 58% of the cases were taken up for emergency LSCS in view of fetal

distress.this study had 100% sensitivity in predicting poor APGAR stores, 95% sensitivity in predicting NICU admissions and 94% sensitivity in predicting prolonged NICU stay

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PROFORMA

Name:

Date of admission: Date of discharge:

Age:

IP NO: Unit:

Education status:

Occupation:

Address

CHIEF COMPLAINTS

Primi/multi:

Months of amenorrhoea:

Pain abdomen :Yes/No Bleeding pv : Yes/No

Blurring of vision : yes/No Upper abdominal pain : Yes/NO

Head ache : yes/No Oliguria : Yes/No

Visual disturbances: yes/No Convulsions : Yes/No

Swelling of limbs:

MENSTRUAL HISTORY

Menstrual cycle: Marital history

LMP: EDD:

OBSTETRIC HISTORY: Score: Married life:

Details of previous pregnancy:

Past h/o pre eclampsia / eclampsia/abruption

FAMILY HISTORY : : h/o diabetes/hypertension/twins/congenital anomalies

PAST HISTORY : h/o diabetes/hypertension/renal disease
/

GENERAL PHYSICAL EXAMINATION : Ht: Wt: BMI:

Pulse : BP : Respiratory rate:

Pallor: Icterus: Edema:

Breast/thyroid/spine:

SYSTEMIC EXAMINATION

CNS:

Pelvis:

GCS score:

CVS:

RESPIRATORY SYSTEM:

PER ABDOMEN

Fundal height;

SFH: AG: EFW:

LIE:

PRESENTATION: Obstetric grips:

Fundal:

Lateral:

First pelvic:

Second pelvic

FHR:

PER VAGINAL EXAMINATION
: MODIFIED BISHOP SCORE:

Cervix: effacement –partial/full/uneffaced

Consistency: firm/medium/soft

Position: anterior/middle/posterior

Dilatation: presenting part: station:

Membranes: present/absent liquor: caput: molding:

Investigations:

Hb
Blood group:
Urine albumin:

Other relevant investigations

Blood Urea: Serum Creatinine Uric acid : SGOT: SGPT: Platelet count :

IUGR: yes/no symmetric/asymmetric

USG: date of scan: gestational age: EFW: AFI: presentation:

DOPPLER INDICES

	Umbilical artery	Middle cerebral Artery	Fetal aortic isthumus EDF
Pulsatility index			
Resistance index			
s/d ratio			
Absence of flow			
Reversal of flow			
Fetal compromise			

CPR

MODE OF DELIVERY: Spontaneous/induced/cesarean section

Duration between Doppler study and termination of pregnancy

Mode Of Induction :

NEONATAL RECORDS:

Sex:

Assessed gestational age in weeks:

Birth weight:

APGAR SCORE:

Fetal/ Placental weight ratio:

POSTNATAL CONDITION OF THE BABY

Admission to NICU

1 Post natal day:

2 nd Post natal day:

During hospital stay:

If dead : date:

Cause of death:

Delivery to death interval:

Condition on discharge:

Mother:

Baby

INFORMED CONSENT FORM

STUDY OF UMBILICAL ARTERY, MIDDLE CEREBRAL ARTERY AND FETAL AORTIC ISTHUMUS DOPPLER IN INTRAUTERINE GROWTH RESTRICTION AND ITS PERINATAL OUTCOME AT A TERTIARY CARE HOSPITAL IN CHENNAI-A PROSPECTIVE STUDY

I agree to participate in the study entitled and have been informed about the details of the study in my own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I understand that I can withdraw from the study at any point of time and even then, I can receive the medical treatment as usual.

I understand that I will not get any money for taking part in the study.

I will not object if the results of this study are getting published in any medical journal, provided my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my full cooperation for this study

Name of the participant :

Signature / Left thumb print:

Date :

Name of the investigator: Dr K.MONISHA

Signature of investigator :

Date :

KEY TO MASTER CHART:

DA	-	Deeply asphyxiated
FD	-	Fetal distress
FI	-	Failed induction
FP	-	Failure to progress
GA	-	Gestational age
LB	-	Live birth
MEC	-	Meconium
MOD	-	Mode of delivery
ND	-	Neonatal death
NEO-OUT	-	Neonatal outcome
pl	-	Previous LSCS
UHT	-	Uncontrolled hypertension
AIEDF	-	Aortic isthmus end diastolic flow
REDF	-	Reversed end diastolic flow
AEDF	-	Absent end diastolic flow
PNM	-	Perinatal mortality