PLACENTAL PLASTICITY INDEX AS A PREDICTOR OF CRITICAL PRENATAL OUTCOME IN GROWTH RESTRICTED FETUSES.

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LIST OF ABBREVIATIONS

UA - Umbilical Artery

UtA - Uterine Artery

PI - Pulsatility Index

PPI - Placental pulsatility Index

UAS - Uterine artery score

AEDF - Absent end diastolic Flow

FGR - Fetal Growth Restriction

IUGR - Intra Uterine Growth Restriction

LMP - Last Menstrual Period

LSCS - Lower Segment Caesarian Section

NICU - Neonatal intensive care unit

NPV - Negative Predictive value

NVD - Normal vaginal Delivery

PPV - Positive Predictive Value

RI - Resistance Index

RDS - Respiratory distress syndrome

CONTENTS

SL NO	**STATISTICAL CHARTS AND TABLE**	PG NO
1	AGE DISTRIBUTION	66
2	PERINATAL OUTCOMES	67
3	ROC CURVE – PERINATAL OUTCOMES AND PPI	68
4	GESTATIONAL AGE IN NORMAL PPI	69
5	BIRTH WEIGHT IN NORMAL PPI	70
6	OUTCOMES IN NORMAL PP	70
7	GESTATIONAL AGE IN ABNORMAL PPI	71
8	BIRTH WEIGHT IN ABNORMAL PPI	72
9	OUTCOMES IN ABNORMAL PPI	72
10	COMPARATIVE STUDY BTN UA, UT.A AND PPI	73
11	PERINATAL OUTCOMES IN DIFFERENT SETTINGS	74
12	TABLE 1 SHOWING STATISTICAL SIGNIFICANCE OF PPI	75
13	ROC CURVE INFERENCE AND PPI	76

INTRODUCTION

Christian Doppler first described the Doppler effect in 1842. He defined it as the "apparent shift in frequency of a light or sound wave when the wave source approaches or travels away from an observer".

An important component of Doppler equation is the insonation angle (Θ). There are three ratios commonly used to describe Doppler waveform, systolic-diastolic ratio (S/D ratio), Resistance Index(RI) and Pulsatility Index(PI). "Doppler has shown to be an effective obstetric technique for more than 30 years". Utility of Doppler is to evaluate both the foetal and placental circulation. UA, MCA, Ut A, and DV are often used obstetric Doppler parameters. Dopplers of the aortic isthmus, atrioventricular valves, and umbilical vein (UV) are more specialised and infrequently performed. [2] Important disorders like foetal growth restriction , foetal anaemia, and TTTS can be diagnosed and monitored more easily thanks to Doppler (TTTS).

According to the American College of Obstetricians and Gynecologists,IUGRis "one the most common and complex problems in modern obstetrics." Worldwide FGR is the leading cause for neonatal morbidity and mortality, stillbirth and long term complications. The incidence of FGR is 3-7%. [7] Fetal growth restriction is used to describe a fetus that is abnormally small for gestational age (SGA) Measures of foetal size percentile (10th percentile) and Doppler anomalies should be combined to define foetal growth restriction (FGR). [6] Diagnosis of FGR is often made in utero based on estimated fetal weight (EFW) less than 10^{th} percentile but not all such foetuses have FGR truly. Hence other sonographic criteria are being considered to improve the diagnostic accuracy of FGR, because EFW has sensitivity of 89% and positive predictive value of 45%. [8]

The Doppler criteria are not reliable for diagnosing FGR however they are useful for fetal monitoring and for guiding management decision. Amongst all the Doppler parameters used for monitoring FGR Umbilical artery Doppler is the most important one. [5] UA Doppler measures resistance in the fetoplacental circulation. Maternal or placental etiologies that cause obliteration of small muscular type of arteries in the tertiary villi causes changes in umbilical artery flow from a further decrease in umbilical arterial End Diastolic flow and then resulting in reversed flow.

As placental impairment further advances, there is REDF in UA, this has been linked to the obliteration of more than 70% of arteries in placental tertiary villi, resulting in severe FGR (EFW-3rd percentile) and oligohydramnios.

MCA PSV is another parameter shown in number of studies may be better in prediction of perinatal mortality in cases of preterm FGR. A phenomenon called brain sparing reflex denotes fetal hypoxaemia and is reflected as increased end-diastolic flow velocity (reflected by a low PI) in the middle cerebral artery. [4] Uterine artery Doppler a progressive decrease in impedance with advancing gestational age due to trophoblastic invasion of the maternal spiral arterioles in the first half of gestation. Early in the pregnancy, uterine can show a notch with relatively low flow in the diastole because of the higher vascular resistance. In later gestation, the diastolic flow increases and the notch disappears as the impedance decreases, if this notch remains in later half of pregnancy it can be a predictor of various abnormalities that can occur. [3]

Apart from the above mentioned Doppler parameters, placental pulsatility index (PPI) which is "calculated as (umbilical artery pulsatility index + mean of the left and right uterine artery pulsatility indices)/2, and mean +2 SD defined as abnormal can be used".

The representative measurements of utero-placental perfusion are the PI of the UA and Ut. arteries. Combining these two could aid in determining the overall placental vascular impedance, potentially enhance the ability to anticipate. [1]

In our study we calculated placental pulsatility index using the above mentioned formula to predict critical perinatal outcome in growth restricted fetuses.

ABSTRACT

PLACENTAL PULSATILITY INDEX AS A PREDICTOR OF CRITICAL PERINATAL OUTCOME IN GROWTH RESTRICTED FETUSES

AIMS AND OBJECTIVES:

1. Correlating placental pulsatility index with adverse perinatal outcomes in growth restricted fetuses

2. To compare placental pulsatility index with conventional umbilical and/or uterine artery Doppler in predicting the outcomes in pregnancies suspected of IUGR.

MATERIAL AND METHODS:

Doppler ultrasonography of growth restricted fetuses between 26 to 40 weeks (diagnosed by fetal biometry on routine/clinically indicated ultrasound examination) and calculation of placental pulsatility index (Umbilical artery PI + mean of right and left Uterine arteries / 2) to predict the critical perinatal outcomes.

RESULTS:

The PPI had higher sensitivity and specificity in predicting critical perinatal outcomes in FGR fetuses when compared to uterine and umbilical arteries alone.

CONCLUSION:

The PPI reflects the vascular impendance on both fetal and maternal side and is therefore valuable predictor of critical perinatal outcomes in FGR fetuses.

KEYWORDS:

Fetal growth restriction, Uterine artery, Umbilical artery PI, Placental Pulsatility Index.

REVIEW OF LITERATURE

HISTORY OF SONOGRAPHY IN OBSTETRICS AND GYNECOLOGY:

The earliest detection of hydatid mole which gives “snowstorm appearance”, using the full bladder approach to visualize early gestational sac, and identification of problems of early pregnancy were all described by Donald and team in 1963 (Donald, 1962). [9]

Placentography: In the early 1960s, pinpointing the placenta's exact placement was crucial for prenatal diagnosis. Because of severe PPH in late gestation, placenta previa was the main factor in maternal mortality. The lower placental edge could not be precisely defined at this time despite the widespread use of radioisotope techniques. The first paper on ultrasound placentography was published in the year 1966 by Gottesfeld et al.

Fetal biometry: James Willocks from Donald's department released a report on head growth in the 3rd trimester revealing differing growth rates between FGR and regularly growing foetuses. This was one of the earliest investigations in foetal biometry. This technique was unreliable, and more accuracy was needed for meaningful biometry. Stuart Campbell, later showed the gray scale technique in 1968, which involved viewing the foetal head in 2D and using A scan for measuring the “biparietal diameter”. A-scan was no longer needed after calipers were invented a few years later. As early as 13 weeks gestation, Campbell showed that the midline echo could be seen clearly. He also quickly demonstrated that second trimester cephalometry was a reliable way to date pregnancies in women whose due dates were unknown. Campbell introduced the idea of EDD on USG (Campbell, 1969). After that, he created the first cephalometry graph, which showed a substantial slowdown in BPD growth in the 3rd trimester, and utilised it to identify the IUGR foetus. This graph was created from 13 to 40 weeks (Campbell and Dewhurst, 1971). Serial cephalometry later became the accepted technique for gauging foetal growth.

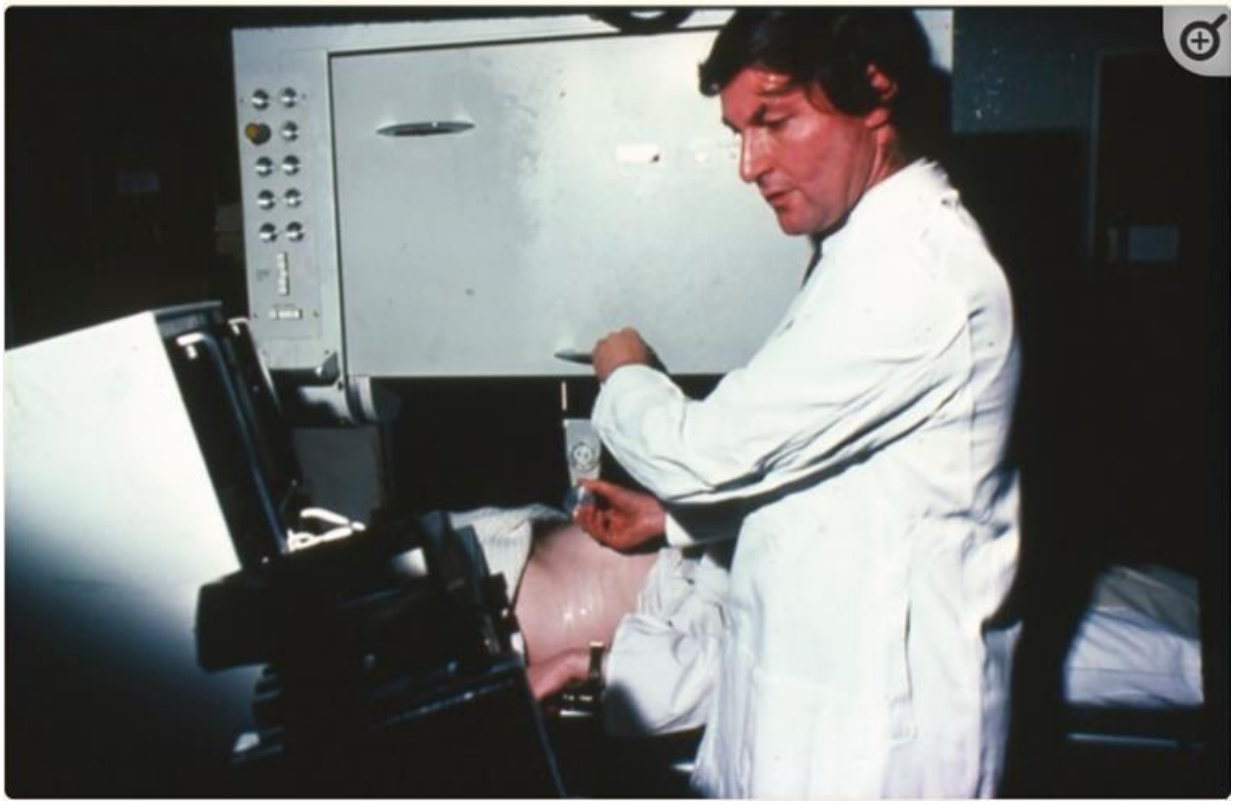


FIG [1]: “CAMPBELL USING NE4102- A SCANNER: SUCCESSOR TO THE DIASONOGRAPH”. [9]

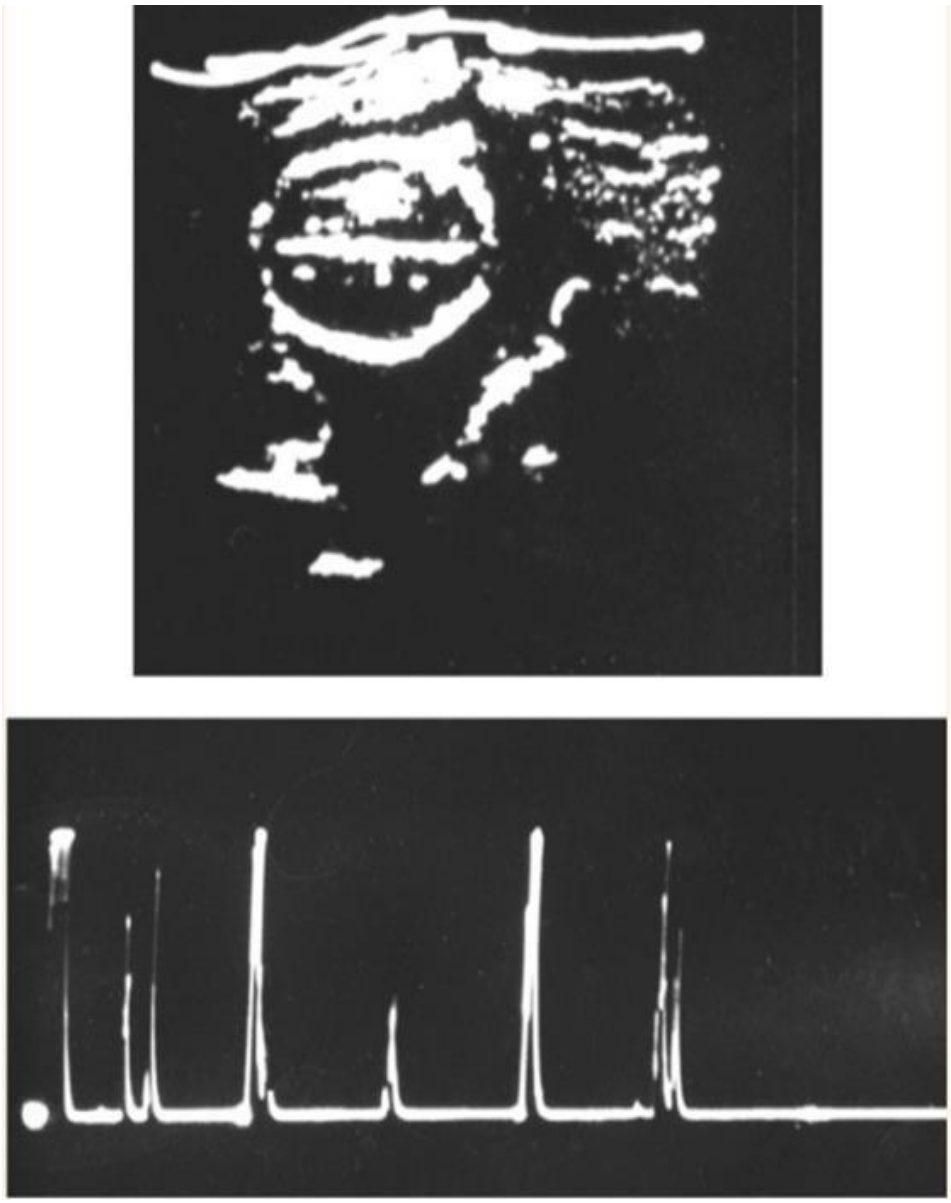


FIG [2] : CAMPBELLS IMPROVISED TECHNIQUE OF CEPHALOMETRY – MIDLINE ECHO VISUALISED ON B MODE SCAN, MEASUREMENTS WERE EARLIER DONE ON A-SCAN. [9]

“Horace Thompson and Ed Makowsky from Denver introduced measurement of the thoracic circumference (TC) and the concept of foetal weight prediction using a combination of this measurement and the BPD in 1971”. This was done to address the drawback of only measuring the head because the brain is affected last in cases of growth restriction (Thompson and Makowski, 1971). These findings were supported by Manfred Hansmann in Bonn in a different study. “The chest of the baby is cone-shaped, and there is no reliable marker to indicate the level of the scan” , according to Stuart Campbell, who is currently employed at Queen Charlotte's Hospital in London. Campbell noted that this poses inherent problems for repeatability with TC

measurements. As a more precise measurement, he proposed the measurement of abdominal circumference “at the level of the intra Abdominal portion of umbilical vein” in the year 1975 by Campbell and Wilkin. Since then, this measurement has become the norm. The “HC:AC ratio” was developed as a way to identify brain sparing in foetuses with FGR since the “AC measurement is done at the level of liver” , an adversely impacted organ in FGR.

Early pregnancy: In 1967, Kratochwil employed a TVS probe to show foetal heart activity using an A-scan at 7 weeks' gestation, however the majority of investigations conducted in the 1960s and the early 1970s were abdominal, using the full bladder approach. For instance, Embryonic heart activity was first seen by Bang and Holm in the year 1968. “Hugh Robinson from the Glasgow school is the author of this study on early pregnancy evaluation. He created the first thorough biometry charts of the foetal crown-rump length from 7 to 16 weeks gestation in 1973 using an upgraded Diasonograph; his measurements were so precise that they are still used today (Robinson, 1973)”.

He then created FHR charts starting from 7 weeks of gestation using the combined A- and B-mode equipment, demonstrating that the detection rate was 100%. He was the first to highlight the predictive value of “embryonic cardiac activity discovered at 8 weeks gestation in relation to foetal death later on (Robinson and Shaw-Dunn, 1973)”. This research had a significant impact on how patients facing threatening abortions were managed.

Fetal abnormalities: In the year 1964 Bertil Sunden and William Garrett in the 1970 both reported cases of prenatal detection of congenital anomalies associated with polyhydramnios in the late 2nd or 3rd trimester. “The Lancet publication by Campbell and his team, published in 1972, described the diagnosis of anencephaly at 17 weeks, which led to the decision to terminate the pregnancy (Campbell et al., 1972). He then meticulously studied the embryonic spine in those mothers who had elevated serum AFP levels and announced the diagnosis of spina bifida in 1975”.

With the development of real-time scanning devices, ultrasonography became widely used for prenatal detection of anomalies.

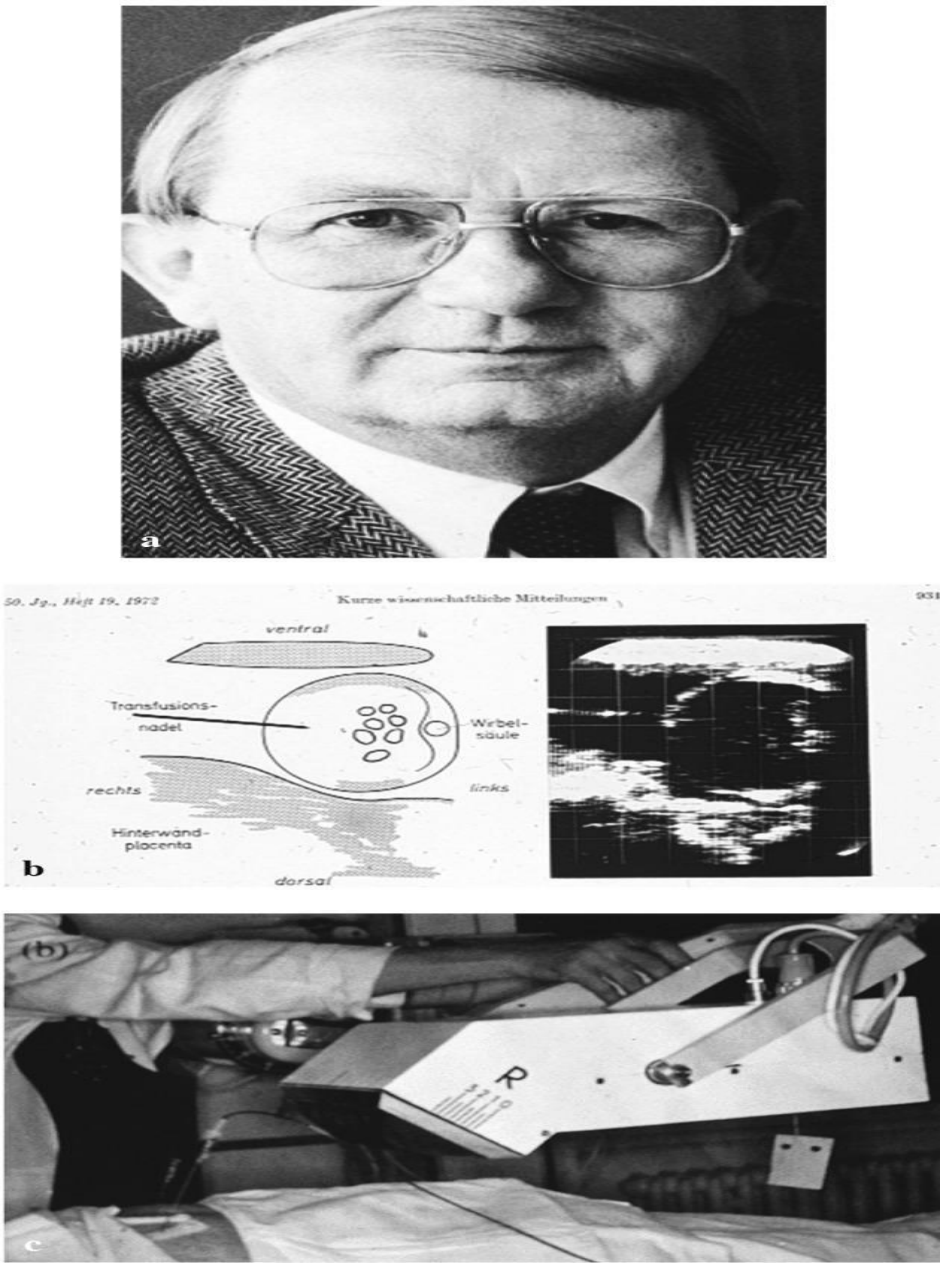
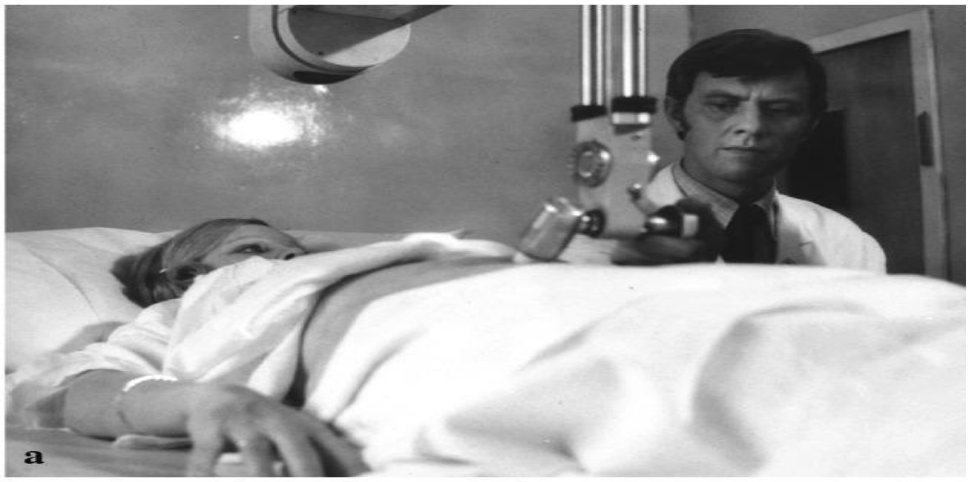
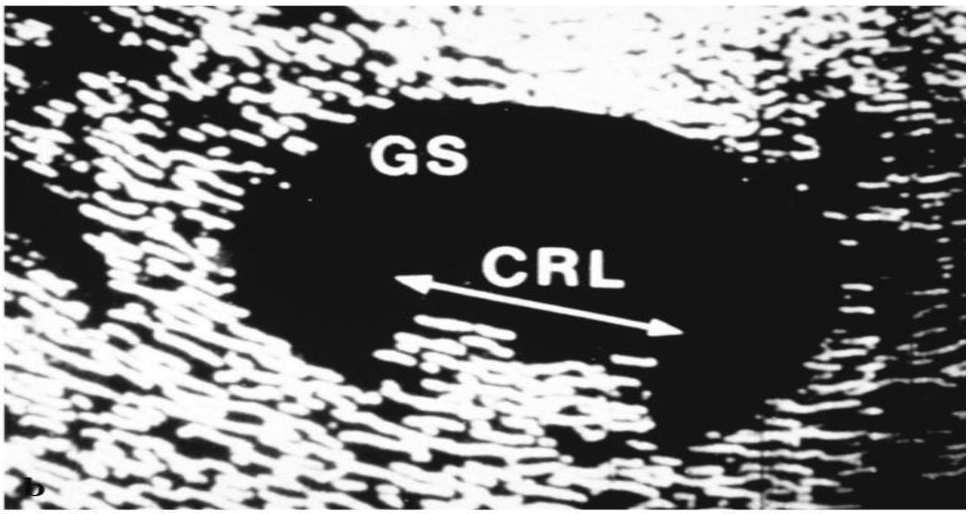


FIG [3]: "MANFRED HANSMANN (A) PIONEERED ULTRASOUND GUIDED INTRAUTERINE THERAPY (B) HIS EQUIPMENT" [9]





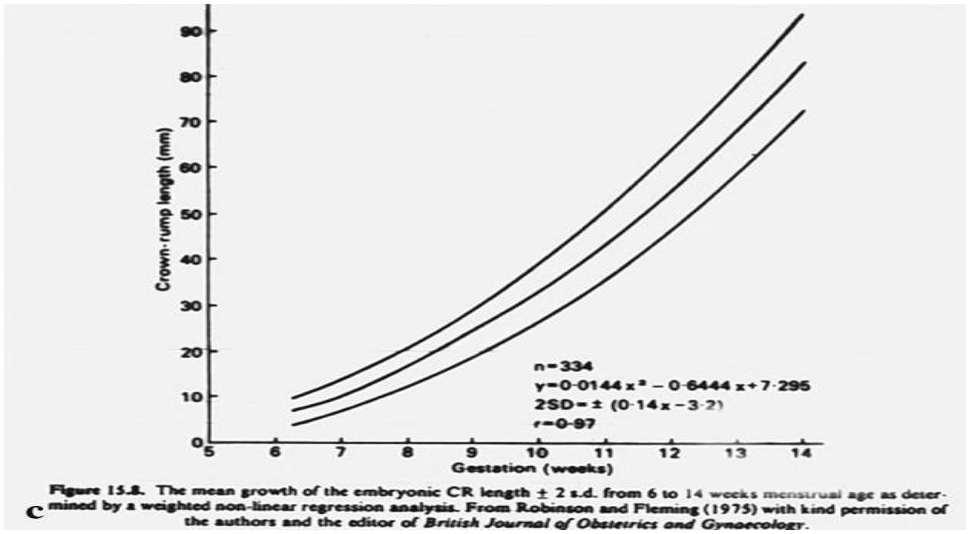


FIG [4]: "HUGH ROBINSON (A) PIONEERED FETAL CRL MEASUREMENT (B) IN 1973" [9]

The evolution of real time sonography

In the middle to late 1970s, scanners with better technology soon superseded the mechanical real-time scanners developed by businesses. Now it was possible to see the foetus' movements and immediately change the angle of the probe to locate the important plane. “The ADR was a tiny business established by Martin Wilcox in Tempe, Arizona, and it produced the first commercial linear array real time scanner. The first version only had 64 lines, and the resolution was low, but the second version, the ADR 2130, released in 1975, had almost 500 lines, phased focusing, and could compete in terms of resolution with static scanners. The majority of major ultrasound manufacturers created real-time equipment over the following few years, passing each other in levels of sophistication, but Sam Maslak's 1983 Acuson 128 with its sophisticated beam forming software (known as "computed sonography") set new benchmarks for spatial and contrast resolution. In order to improve the method of oocyte collecting in in vitro fertilisation, Kretztechnic created the first usable endovaginal mechanical sector transducer in 1985”. However, probe vibrations were a drawback of these transducers, which produced great images. By the end of 1990s, the manufacturers created probes with better resolution.

Color Doppler imaging, initially known as colour flow mapping, was integrated into Aloka's real-time technology by 1985, and other manufacturers soon followed suit. By 1990, the TVS probe for gynaecological inquiry had colour capabilities. Harmonic imaging was made available by the year's end of 1990, considerably enhancing image resolution. Although Kazunon Baba initiated early research on 3D imaging in Japan in 1984, it wasn't until “the third generation 530D Voluson” was developed that the public came to the conclusion that “3D/4D ultrasound” Played a major role both Obs and gyn imaging. “The present real-time scanning device with high resolution abdominal and endovaginal transducers, harmonic imaging, colour and

power Doppler choices, and a 3D/4D option might thus be claimed to have been available by the year 2000".

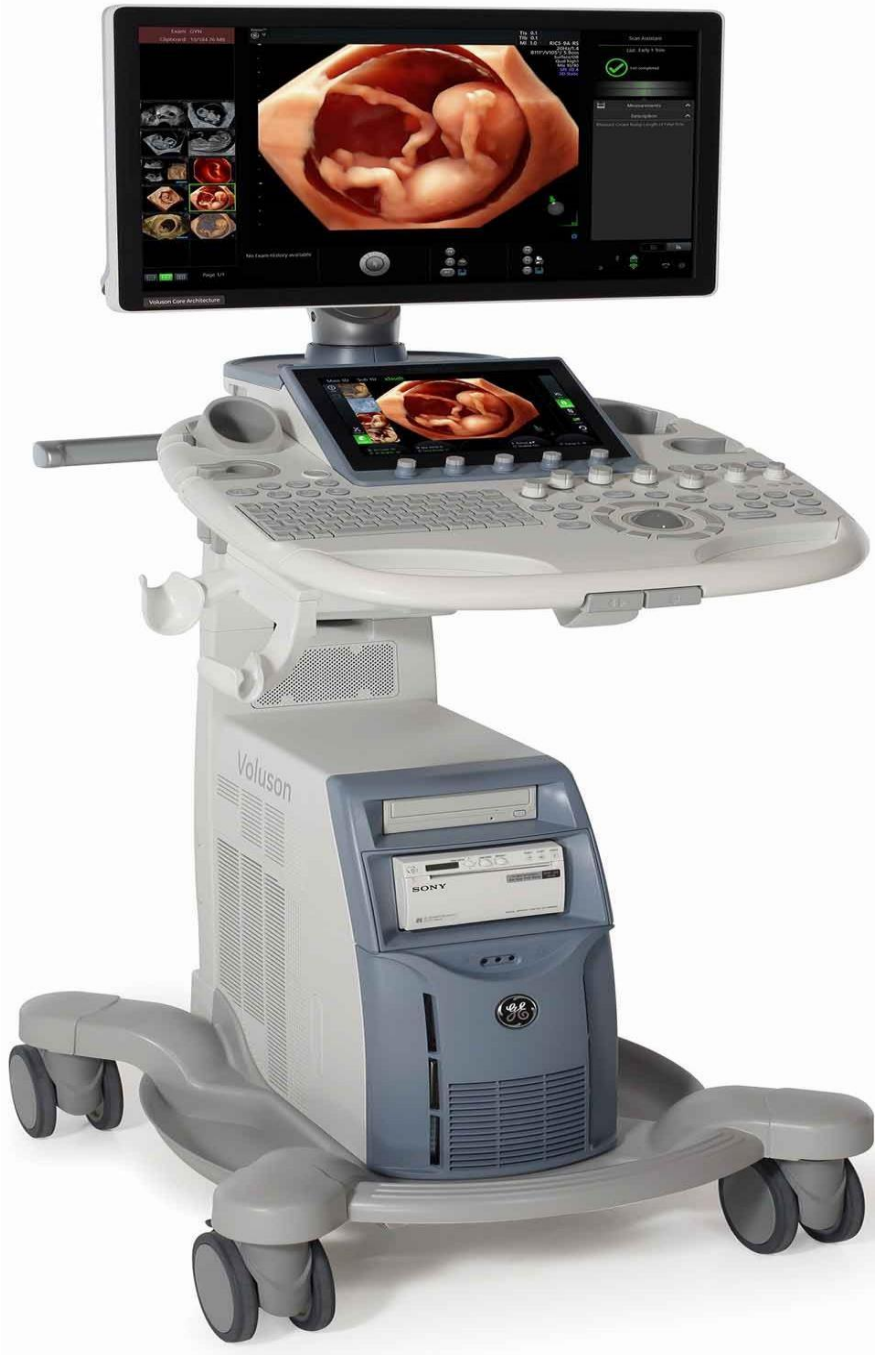


FIG [5] :MODERN DAY REAL TIME ULTRASOUND MACHINE

Obstetric ultrasonography was greatly impacted by the modern day scanners because it was no longer the domain of a small number of specialists in a few big centres, these scanners are now available at almost every centre, they're affordable and many experts were amazed how fast the junior staff learnt the scanning technique in less than a day.

Fetal biometry: Due to the probe's simplicity of use, numerous foetal structures were assessed, and numerous charts of various planes and organs were created. However, easier to measure femoral length was included in formulae for foetal weight and growth predictions; “the standard measurements CRL, BPD, HC, and AC that were developed during the static era continue to be the standard foetal biometric measurements for assessing growth (Hadlock et al., 1985)”.

Fetal activity: The capacity to monitor foetal movements via ultrasound has generated a lot of interest in whether quantifying the motions, particularly foetal breathing movements, may be useful in determining the welfare of the foetus. The frequency, duration, and quantity of foetal breaths or movement episodes were counted and recorded. The idea of assessing overall “foetal activity over a 30 minute period was taken into consideration because foetal breathing movements and activity are both episodic and rarely coincide with one another”. “Due to the significant physiological variability in the incidence of both respiratory and motor activity, the test exhibited a low predictive value for a positive test even if there was a relationship between reduced overall activity and IUGR (Marsal, 1978). For the same reason, foetal activity assessment as a method of gauging foetal health was no longer favoured in Europe. However, in the USA, Frank Manning and Larry Platt in 1980 combined both of these measurements into a 30-minute foetal biophysical profile exam (Manning et al., 1980) that also included a non-stress test (CTG) of the foetal heart and an evaluation of amniotic fluid and foetal tone. For more than 20 years, this test—with some slight modifications—became the cornerstone of foetal welfare assessment in the United States. However, Doppler ultrasound was used more and more in Europe by researchers to address the issue of how to accurately measure foetal welfare and optimise the time of delivery when there is foetal compromise”.

Doppler Assessment: Using 2D static scans to determine where the probe should be placed, “D.E. Fitzgerald and John Drumm from Dublin reported the blind continuous wave (CW) Doppler demonstration of the umbilical artery waveform as early as the mid 1960s”, but none of these two groups followed up on their results. Pulsed Doppler foetal imaging research were started by two organisations. However, the Octason's long route length made it unable to monitor high-velocity artery flow, making this instrument unsuitable for use in clinical Doppler research. The first duplex linear array system, in which a pulsed Doppler probe was mounted at a 52-degree angle, was described by Sturla Eik-Nes while she was a researcher at Karel Marsal's Malmo laboratory (Eik-Nes et al., 1980). He observed that IUGR foetuses had decreased flow velocities from the foetal aorta. Workers in various academic units in Europe employed equipment resembling the Malmo duplex Doppler system in the early to mid-1980s to describe the embryonic cardiac response to hypoxia. Absolute velocity measurements were discovered to be inferior to waveform analysis, particularly the pulsatility index in the evaluation of foetal circulation changes in response to hypoxia. The compensatory centralization of the foetal circulation, or "centralization of the foetal circulation," linked with IUGR foetuses was originally noted by Yuri Wladimiroff in Rotterdam (Wladimiroff et al., 1986). “The significance of the umbilical artery waveform and the importance of absent and reversed end diastolic flow were rediscoverys by Australian researchers Brian Trudinger and Warwick Giles (Trudinger et al., 1986)”. Giancarlo Mari and the team at Yale University highlighted the use of Doppler as a non-invasive means of identifying anaemia in foetuses with the Rh immunisation.

In a very sizable multicenter study, Nicolaides looked further into the uterine artery Doppler's potential for predicting pre-eclampsia and IUGR. In 2001, it was demonstrated that a “uterine artery PI conducted at 23 weeks could accurately predict 85% of women who will experience severe pre-eclampsia for just a 5% screen positive rate (Papageorghiou et al., 2001)” . One problem is that it doesn't look like low-dose aspirin or other preventative measures are very effective. “Pre-eclampsia screening with uterine artery Doppler and biochemical indicators like PlGF and PAPP-A may be possible in the first trimester (when preventive medication appears to be beneficial)”, according to research by Nicolaides and colleagues (Akolekar et al., 2013).

Christian Andreas Doppler and Doppler theory

Christian Andreas Doppler is renowned for his ground-breaking hypothesis of the Doppler effect, which has had a significant impact on numerous fields of contemporary science and technology, including medicine. More than a century after his passing, his concepts are still stimulating discoveries. His work created the groundwork for contemporary ultrasonography. Due to his extensive understanding of physics, mathematics, and astronomy, as well as his tireless search for novel theories and his brilliant mind, Doppler may very possibly be considered the first Homo Universalis. Bolzano stated that it was "difficult to realise what a productive talent Austria has in this man." The ultimate testament to Doppler's work is the innumerable allusions to the eponymous medical eponym. His scientific legacy has seen Doppler honoured in later years on coins and money, names of streets, educational institutions, rock groups, and even of a lunar crater.

DOPPLERS LIFE AND WORK: In Salzburg, Austria, on November 29, 1803, Christian Andreas Doppler was born. He came from a family of stonemasons. His poor health turned out to be both a benefit and a curse because it allowed him to quit the family company and go to college. [10] He excelled in mathematics at the brand-new Vienna Polytechnic Institute after finishing his elementary and secondary education in Salzburg and Linz. Later, he studied higher mathematics, mechanics, and physics at the University of Vienna. [11] He authored four mathematical papers after finishing his studies and worked for Professor Burg for four years as an assistant. [12] Despite his obvious talent and expertise, Doppler was not hired for an academic position once his assistantship ended, thus he was forced to work for 18 months as a bookkeeper in a cotton factory to make ends meet. He was on the verge of leaving for America during this depressing period, but instead he was hired as a lecturer at the technical secondary school in Prague and afterwards at the polytechnic school in the same city. [11]

He married, had five children, and authored more than 50 articles on mathematics, physics, and astronomy while working as a professor in Prague. His most well-known essay, Über das farbige Licht der Doppelsterne ("On the Colored Light of Double Stars"), was published in 1842 and included his initial explanation of the Doppler phenomenon. He was appointed Professor of Mathematics, Physics, and Mechanics at the Academy of Mines and Forests in Schemnitz in 1947, but because to the industrial unrest, he and his family were forced to move back to Vienna.

[13] He was named Director of the newly established Institute of Physics at Vienna University in 1850 and promoted to Full Professor of Experimental Physics at the institution. His health deteriorated when he was employed in Vienna. He had to go to Venice because of severe chest problems (perhaps caused by tuberculosis), and there he passed away on March 17, 1953, a few months later

FIG [6] : CHRISTIAN ANDREAS DOPPLER

When there is relative motion between the source of the waves and an observer, a wave's apparent shift in frequency or wavelength is the Doppler effect. When the wave source is travelling in the direction of the observer, the perceived frequency is higher than the actual frequency emitted, and it is lower when the wave source is receding. The Doppler effect or Doppler shift is the term used to describe this apparent change in the pitch (or frequency) of sound. All waves, including gamma, x-ray, ultraviolet, light, microwave, RF signals, and sound, that are subject to relative motion are affected by the Doppler effect.

The formula v=c x DF/[2 FT (cos)], where c is sound speed, DF is frequency shift, and is intercept angle, provides a mathematical expression for Doppler's effect.

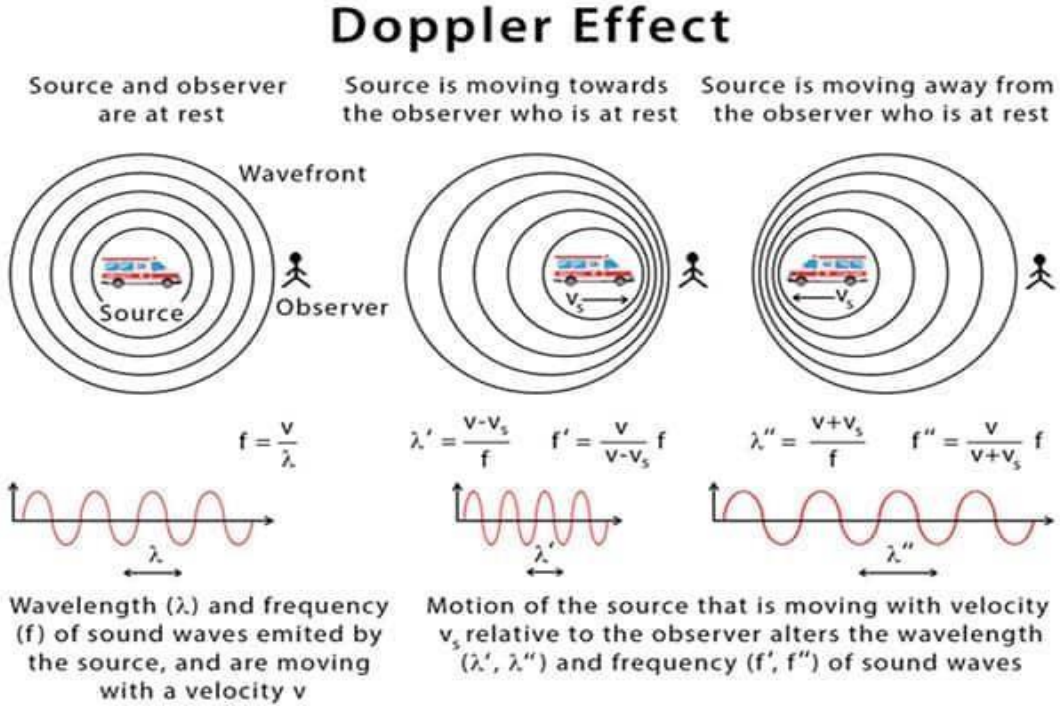


FIG [7] : DOPPLER EFFECT

Placentation & Development of placenta: [14]

After fertilisation, the two-celled zygote undergoes cleavage; the resultant cells are referred to as blastomeres. The zona pellucida still surrounds the blastomeres and polar body in the two cell zygote. While in the fallopian tube, the zygote undergoes cleavage for a further three days. A firm ball of cells, called the morula, resembling a mulberry, is created when the blastomeres continue to divide. Three days following fertilisation, the morula makes its way into the uterus. Gradual buildup of fluid between the morlua cells causes the formation of an early blastocyst (as early as 4 to 5 days after fertilisation), which is then released from the zona pellucida as a result of protease secretion. This release increases the endometrial receptivity, and so the blastocyst implants onto the uterine wall 6 to 7 days after fertilisation. A receptive endometrium primed with oestrogen and progesterone by the copurs luteum, which is only present for 20 to 24 days, is necessary for successful implantation. It has between 100 and 250 cells at the moment of its interaction with the embryo.

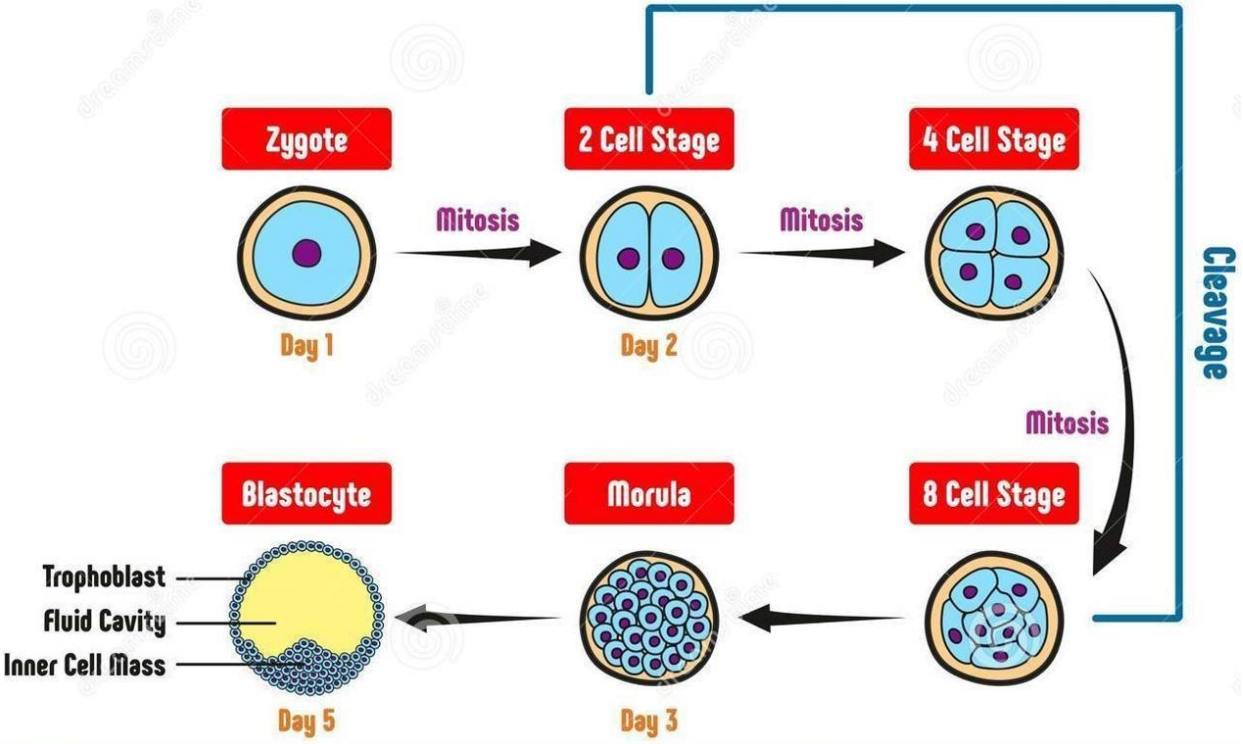


FIG [8] : EMBRYOGENESIS

The trophoblast differentiation:

The trophoblast divides into an exterior multinucleated synctium-primitive synctiotrophoblast and an inner layer of primitive mononuclear cells—cytotrophoblast—by the eighth day post fertilisation after first implantation. Following successful implantation, trophoblast continues to

differentiate into villous and extravillous trophoblast. The chorionic villi are produced by the villous trophoblast, which largely distributes nutrition, oxygen, and other substances between the mother and foetus. Extravillous trophoblast penetrate the maternal vasculature, travel into the decidua and myometrium, and come into contact with a variety of maternal cell types.

Placental organization:

Chorionic villi:

The extravillous cytotrophoblasts give rise to solid primary villi made up of a cytotrophoblast core covered by synctiotrophoblast with deeper blastocyst penetration into the deciduas. These initial villi are then invaded by the mesenchymal cords to create secondary villi, which are then transformed into tertiary villi once angiogenesis starts.

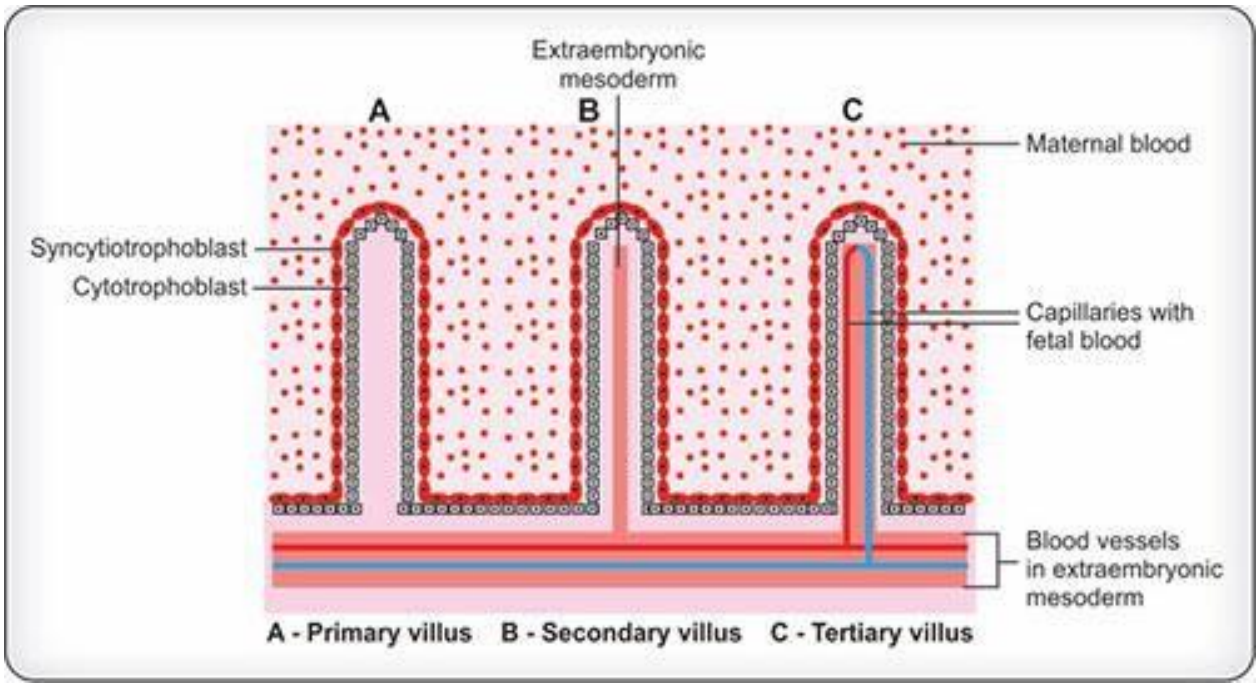


FIG [9] : VILLOUS REMODELLING

Invasion of spiral arteries:

The significant alteration of the maternal vasculature throughout human placental development by trophoblasts, which are by definition of foetal origin, is one of the most striking characteristics of placental development.

These prenatal occurrences, which are also essential to several pathological situations like preeclampsia, FGR, and premature birth, take place in the early half of the pregnancy. Two populations of extravillous trophoblasts—interstitial trophoblasts that surround the arteries and endovascular trophoblasts that pierce the arteries—are responsible for spiral artery remodelling. Invading the spiral arteries and forming a clog, the endovascular trophoblasts later obliterate the

vascular endothelium and alter the arterial media. Thus, the smooth muscle and connective tissue of the vessel media are replaced by a fibrinoid substance. Uteroplacental vascular formation is characterised by Ramsey and Donner (1980) as occurring in two waves or stages. Before 12 weeks post-fertilization, the first wave occurs, and between 12 and 16 weeks, the second wave. Remodeling turns muscular spiral arteries with limited lumens into dilated, low resistance uteroplacental vessels.

This invasion is not optimal, and the spiral arteries stay in high resistance, which is reflected in the foetal circulation, unlike in patients with preeclampsia, FGR, and preterm birth.

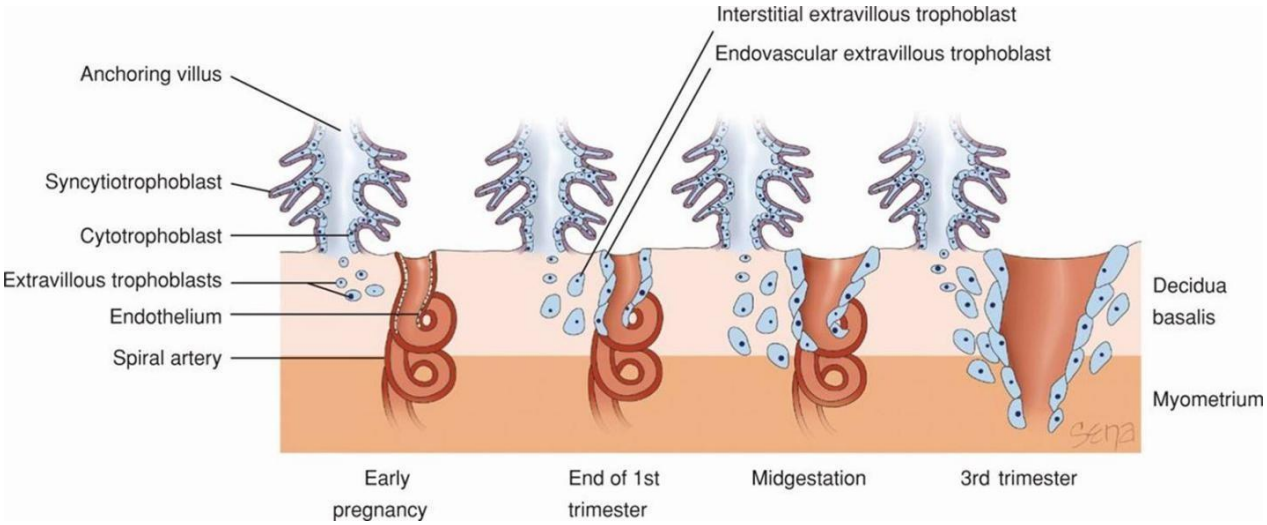


FIG [10] : INVASION OF SPIRAL ARTERIES

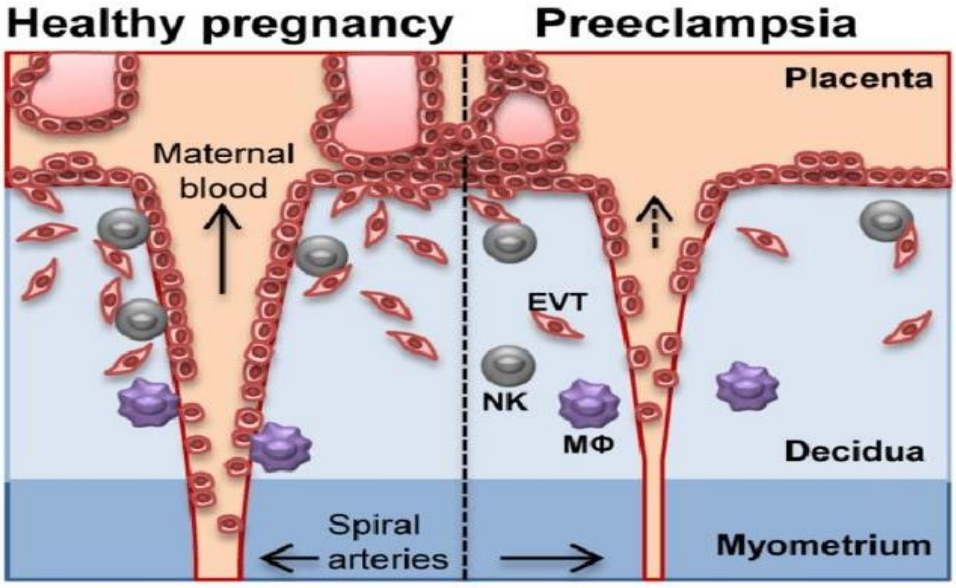


FIG [11]: DEFECTIVE TROPHOBLASTIC INVASION IN PE

Structure of placenta:

Fetal circulation:

The placenta receives deoxygenated blood through two umbilical arteries. These umbilical veins regularly branch beneath the amnion and within the villi as the cord attaches to the placenta, eventually generating capillary networks in terminal villous branches. Oxygenated blood returns to the foetus from the placenta through just one umbilical vein.

Placental surface or chorionic vessels (chorionic arteries and veins) are the branches of the umbilical vessels that travel along the foetal surface of the placenta in the chorionic plate. Chorionic arteries first form a network supplying the cotyledons before bending downward to pierce the chorionic plate. Conclusion diastolic flow does not develop in the umbilical artery until 10 weeks following the end of the foetal cardiac cycle; it then persists throughout a typical pregnancy.

Maternal circulation:

Maternal blood enters through the basal plate and is laterally dispersed after being pushed by artery pressure all the way up to the chorionic plate. Maternal blood drains back through the venous orifices in the basal plate and enters the uterine veins after bathing the exterior micovillous surface of chorionic villi. Using serial sonography during a typical labour, Bleker and associates (1975) discovered that placental length, thickness, and surface area increased during contractions. Therefore, more blood is accessible for exchange during contractions.

Similar to this, Doppler velocimetry has demonstrated that spiral artery diastolic flow velocity decreases during uterine contractions.

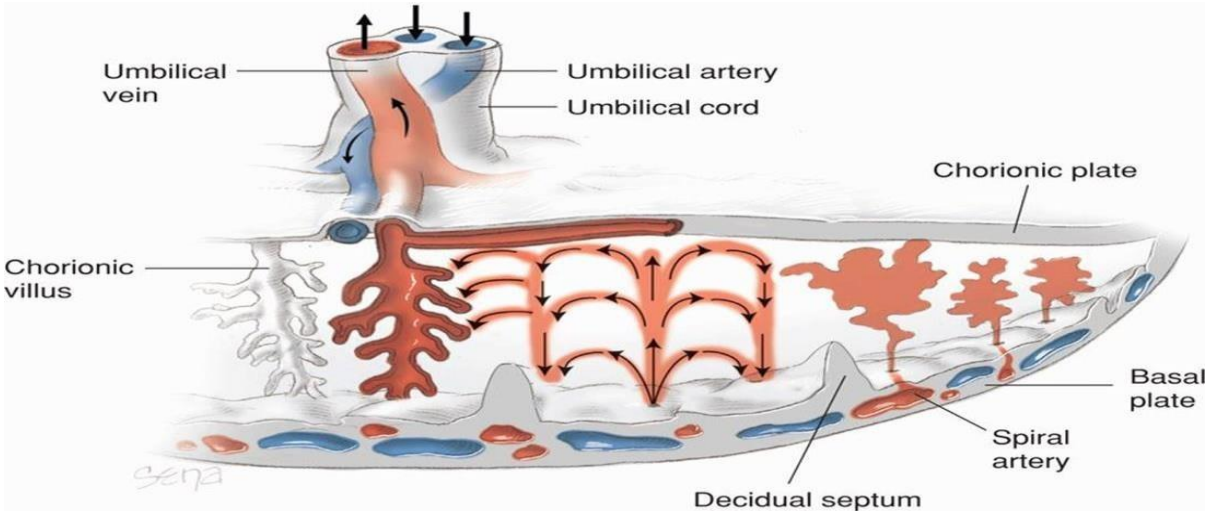


FIG [12] : STRUCTURE OF PLACENTA

The placental alterations observed in cases of FGR of noninfectious and nongenetic origin are part of a spectrum of pathologies linked with various degrees of inadequate remodelling of the uterine spiral arteries, according to a study by Burton GJ, Jauniaux E, et al. [15]

FETAL GROWTH RESTRICTION:

The most common definition of foetal growth restriction (FGR) is a foetal weight determined by prenatal ultrasound evaluation to be less than the third percentile for gestational age or less than the tenth percentile for gestational age linked Doppler alterations. [16] FGR is linked to both immediate and long-term issues that may have a negative effect on one's quality of life.

The foetus in FGR is unable to grow to its full genetic potential. As foetal growth cannot be determined by a single biometric measurement of the foetal size and growth potential is speculative, the identification of FGR is typically indirect.

“SGA is defined as EFW or AC below the 10th percentile of the specified reference ranges. The risk of stillbirth and perinatal mortality increases for foetuses with birth weights below the 10th percentile, with the largest risk occurring for those with birth weights below the 3rd percentile. To determine FGR at any gestational age, foetal size at the lower end of the growth charts, such as AC or EFW below the third percentile for a given growth chart, can be utilised alone”. [16]

Causes: [17]

Fetal, placental, or maternal reasons might be used to categorise the causes.

Fetal causes: In 5% to 20% of these cases, foetal genetic abnormalities are found. The ring chromosome, aneuploidy, uniparental disomy, single-gene mutations, partial deletions or duplications, abnormal genomic imprinting, and single-gene mutations are some potential causes. Aneuploidy is indicated if symmetric FGR is found before 20 weeks of gestation. For 5% to 10% of FGR instances, foetal infection is to blame; CMV and toxoplasmosis are the most frequent culprits. Malaria, syphilis, varicella-zoster virus, and herpes simplex are some other infectious agents that have been linked. Growth restriction may also occur in foetuses with non-chromosomal congenital abnormalities or certain disorders.

Fetal, placental, or maternal reasons might be used to categorise the causes.

Maternal causes: FGR can be brought on by maternal morbidities that disrupt uteroplacental-fetal blood flow. “Chronic hypertensives, GDM, systemic lupus erythematosus, APLA, severe cardiopulmonary or renal diseases, severe anaemia and malnutrition, sickle cell disease, substance abuse (alcohol, cocaine, nicotine, heroin, marijuana, and others), anti-neoplastic drugs or radiation exposure, chronic antepartum haemorrhage, low pre-pregnancy weight or poor gestational weight gain, and extremes of maternal age” , A foetal weight's variability of roughly 10% can be attributed to maternal diet.

Placental/umbilical cord causes: “10% of idiopathic cases of FGR and 33% of FGR with placental infarction and decidual vasculopathy are found to have chromosomal placental mosaicism (CPM), which manifests as placental trisomy (most frequently trisomy 21) and a chromosomally normal foetus”. Other causes of FGR include placental anomalies (such as a bilobate or circumvallate placenta, a tiny placenta, or a placenta with mesenchymal dysplasia), as well as umbilical cord anomalies (such as a single artery or a velamentous or marginal cord insertion). Through their detrimental effects on placental functioning, maternal morbidities have an impact on foetal growth.

Epidemiology:

About 3% to 7% of pregnancies result in foetal growth restriction (FGR). [18] Depending on the population investigated, the foetal gestational age, and whether or not SGA foetuses were included, the incidence varies. According to reports, it is 6 times greater in developing and undeveloped nations than in developed ones. [19] In underdeveloped nations, one in four newborns are undersized for gestational age at birth, and this condition affects 20% of all infants. 75% of the affected infants are from Asian continents. Preeclamptic women who have had previously growth-restricted foetuses show a 20% recurrence rate in subsequent pregnancies. Idiopathic FGR cases, or those without a known aetiology, make up about 40% of all cases. A genetic anomaly accounts for one-third of the remaining 60% of instances with known causes, with environmental factors accounting for the remaining 40%.

Pathophysiology:

The fetus's body fat and muscle mass are drastically decreased, which causes the subcutaneous fat as well as the body's nitrogen and protein stores to be depleted. Reduced mineral and glucose deposition in the bones as well as impaired maternal-fetal transfer of nutrients such minerals,

amino acids, and glucose as a result of placental insufficiency. The blood flow is shifted away from less important organs and prioritised toward the brain, heart, adrenal glands, and placenta as the foetus continues to experience stress.

"Causes of FGR:

- Previous H/o FGR
- Previous H/o preeclampsia
- H/o smoking & substance abuse
- Multiple gestations
- Assisted Reproduction
- Chronic diseases
- Advancing maternal age"

Examination findings:

Maternal Findings

By measuring the distance between the pubic symphysis and the top of the uterus, the fundal height that determines gestational age is reduced.

Neonatal Findings

The newborn with FGR weighs less than the third percentile and often appears malnourished at birth with reduced muscular mass and subcutaneous fat. Depending on the aetiology of intrauterine growth restriction, the head may appear proportionately large or tiny. The umbilical cord may seem shorter and the face may appear thinner. The cranial suture may be wide and the fontanels may be big as a result of insufficient bone mineralization and bone growth. Particularly with asymmetric FGR, "the Ponderal index (PI) [PI=weight (g) x 100/height (cm)] is a reliable measure of the degree of foetal malnutrition. Malnutrition is indicated by an index below the 10th percentile".

"Depending upon the etiology, physical findings may be noted in a growth-restricted infant at birth, such as:

- Hepatomegaly, sensorineural hearing loss, chorioretinitis, blueberry muffin spots in congenital CMV infection.
- Low set ears, cleft palate, clenched fist with overlapping fingers, and rocker bottom feet in trisomy 18.
- Scalp defect, close-set eyes, coloboma, micrognathia, and umbilical hernia in trisomy 13.

Other findings in FGR with known etiology may be relatable to the primary cause and manifest according to the specific syndromes involved".

Evaluation:

Every antenatal appointment should include a serial fundal height measurement, according to the ACOG. [20] If the fundal height is 3 cm or more or less than the gestation in weeks, a serial USG study is advised. The ultrasound scan also finds any anatomical anomalies in the developing foetus. To distinguish FGR from a misdated pregnancy, the gestational age must be determined accurately.

The recommendations emphasise the importance of identifying high-risk pregnancies as soon as possible, "including those with a H/o FGR, substance addiction (tobacco, alcohol, and others), advanced maternal age, preeclampsia, or a previous pregnancy complicated by preeclampsia, among others". If risk factors are found, serial USG is strongly advised. Estimates of amniotic fluid volume and umbilical arterial Doppler should be carried out if FGR is found. In low-risk pregnancies, routine ultrasound screening throughout the third trimester is not advised. [20]

Management:

The evaluation of foetal growth velocity can be done in a number of ways, including by using growth charts, evaluating deviations from growth-velocity charts, and doing an individual growth assessment. Overall, the primary objective is to assess the foetal growth trajectory and identify those foetuses that are deviating from their unique trajectory, which indicates a failure to meet their growth potential. There is evidence to show that a third trimester with slower foetal growth velocity is linked to a higher chance of unfavourable outcomes. Reduced growth velocity is typically understood to be a drop of > 50 percentiles for AC or, more frequently, EFW between two consecutive ultrasound exams. [16]

DOPPLER EVALUATION:

The Doppler in the evaluation of foetal development is of great use, the ideology is that it can look at the umbilical and uterine arteries to assess uteroplacental function. Uteroplacental insufficiency is mediated by the sick villous vascular tree and spiral artery maladaption. Measurements of the middle cerebral artery (MCA) and ductus venosus are made possible by Doppler velocimetry. "The failure of the uterine arteries to physiologically transition from high- to low-resistance vessels is attributed to a defective trophoblastic invasion of the spiral arteries, which results in a high-resistance circulation. High uterine artery mean PI is linked to placental insufficiency and maternal vascular malperfusion of the placenta (above the 95th percentile)". Placental vascular insufficiency, which is indicated by REDF and AEDF in the UA, is related with progressively rising PI in the UA. This increases the foetal afterload resistance and further lowers the placental surface area accessible for gas and nutrition exchange. Foetal MCA-PI declines as a result of vasodilatation, often known as the "brain-sparing" effect which occurs as a reaction to the hypoxemia in fetus by the oxygen sensitive vascular beds in the brain, next organs to receive relataively high blood volume are the adrenals and coronaries. In an effort to compensate for the severe oxygen deprivation, the DV gradually enlarges to increase cardiac flow. As a result, the ductus venosus flow velocity waveform changes, specifically the presence or absence of a-waves. Doppler velocimetry is essential in the diagnosis, monitoring, and therapy of FGR. It is crucial to highlight that different Doppler velocimetry patterns can discriminate between the Early FGR and late FGR.

Biophysical profile: “The BPP score is determined after a 30-minute study of the foetal tone, general body movement, breathing movement, amniotic fluid volume, and heart rate reactivity”. Fetal pH and outcome can both be predicted by BPP score. Across gestational ages, there appears to be a continuous correlation between the changed BPP score and foetal pH. A score of 2 has a 100% sensitivity for acidemia, while a score of 4 is connected to a foetal pH of less than 7.20. The STV is an indicator of autonomic nervous system activity acquired by computerised CTG (cCTG). “”=cCTG and evaluation of STV are used in place of invasive testing in cases of foetal hypoxemia and acidemia and represent the only objective measure of foetal heart rate. In the context of FGR and the presence of severe hypoxemia or hypoxia, the foetal sympathetic and parasympathetic activity is altered, resulting in reduced foetal heart rate variation and, therefore, reduced STV”.

ROLE OF DOPPLER IN OBSTETRICS:

The flow in the umbilical cord was made audible by the use of CD also known as the Continuous-wave Doppler which also happened to be the first application of Doppler in the field of obstetrics. The development of gray scale ultrasound and PW ultrasound allowed for the visualisation of particular vessels and the sampling of waveforms, opening an access into the fetoplacental unit. [27] The identification of typical anatomical structures was made easier with the addition of colour Doppler flow US for eg A three-vessel cord confirmation by demonstrating the umbilical arteries on both sides of the bladder. Amniotic fluid volume is also prevented from being overestimated by using colour Doppler flow to identify cord that seem like pockets of fluid, site of insertion of the cord is much easier using the colour Doppler than with gray-scale alone. A preferred obstetric scan should consider whenever possible, documentation of the site of cord insertion onto the placenta. [28,29] “Because marginal or velamentous insertions increase the risk of growth restriction, unequal placental sharing, and vasa previa, identifying the placental sites of the umbilical cord insertions is crucial in multiple gestations”. [30] “Even though many various vessels have been the focus of research studies, only the umbilical artery's spectral analysis has been demonstrated to have an effect on the course of pregnancies impacted by foetal growth limitation”. [31] “The guidelines for the publication "Doppler Assessment of the Fetus with Intrauterine Growth Restriction" by the Society for Maternal-Fetal Medicine. [31] Doppler in Obstetrics, a free online textbook, is another resource for in-depth technical information”. [32]

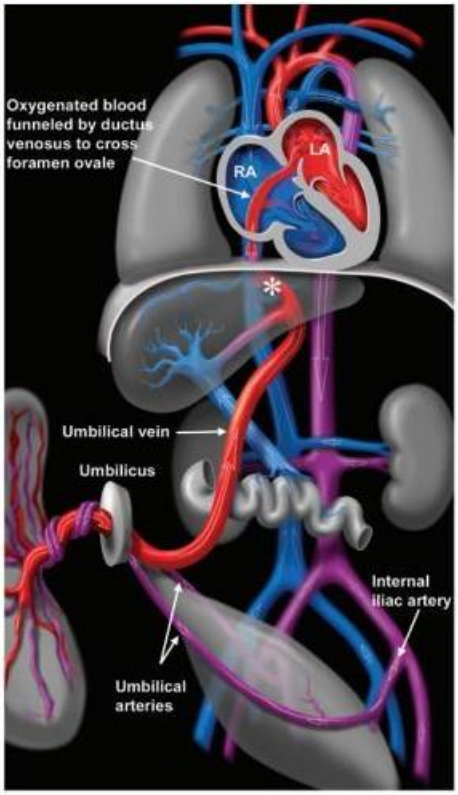
Safety of Doppler in Obstetrics:

“Without a discussion of safety, no discussion of imaging during pregnancy is complete. Despite the fact that ultrasound does not emit ionising radiation and is safe for use at all gestational ages, spectral Doppler ultrasound can produce a significant amount of energy.

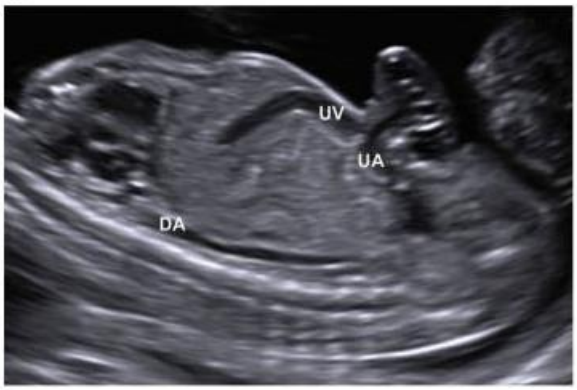
In accordance with the ALARA principle, all foetal imaging, including Doppler US, should only be carried out when necessary for legitimate medical reasons and with the use of measures to reduce foetal exposure to a level that is as low as practically possible. Numerous variables, including as the power output, the depth and kind of structures being probed (soft tissue vs. bone), the duration of the examination, and the transducer type, all have an impact on the amount of energy that is exposed to the foetus during an ultrasound. Because the energy output with Doppler US is larger than that with B-mode US, special attention should be made to safety. On-

screen indicators of the relative risk of possibly adverse US-induced bioeffects are the mechanical index and the heat index. [33] The mechanical index, which measures the likelihood of nonthermal bioeffects such as cavitation (the interaction of the US with gas bubbles), should be 1.0 or lower. There may be a threshold below which no effect is felt, and this threshold may differ depending on the kind of tissue. [34] The mechanical index is thought to be less significant than the thermal index in obstetric imaging because foetuses lack gas. The thermal index is a relative measure of temperature increase and probable thermal tissue damage. The amount of energy absorbed, which varies by tissue type (bone > soft tissue > amniotic fluid), is a factor in the thermal risk. Before bone ossification is visible in the first trimester, a heat index for soft tissue should be used; once it appears, a thermal index for bone should be utilised (typically after 10 weeks). These indices should be carefully watched throughout the evaluation because they fluctuate with different machine settings and power output. [34] The amount of power emitted rises with colour Doppler flow US. The depth and size of the colour box, which should be maintained as small as possible to just encompass the region of interest, affect the power output. Even more energy is produced by Spectral Doppler US, increasing its heating potential. The fact that the transducer is fixed in place and the power is concentrated down a single line makes the issue worse. The displayed thermal index should be 1.0 or less, according to the most recent recommendations for Doppler US use at the time of first-trimester screening (11 to 13 weeks, 6 days), and the exposure time should be as brief as possible, typically no longer than 5 to 10 minutes and no longer than 60 minutes. [35]

All imaging should follow the ALARA approach for the rest of the pregnancy. The way the mechanical and thermal indices are shown differs from vendor to vendor. All operators doing obstetric US should confirm with their application specialists that the operators are aware of where the thermal index and mechanical index are displayed and that they are aware of how to change levels. Many specialty imaging packages are set up to ensure low energy output. Start with a modest power level for both indices and gradually increase to levels that are just high enough to produce a diagnostic examination".



a.



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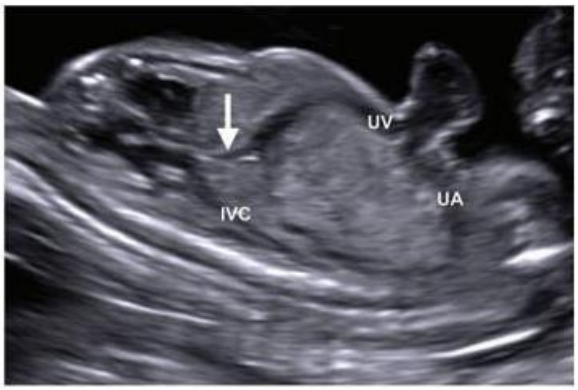


c.

FIG 13: A. FETAL CIRCULATION, B. GRAY SCALE ULTRASOUND PARA-SAGGITAL VIEW, UV: UMBILICAL VEIN, UA: UMBILICAL ARTERY, DA: DUCTUS ARTERIOSUS, C: SLIGHT RIGHT PARA-SAGGITAL VIEW SHOWING DUCTUS VENOSUS IN WHITE ARROW CONNECTING UV AND INFERIOR VENA CAVA. [73]

Fetoplacental Flow unit:

The deoxygenated blood is carried by the umbilical arterial system which are 2 in number, that arise from the internal iliac arteries, this blood is taken to placenta. The ductus venosus, left portal vein, inferior vena cava, and umbilical vein are all used to transport oxygenated blood back to the right atrium from the placenta. “A defined stream of oxygenated blood is created by flow across the trumpet-shaped ductus venosus, and this stream preferentially passes through the foramen ovale to the left atrium, left ventricle, and aorta, diverting the most oxygenated blood to the head and neck veins and the coronary arteries” (Fig 13). [36] Large portions of the foetal right ventricular flow skip over the lungs. Instead, it is redirected to the descending aorta via the ductus arteriosus to perfuse the foetal torso. The internal iliac arteries give rise to the umbilical

arteries, which are in charge of delivering foetal blood depleted of oxygen to the placenta. Rise in the placental resistance reflects onto the right ventricular function which produces more than half of the heart's CO, any process that has a detrimental impact on the organ's health will also have a negative impact on the foetus. [37] The uterine artery is a representation of the maternal half of the fetoplacental circulatory unit. In pregnant state, the uterines distend as a result of the trophoblastic activity in first trimester resulting in efficicent remodeling rendering them resistant to parasympathetic activity [38] therefore , there is steady low resistance flow during the diastole. The US, MCV, DV and UT A are among the arteries sampled to evaluate the fetoplacental unit. “In the first trimester, Doppler ultrasound is used to screen for women who are more prone to develop preeclampsia by evaluating the uterine artery waveform and (a) detecting aneuploidy and an elevated risk for congenital heart disease. Doppler US is used in the second and third trimesters to assess risk in foetuses with growth restrictions, those with high output conditions, and to detect monochorionic twinning complications (umbilical artery, middle cerebral artery, umbilical vein, ductus venosus), as well as to noninvasively detect foetal anaemia by measuring the middle cerebral artery's peak systolic velocity. To make waveform analysis as simple as possible, the results of all spectral Doppler US exams should be presented with an appropriate baseline (Fig 14a), scale (Fig 14b), and sweep speed (Fig 15). Misinterpretation of results and management mistakes may result from technical errors in the angle of insonation (Fig. 16), sample volume size and location, and selection of the wall filter (Fig. 17)”. The umbilical artery's normal and aberrant waveforms are depicted in a composite in Figure 18.

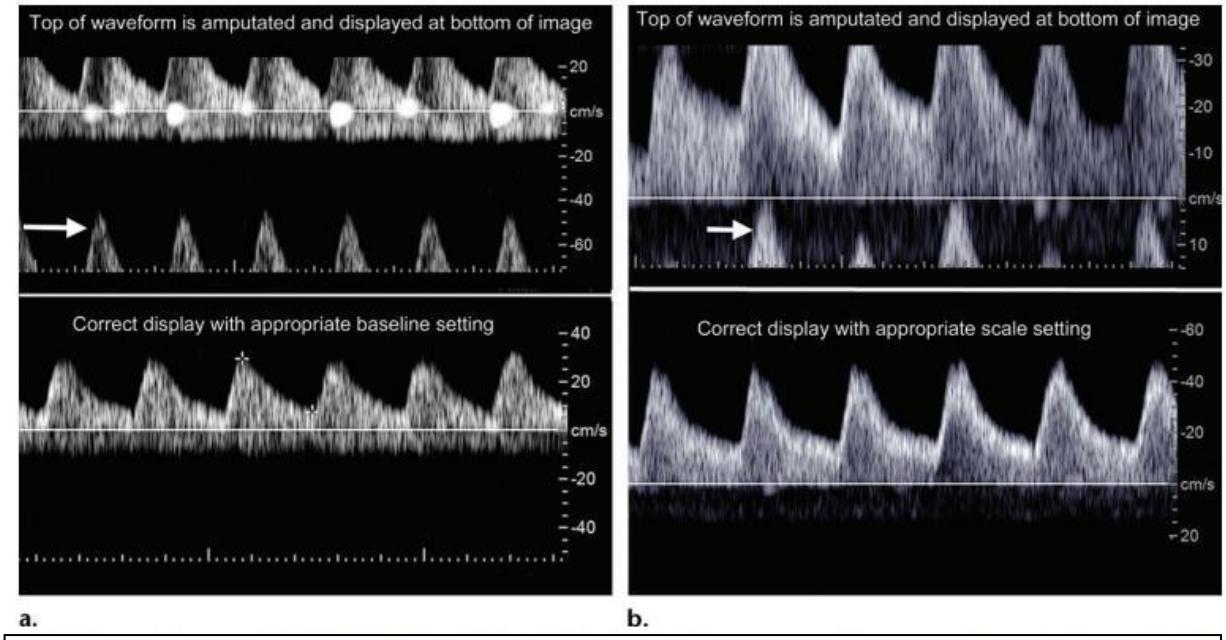


FIG 14: [73]

A: CORRECTION OF BASELINE

B: CORRECTION OF SCALE.

Obstetric Doppler US in the First Trimester:

The umbilical portal venous system and IVC are connected by a tiny trumpet-shaped structure called the ductus venosus. Due to the right atrium's unique structure, oxygenated blood returning from the placenta flows straight into it, allowing for easier passage through the foramen ovale and into the left atrium. The waveform and sound produced by the ductus venosus are distinctive. The latter has been compared to a washing machine's noise. To ensure proper cursor positioning, it is helpful to listen while sampling. The ductus venosus should be sampled using proper procedures. “Locate the point of aliasing between the left portal vein and the inferior vena cava using colour Doppler flow US. When screening for nuchal translucency in the first trimester, this aliasing is best detected on a sagittal plane. Axial images at the level used for measuring belly circumference can be employed later in pregnancy”. (Fig 19).

Use a tiny sample size (0.5 to 1 mm) for the best results to prevent mixing of the flow from the nearby vessels (Fig 20). [36] “To achieve a nice waveform and maximise Doppler shift, the insonation angle should be less than 30°. Avoid probing the ductus venosus at a 90° angle (that is, perpendicular to the direction of flow), as with all Doppler US investigations, as this results in zero Doppler shift and no flow information. frequency (50–70 Hz) possible. A high sweep speed (2–3 cm/sec) should also be used to spread the waveform. [31,32] Determine the three waves that make up the waveform: the S wave, the D wave, and the A wave. The S wave, D wave, and A wave all represent different phases of ventricular contraction: systole, diastole, and contraction of the atrium”. A wave's reversal is never normal. Reversed A wave in twins is a sign for an increased chance of developing the TTTS. Other associations include an increased risk of aneuploidy [39,40] and congenital cardiac disease [41]. [42] The absence or inversion of the A wave are examples of abnormal findings (Fig 19b). In research settings, many metrics, like the venous pulsatility index, are used. Between 10 and 14 weeks of gestation, the ductus venosus is subjected to Doppler US for aneuploidy screening, sometimes in conjunction with the assessment of NT and first trimester structural features. Doppler of DV is also carried out in the 2^{nd} and 3^{rd} trimesters to evaluate cardiac strain in foetuses with foetal growth limitation attributable to aberrant placentation and to evaluate cardiac dysfunction in foetuses with high-output situations. When the ductus venosus is sampled, the foetus should be at rest and not breathing.

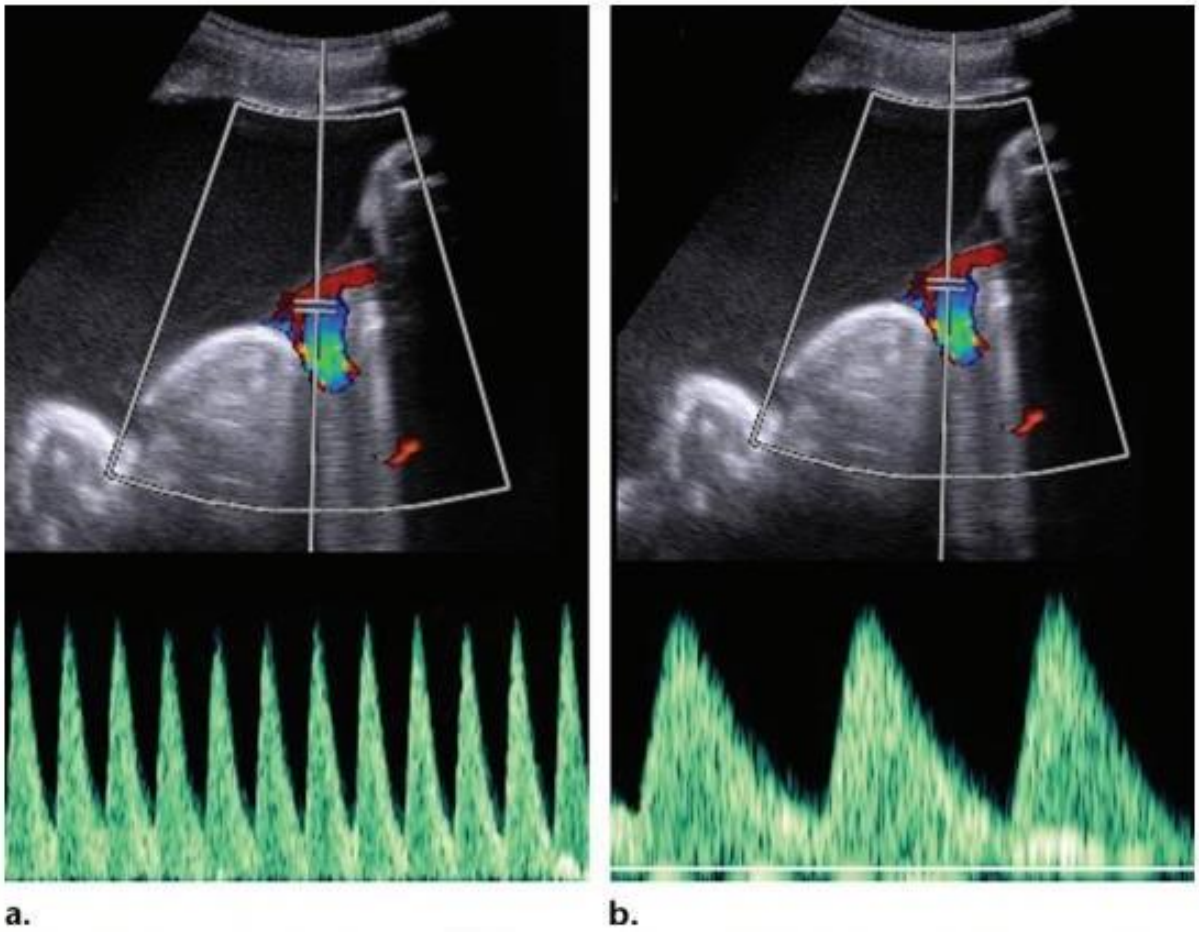


FIG 15: [73]

A: INCORRECT SWEEP SPEED,

B: CORRECT SWEEP SPEED.

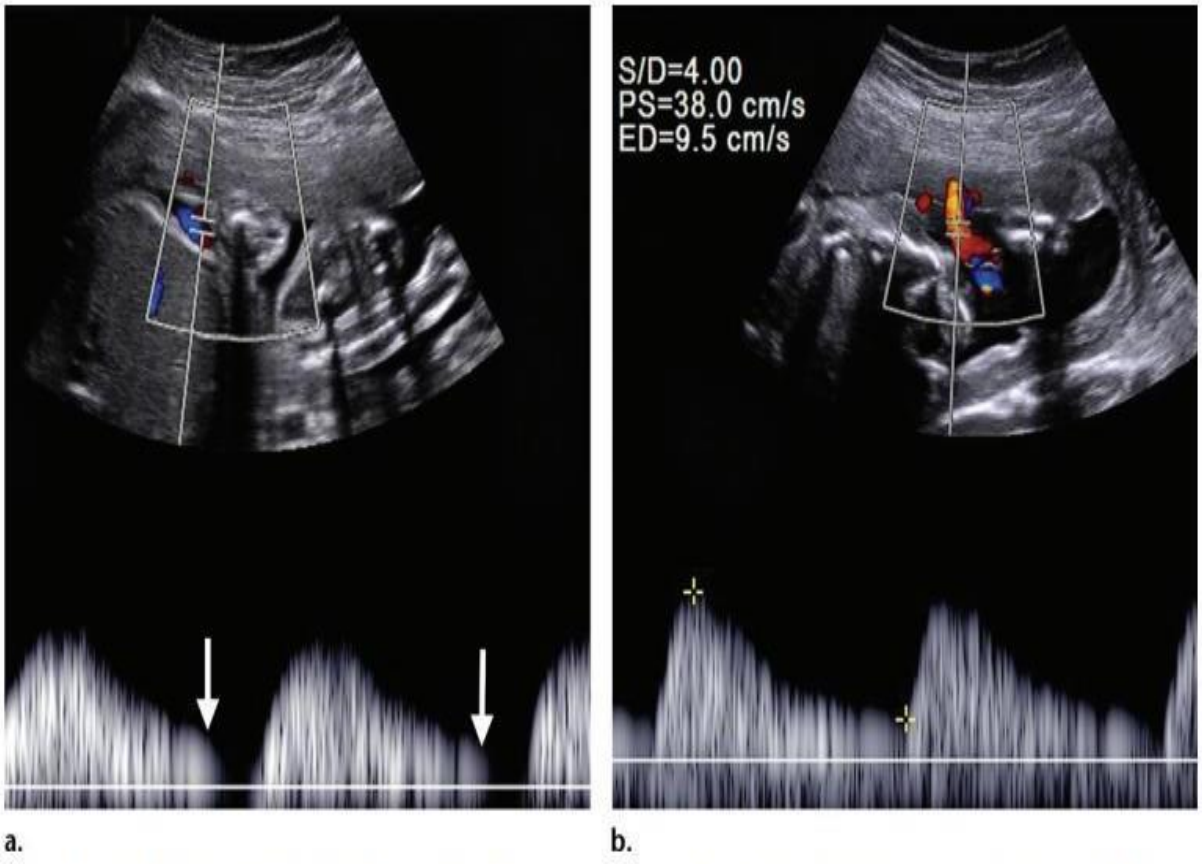


FIG 16: [73]

A: INCORRECT (70-80 degree) ANGLE OF INSONATION

B: CORRECT – NEAR TO O DEGREE OF ANGLE OF INSONATION.

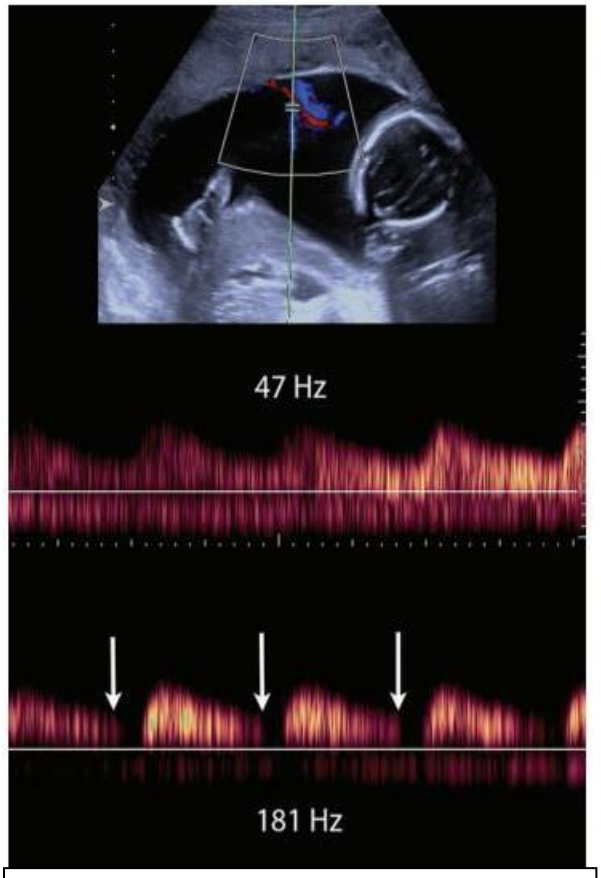


FIG 17: [73]

SELECTION OF WALL FILTER

INCORRECT WALL FILTER (181 HZ SHOWING ABSENT END DIASTOLIC FLOW)

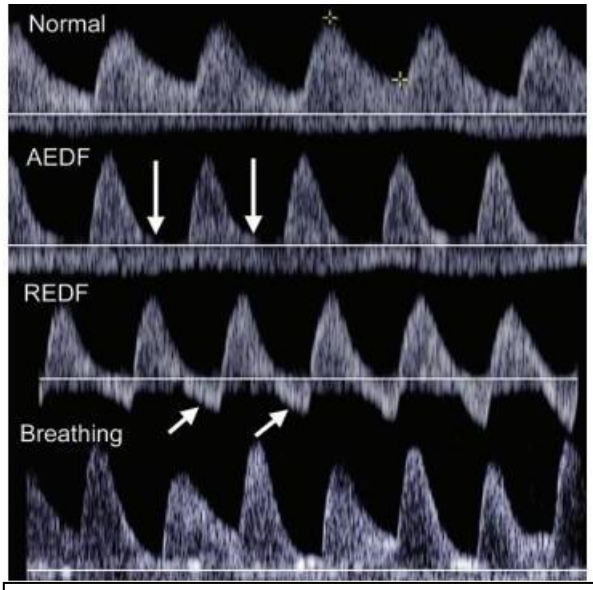


FIG 18: [73]

NORMAL UMBILICAL ARTERIAL FLOW

ABSENT END DIASTOLIC FLOW

REDUCED END DIASTOLIC FLOW

VARIATIONS DURING RESPIRATION

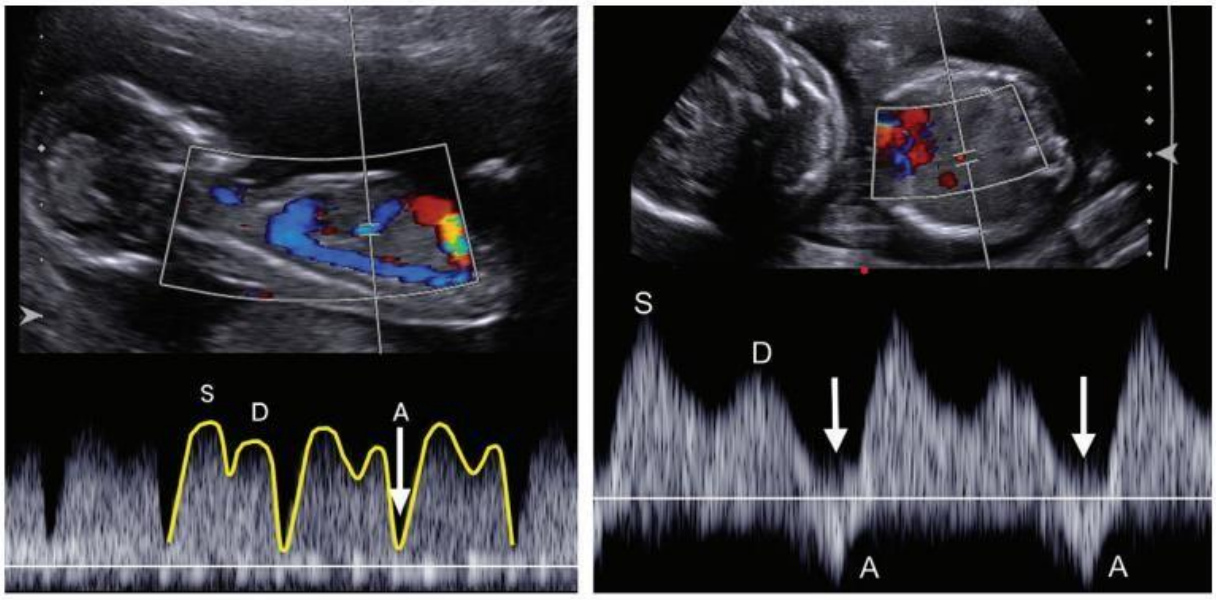


FIG 19: [73] A: NORMAL DUCTUS VENOSUS FLOW SHOWING "S WAVE, D WAVE AND A WAVE ABOVE THE BASELINE"

B: "REVERSAL OF A WAVE IN A CASE OF SEVERE GROWTH RESTRICTION IN SECOND TRIMESTER".

Obstetric Doppler US in the 2nd and 3rd Trimesters:

Doppler US is used to evaluate foetal health in the second and third trimesters. The MCA and the umbilical artery are the two most crucial blood arteries to examine; ductus venosus and umbilical vein analysis can provide additional data. Uterine Artery Throughout the cardiac cycle, the normal placental vascular bed has constant forward flow and low resistance. "With increasing gestational age, the diastolic flow increases and the S/D ratio decreases. The S/D ratio's 50th percentile at 20 weeks is 4.At 30 weeks, the 50th percentile is 2.83; and at 40 weeks, the 50th percentile is 2.18". [43] To manage FGR and staging of TTTS, current clinical practise uses the S/D ratio and the presence of AEDF and REDF. Doppler of the UA is typically used for viability (i.e., 24 weeks) in clinical settings; however, in the twin-twin transfusion syndrome, it is performed as part of the staging system. Therefore, regardless of gestational age, it is carried out whenever that diagnosis is thought to exist. "To study blood flow throughout the cardiac cycle in research studies, researchers use the pulsatility index. The peak systolic velocity less the end-diastolic velocity is subtracted from the time-averaged velocity to get the pulsatility index. Along the umbilical cord's length, the umbilical arteries' flow resistance varies". When the umbilical cord is inserted, resistance is greatest at the abdominal site, intermediate in the free-floating loops of the cord, and minimal at the placental location [44]. (Fig 21). Therefore, it's crucial to sample consistently when doing pregnancy-related serial examinations. " The abdominal site of umbilical cord insertion was recommended for sampling by the Society for Maternal-Fetal Medicine in 2012 [31], although this location can be difficult in later stages of pregnancy when the foetal lower extremities may cover it or when oligohydramnios restricts acoustic access (as often occurs in association with foetal growth restriction)". To assure the right comparative evaluation of the same fetus throughout the pregnancy, it is very important to sample at or

closest to fetal insertion of the cord, while performing the Doppler evaluation in 2013, the International Society of Ultrasound in Obstetrics and Gynecology suggested the use of free loop in singleton feuses. [45] The foetus should ideally be at rest and not breathing because these activities alter the spectral waveform. Since all measurements used in clinical practise are ratios, an angle of insonation close to 0° although not essential yields the best Doppler shift and waveforms. Compare the values by measuring the S/D ratio, "which is the peak systolic velocity divided by the end-diastolic velocity". [43] The S/D ratio numbers should not be averaged. Note whether there is no end-diastolic flow or if it is reversed, as well as whether it is intermittent or persistent. It is significant to highlight that screening for low-risk pregnancies does not involve Doppler of the fetoplacental unit. Doppler of the umbilical cord is only aberrant when significant portions of the placental tertiary villous system is severed, making it a rather basic indicator of placental health. Before reversed end-diastolic flow is observed, up to 70% of the placental vascular bed is believed to have to be destroyed [46,47]. (Fig 18). Doppler US results, however, could appear before variations in the FHR that show up as abnormal foetal nonstress test outcomes. "A clinical recommendation for Doppler US evaluation of the foetus with growth limitation was released by the Society for Maternal-Fetal Medicine in 2012; it is still valid today. The Society for Maternal-Fetal Medicine's recommendations urge weekly Doppler US of the umbilical artery in cases of foetal growth restriction. The recommended gestational age for delivery is 38–39 weeks if the Doppler US results are still normal. The severity of the finding governs management when these results are aberrant. Reduced diastolic flow necessitates more frequent antenatal testing (such as nonstress tests, amniotic fluid measurements, and biophysical profiles), weekly Doppler US, and consideration of delivery after 37 weeks. Doppler US is conducted two to three times per week in addition to conventional antenatal examinations of foetal well-being when absent end-diastolic flow or reversed end-diastolic flow is observed. Corticosteroid therapy is also administered in expectation of preterm delivery. [31] If end-diastolic flow is missing, the goal gestational age for birth is 34 weeks or more; if end-diastolic flow is reversed, the goal gestational age is 32 weeks or more. Figures 10 and 11 show the role of umbilical artery Doppler US in the evaluation of unequal placental sharing and time of delivery in twins".

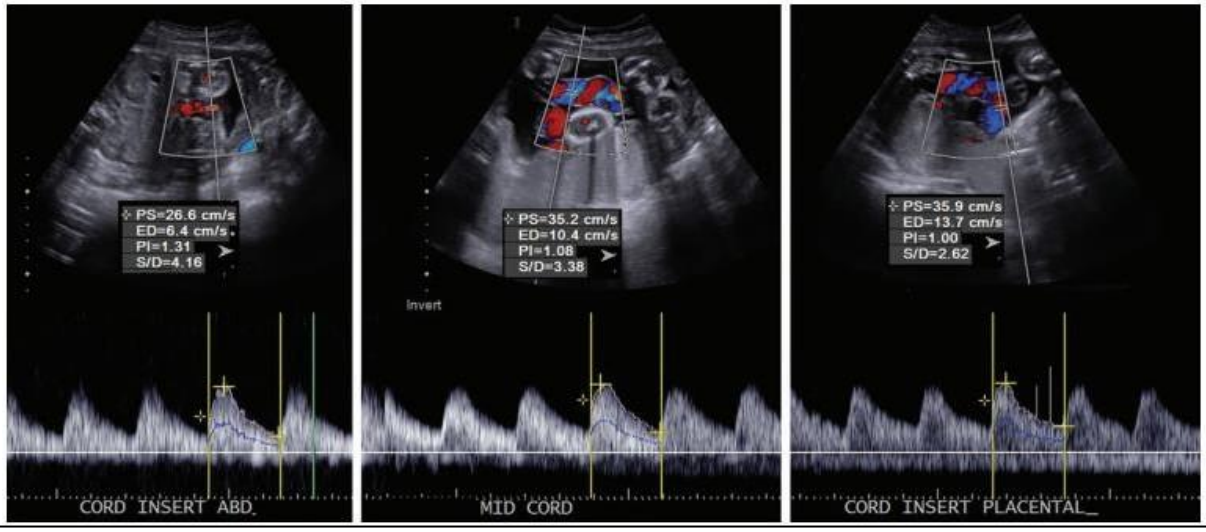


FIG 21 : [73] LEFT TO RIGHT SHOWING DIFFERENCE IN S/D RATIO

FROM THE ABDOMINAL CORD INSERTION

FROM THE FREE LOOP OF CORD

FROM THE PLACENTAL INSERTION

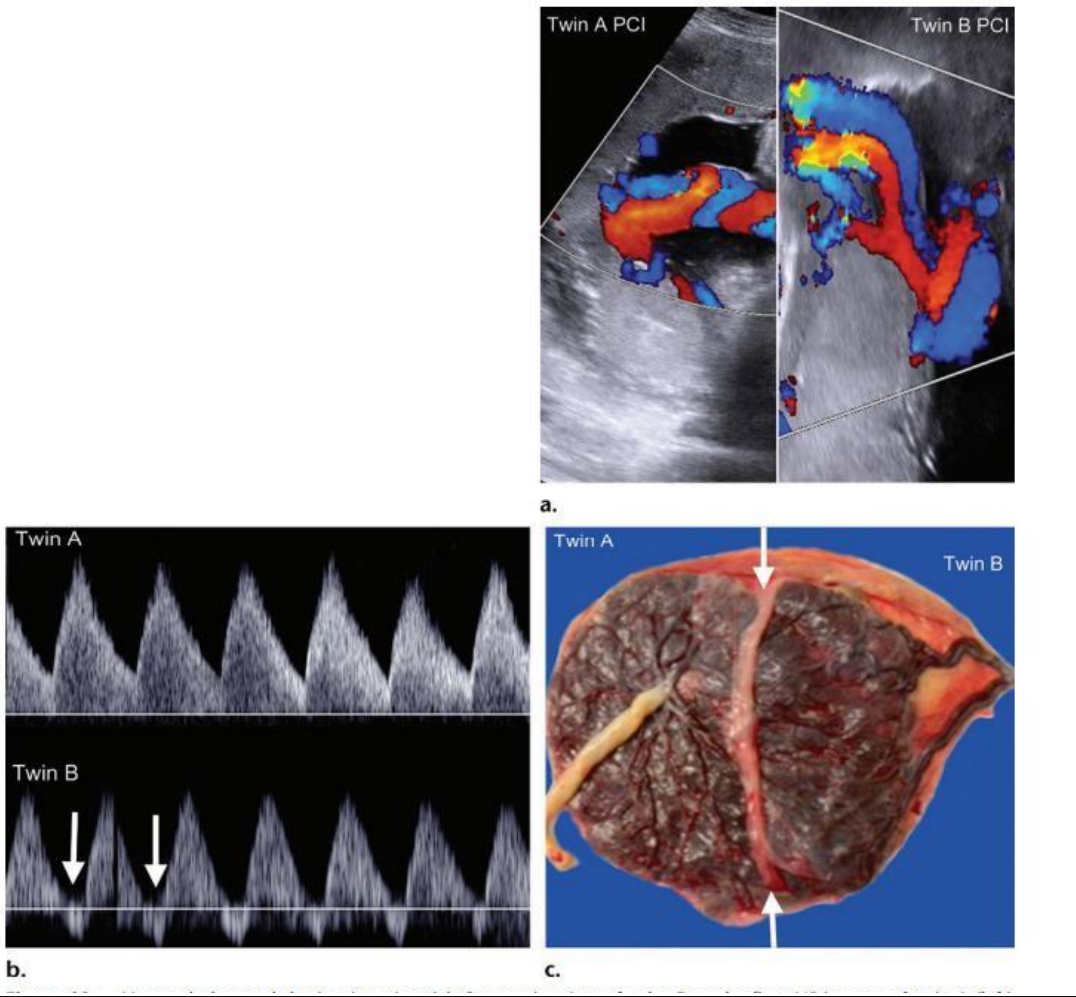


FIG 22 : [73]

UNEQUAL SHARING OF PLACENTA IN A TWIN GESTATATION

A: CENTRAL INSERTION IN TWIN A AND VELAMENTOUS INSERTION IN TWIN B

B: SPECTRAL DOPPLER US OF CORD SHOWING NORMAL FLOW IN TWIN A AND REDF IN TWIN B

C: "THIN INTER TWIN MEMBRANE" – WHITE ARROW CAUSING UNEQUAL DIVISION OF PLACENTA, NOTE THE VELAMENTOUS INSERTION

Umbilical Vein:

The oxygenated blood derived from the placental circulation goes to the fetus which is a typical continuous flow (Fig 24). In the third trimester, it's common to see a foetus breathing. Variations in intrathoracic pressure affects the dynamics of the flow in the vein, causing the umbilical vein waveform to undulate in a way that is unrelated to the cardiac cycle (Fig 24). The umbilical vein's pulsatile flow is a concerning discovery this means that the raised pressure in the placenta has reflected on to the right heart which fails to pump the flow in a forward direction concomitantly resulting in raised right atrial and DV pressure where is seen as a reversal of A wave then resulting in pulsatility of UV (Fig 24). Use singletons to sample in a free-floating loop of the umbilical cord for the best results. To determine which vein belongs to which foetus when

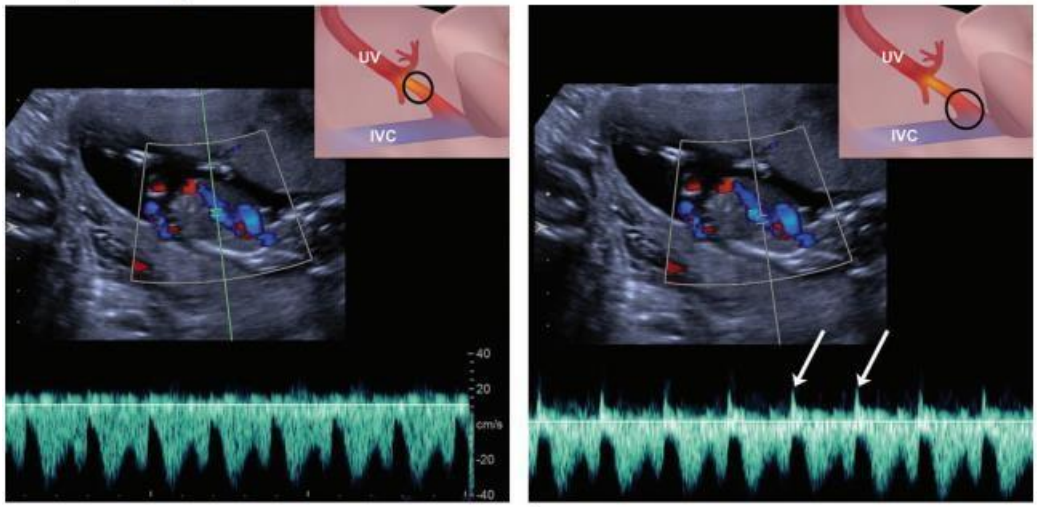
there are many pregnancies, take a sample not far from where the umbilical cord was inserted into the abdomen. [45] There are no velocity data, hence the insonation angle is not important. The foetus should ideally not be breathing and be at rest. When examining the waveform, be sure to distinguish between pulsatile venous flow and the typical undulations associated with foetal breathing.

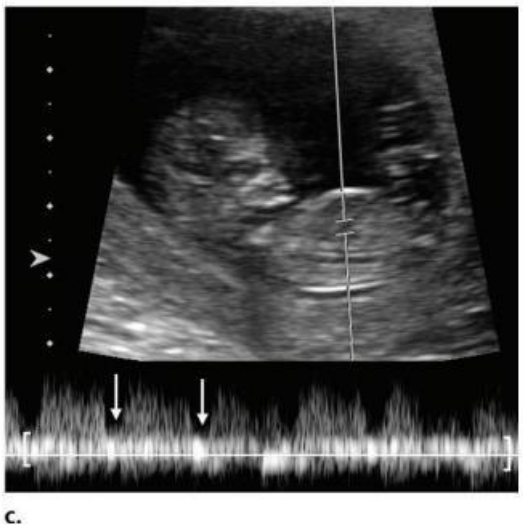
FIG 20 : SAMPLING OF DUCTUS VENOSUS [73]

A: CORRECT SAMPLE VOLUME PLACED OVER THE ALIASING

B: RATHER LARGE SAMPLE VOLUME PLACED CEPHALAD (NOT OVER THE ALIASING), CONTAMINATION OF THE WAVEFORM WITH IVC FLOW RESULTING IN SPURIOUS REVERSAL OF A WAVE

C: RATHER LARGE SAMPLE VOLUME PLACED OVER THE PORTAL VEIN SIMULTANEOUSLY RESULTING IN OBSCURATION OF A WAVE





Doppler evaluation of Ductus Venosus :

DV Doppler is a measure of strain on cardia in the 2nd and 3rd trimesters, in contrast to its role in the first trimester as a screening tool for aneuploidy and congenital heart disease. “Under normal circumstances, the liver is bypassed by around 30% of the inbound placental return in the second trimester, and by 31 weeks till term, this percentage has decreased to about 18%. A greater proportion of umbilical vein blood flow is diverted to the left side of the heart when placental function is compromised (the head-sparing effect). This shunting reduces blood supply to the liver, which stunts liver development and restricts foetal weight gain.” [48]

“Afterload (for example, higher placental resistance), myocardial performance (for example, cardiomyopathy), and preload are some of the variables that affect heart function (eg, the recipient twin in the twin-twin transfusion syndrome) . The most common and sensitive observation when any one of these parameters is altered is decreased forward flow during atrial systole (i.e., attenuated or reversed A wave)”. [49,50] (Fig 19). Reversal of A wave in DV is a prime marker of cardiac dysfunction, researches have been going on to use the venous PI that shows the extent to volume redirected to the brain. It has been demonstrated that a ductus venosus A wave that is absent or reversed is a reliable indicator of stillbirth. Reversal of a wave mosty suggested less likelihood of a week of survival of FGR fetus . [51]

Middle Cerebral Artery Doppler evaluation :

In order to calculate the cerebroplacental ratio, a metric for foetal brain sparing, and to noninvasively diagnose foetal anaemia, Doppler evaluation of middle cerebral artery is used, also to assess anaemia in fetus which can be early in the gestation from 18 weeks onwards. The PI is used to calculate the CP ratio. The angle of insonation is of less value in middle cerebral artery Doppler to assess anaemia because the cerebroplacental ratio compares the flow of the middle cerebral artery to the flow of the umbilical artery using data from the pulsatility index. The cerebroplacental ratio contrasts the perfusion of the placenta and the foetal brain. Normal flow in the umbilical artery should be low resistance In contrast to normal flow in the middle cerebral artery which is high resistance. As a general rule, the umbilical artery's S/D ratio ought to be lower than the MCA. The fetal adaptation occurs when there is hypoxia, the blood is majorly supplied to the brain that raises the (Fig 25). FGR prone fetuses with abnormal CP ratio which is “defined as the ratio of the middle cerebral artery pulsatility index divided by the umbilical artery pulsatility index that is less than the 5th percentile for gestational age” —but this was only seen till 34 weeks gestation in studies, Bahado-Singh et al [52] saw a significant rise in perinatal morbidity and mortality with loss of correlation later. [52] “Researchers hypothesised that an abnormal cerebroplacental ratio at more than 37 weeks is strongly associated with poor obstetric outcomes based on the findings of other studies”. [53] Despite all the evidences that show CP ratios potential to guide management, two recent reviews show theres no enough data and more improvised clinical trials are needed to ascertain its function and test its ability to perform as a stand alone test. [54,59] The MCA flow increases in foetal anaemia for a number of causes. Because fluids flow more quickly through a tube that has a fixed diameter when their viscosity drops, Figure 26's foetal hematocrit value increased. A 0° insonation angle should be used to sample the middle cerebral artery. The ultrasound beam's orientation is indicated by the vertical white line. The middle cerebral artery's orientation is indicated by the arrow. The angle formed by the vertical line and the arrow is known as the angle of insonation, and it should be 0°. (The difference at this gestational age (34 weeks) is 1.1 to 1.25 MOM. Cerebral vasodilatation also

redirects blood flow to the brain in a challenged foetus. Fetuses with anaemia experience increased cardiac output. Using colour Doppler to locate the COW in an axial image of the foetal head is the best way to determine the PSV in the MCA. The Sylvian fissure is where the middle cerebral artery enters the circle of Willis. The near-field middle cerebral artery will therefore be travelling toward the maternal abdomen wall in the majority of foetuses with cephalic presentation. To sample the middle cerebral artery with the beam parallel to the vessel's long axis and a 0° angle of insonation, the transducer position can be changed in relation to the foetal head in real time (Fig 26b). The image has been enlarged such that the middle cerebral artery can be seen for its entire length, and the colour image of the Willis circle takes up half of the image. When the fetus is at rest with no breathing movements, a sample size of 1 mm is kept within 2 milimeters of the origin of MCS at an insonation angle of 0 Degrees, [56] PSV and MOM are also recorded. MOM is easily calculated using an online calculator. [57] PSV >1.5 MOM is a higher risk of foetal anaemia. [58] this technique is essential in the evaluation of foetal anaemia. Serial Doppler US exams have taken the place of serial amniocentesis; invasive treatments are now carried out with the intention of treating anaemia with intrauterine transfusion (Fig 26). It is crucial to look for foetal anaemia as a potential cause whenever unexplained foetal hydrops is noticed. In this situation, a transfusion might save your life. [59] Measuring the peak systolic velocity of the middle cerebral artery is most frequently used to monitor patients who are at risk of developing foetal anaemia as a result of alloimmunization. This measurement may also be used in the evaluation of monochorionic twin pregnancy complications, as well as with other possible causes of anaemia, such as viral infection (e.g., parvovirus), anemia occurring due to bleeding into a foetal tumour. [60,61]

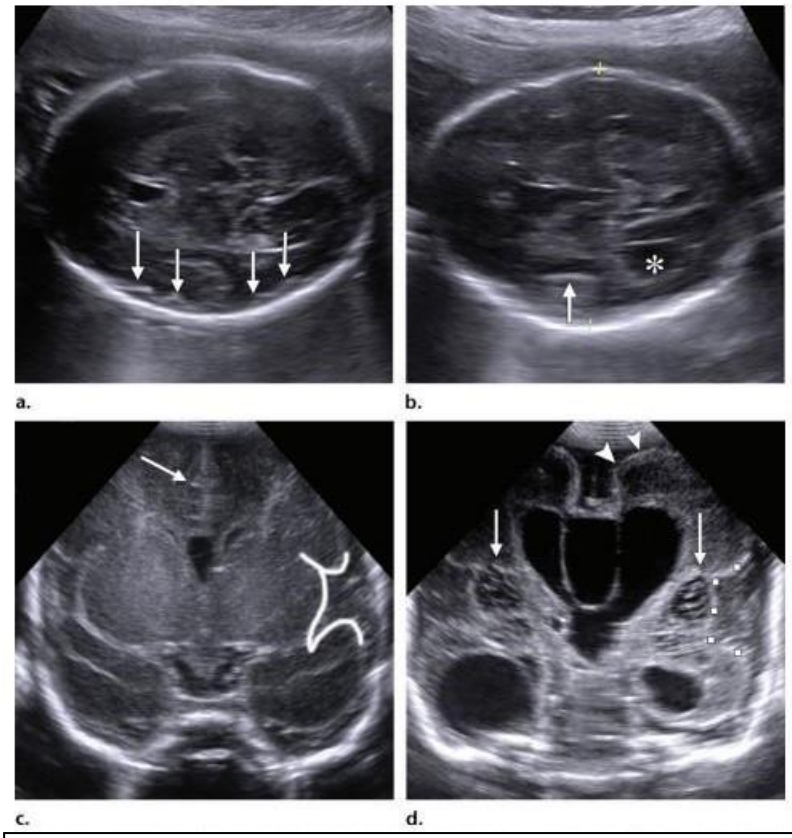


FIG 23 : UNEQUAL SHARING OF PLACENTA [73]

A: AXIAL GRAY SCALE IMAGE OF FETUS A SHOWING NORMAL DEVELOPMENT AT SECOND TRIMESTER SCAN

B: AXIAL GRAY SCALE IMAGE OF THE FETUS B SHOWING “VENTRICULOMEGALY (*) SMOOTH CORTEX AND OPEN SYLVIAN FISSURE”

C: CORONAL NEONATAL NEUROSONOGRAM (TWIN A) GREY SCALE IMAGE OF THE HEAD SHOWING NORMAL ANATOMY

D: CORONAL NEONATAL NEUROSONOGRAM (TWIN B) GREY SCALE IMAGE OF THE HEAD SHOWING “MULTICYSTIC ENCEPHALOMALACIA , VENTRICULOMEGALY, SMOOTH CORTEX”.

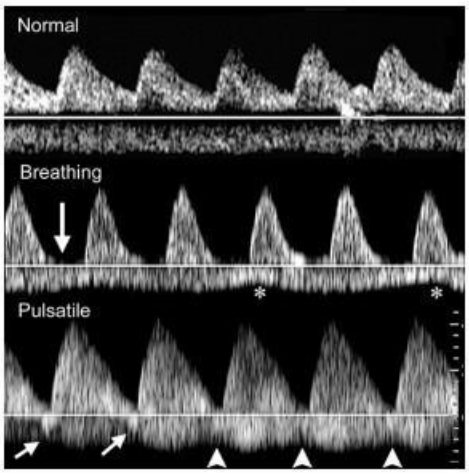


FIG 24 :UMBILICAL VEIN WAVEFORMS [73]

NORMAL

BREATHING FETUS

PULSATILE UV FLOW

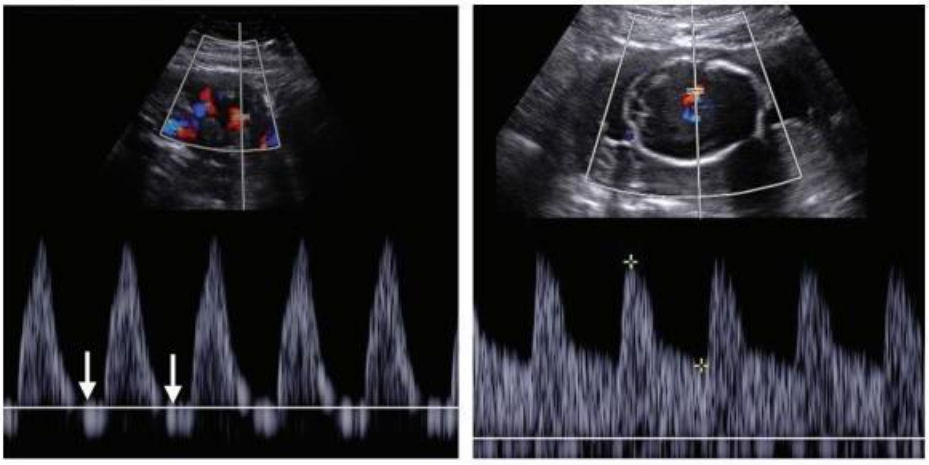


FIG 25 : ABNORMAL CP RATIO [73]

LEFT : REVERSAL OF EDF IN UMBILICAL ARTERY

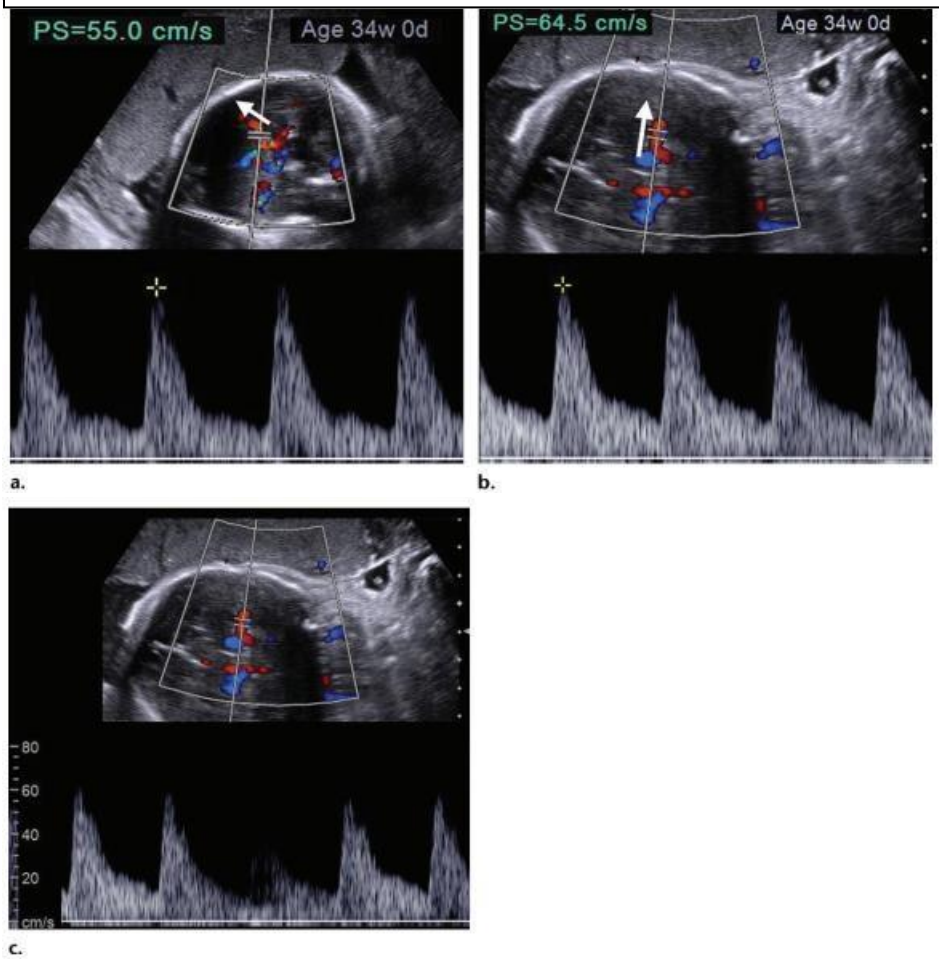
RIGHT: RAISED DIASTOLIC FLOW IN MCA WITH RESULTANT BRAIN SPARING

FIG 26: DOPPER ULTRASOUND OF MCA [73]

A: COPPLER DOPPLER ULTRASOUND IMAGE SHOWING SAMPLING OF MCA WITH INCORRCT ANGLE OF INSONATION

B: WITH CORRECT ANGLE OF INSONATION (0)

C: CORRECT ANGLE OF INSONATION BUT WAVEFORM IS COMPROMISED DUE TO FETAL BREATHING



Uterine Artery Doppler:

Pre-eclampsia screening done in first trimester and screening of other unfavourable outcomes in pregnancy like FGR are usually predicted doing the uterine artery Doppler. [62]. The internal iliac artery's branch known as the uterine artery travels anteriorly via the pelvis to the junction of the uterine body and cervix, where it enters the myometrium It hasa strong resistance, low diastolic flow, and early diastolic notching in the non-pregnant state. Successful placentation depressurizes the uterine artery branches which is steady flow with low resistance during the diastole. “This placental blood flow recruitment occurs quickly; notching should vanish by 13 weeks [63] and low-resistance flow should be achieved by 20 weeks at the latest. [64] Increased resistance and the presence of a diastolic notch through the late second trimester are signs of an aberrant waveform. One definition of a diastolic notch is a decrease in forward flow at the beginning of diastole, which is assumed to signify aberrant uteroplacental flow”. Negative

consequences have been linked to a diastolic notch. [65-67] “The probe is positioned in the medially-angled lower lateral quadrant of the abdomen. The uterine artery is seen with colour Doppler flow US since it seems to cross the external iliac artery and runs anteriorly (Fig 27). [36] Aim for as close to 0° as possible. The orientation of the vessel permits a modest angle of insonation, often 15°–30°”. Foetal activity does not change the waveform of the uterine artery. Samples can be taken while a mother is breathing normally. The existence of a diastolic notch is the most significant finding, but several Doppler US characteristics may be examined in a research environment (Fig 28). Color Doppler Flow Clinical Applications As part of the routine obstetric US examination, the placental insertion of umb Cord should be documented. When the placenta is posterior or when dealing with numerous pregnancies, colour Doppler flow ultrasound is more straightforward to use for this documentation than grayscale ultrasound alone. The umbilical cord usually attaches to the placental disc, however it can also attach marginally or velamentously. The term "marginal insertion" refers to placental attachment that occurs within 2 cm of the placental disk's edge. Instead of attaching to the placental disc, the velamentous cord inserts on the membranes to the placenta without being protected by Wharton jelly or the thick umbilical cord coverings (Fig 29). Vasa previa is regarded as a crucial discovery. “Antenatal corticosteroid medication between weeks 28 and 32 of pregnancy, consideration of preterm hospitalisation at weeks 30-34 of pregnancy, and scheduled caesarean birth at weeks 34 to 37 of pregnancy are all part of the management of vasa previa that is discovered during pregnancy” (Fig 30). It has been demonstrated that specialised imaging techniques using colour Doppler flow US and endovaginal US improve antenatal identification of vasa previa. [68,69] Antenatal detection then leads to better outcomes. [70] Additionally, foetal growth limitation and discordant growth in many gestations are linked to velum insertion [71,72]. (Figs 22, 23).

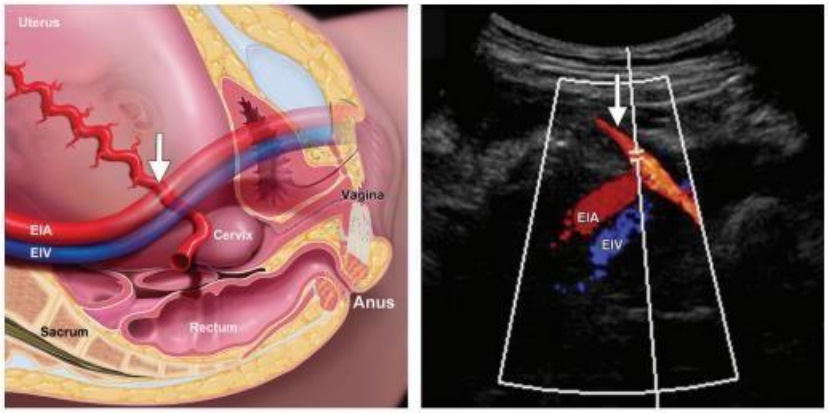
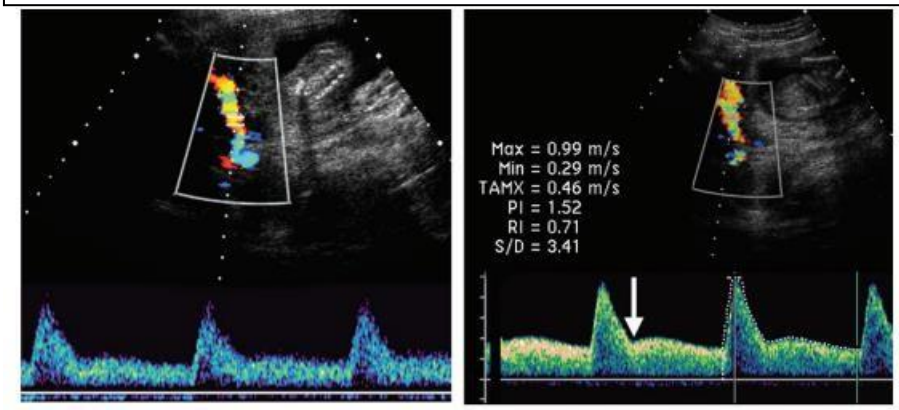


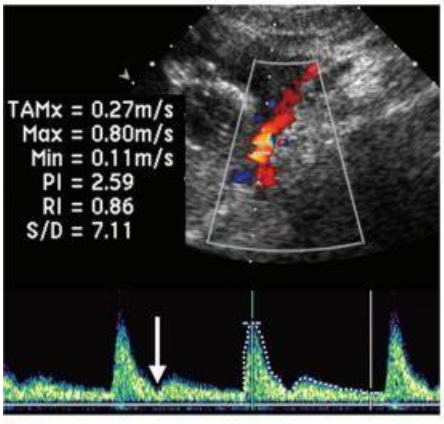
FIG 27: UTERINE ARTERY [73]

LOCATION OF UTERINE ARTERY AT THE "CERVICO-ISTHMIC JUNCTION" (LEFT)

COLOR DOPPLER US OF "UTERINE ARTERY SEEN CROSSING THE ILIAC VESSELS IN SECOND TRIMESTER WITH PROBE PLACED IN LOWER LATERAL QUADRANT"



a.



c.

FIG 28 : UTERINE ARTERY WAVEFORM [73]

A: NORMAL

B: "EARLY DIASTOLIC NOTCHING" – A NORMAL FINDING IN FIRST TRIMESTER

C: "EARLY DIASTOLIC NOTCHING" WITH SIGNIFICANTLY RAISED PI IN SECOND TRIMESTER

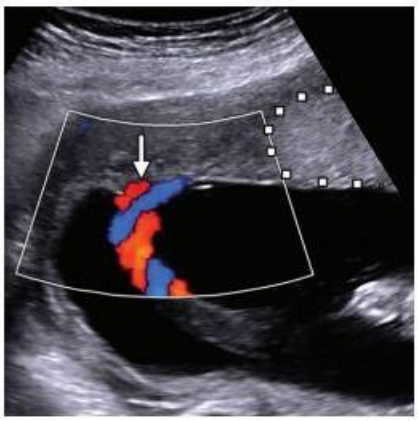
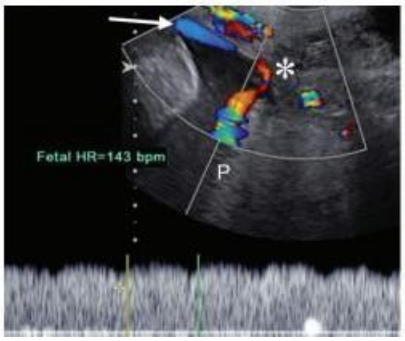


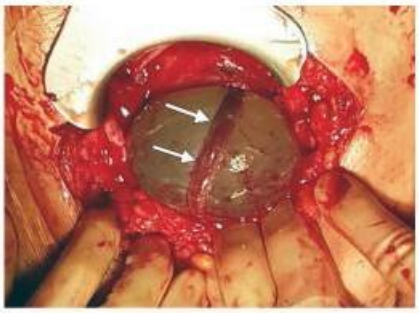
FIG 29 : [73] VELAMENTOUS INSERTION OF CORD SEEN ON COLOR DOPPLER ULTRASOUND

FIG 30: [73]

COLOR DOPPLER ULTRASOUND SHOWING VASA PREVIA

POST OPERATIVE IMAGE (B)





b.

PLACENTAL PULSATILITY INDEX:

Doppler ultrasound has developed into a useful tool for assessing foetal and placental circulation, as well as for predicting the health of the foetus and the course of the pregnancy. [21,22] Fetal growth limitation and warning symptoms of impending asphyxia are usually linked to Doppler signals of increased placental vascular resistance. In high-risk pregnancies, umb artery (UA) Doppler is currently a standard component of surveillance of fetal well being. The ut.artery (UtA) Doppler has also demonstrated its efficacy in predicting the fate of high-risk pregnancies after initially experiencing technical challenges, and in recent years it has been reported to be comparable to the UA Doppler in that regard. [23] Ut A Doppler abnormalities and decreased blood volume in the umbilical vein are thought to act as stand-ins for decreased placental perfusion in late pregnancy. [24] Uterine Artery screening during the first trimester and early second trimester has also demonstrated its effectiveness in identifying instances that require particular surveillance and predicting unfavourable outcomes in highrisk pregnancies. [25,26] The SD ratio of the Umbilical Artery and Uterine Artery, the resistance index, and the pulsatility index (PI) are frequently used to express placental vascular impedance. AEDF and REDF in the UA, placental position, and early diastolic notching in the UtA are occasionally also noted. The work by Gudmundsson et al. set out to create a “new reference chart for the placental pulsatility index (PPI), which measures the combined vascular impedance of the placenta's maternal and

foetal sides". To determine whether the novel index performs better at predicting unfavourable outcomes in suspected FGR pregnancies , they also compared it to UA and UtA Doppler values and the information may be useful in scrutinizing the pregnancies that need closer monitoring because of a placental vascular source of FGR.

METHODOLOGY

This is a prospective study done at Shri B.M Patil medical college, hospital and research Centre, Vijayapura over a period of 2 years from. 90 women with singleton pregnancy with suspected FGR (diagnosed by fetal biometry on routine/clinically indicated ultrasound examination), all the subjects underwent Doppler study that included uterine artery and umbilical artery along with the growth scan/biometry after satisfying the inclusion criteria. Placental pulsatility index was calculated : using the formula (UA PI + mean of rt and lt Ut.A/ 2). The study is prospective cohort study.

AIMS AND OBJECTIVES:

1. correlating placental pulsatility index with adverse perinatal outcomes in growth restricted foetuses

2. To compare placental pulsatility index with UA and/or uterine artery Doppler in predicting the critical perinatal outcomes in FGR suspected pregnancies.

INCLUSION CRITERIA:

All Singleton pregnancies with growth restricted foetuses - from 26-40 weeks
(primigravida/multigravida, irrespective maternal health status)

EXCLUSION CRITERIA:

1. Women with multiple pregnancy.

2. Fetal anomalies.

3. Uterine anomalies.

4. Placental anomalies.

5. Umbilical cord anomalies.

6. Dropouts/loss to follow-ups.

7. Those who do not consent to be a part of the study.

PROCEDURE

Data collected by SIEMENS ACUSON S3000 and GE VOLUSON machines.

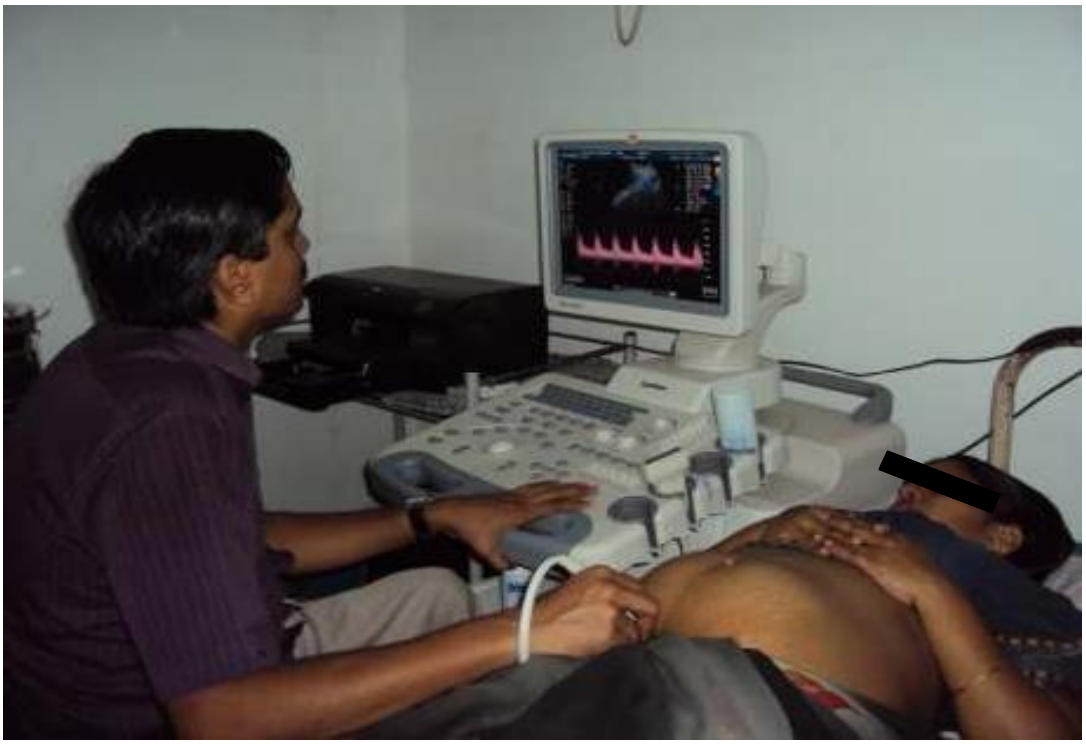
All the patients with suspected FGR were referred to the Dept of Radio-diagnosis, ultrasound examination was performed beginning with biometry. FGR was defined as EFW/AC < 3rd percentile, cases with EFW/FGR <10th percentile were included under the suspected FGR, the hadlock growth centiles were used as reference. Further, right and the left uterine artery Doppler was performed proximal to the crossing of the external iliac vessels and free loop of umbilical cord was used for UA Doppler.

PI of each was noted.

Placental pulsatility Index was calculated and was defined abnormal if greater than +2SD from the mean for a given gestational age – Cut off's were referred from parent article.

Follow up till the delivery was done, all the events during the pregnancy, throughout the labour and perinatal outcome of the neonate were properly noted. Critical Perinatal outcomes considered were Intrauterine Death, Still birth, NICU admission i/v/o RDS,low birth weight, birth asphyxia etc.,

FIG 31 : RADIOLOGIST PERFORMING OBSTETRIC DOPPLER.



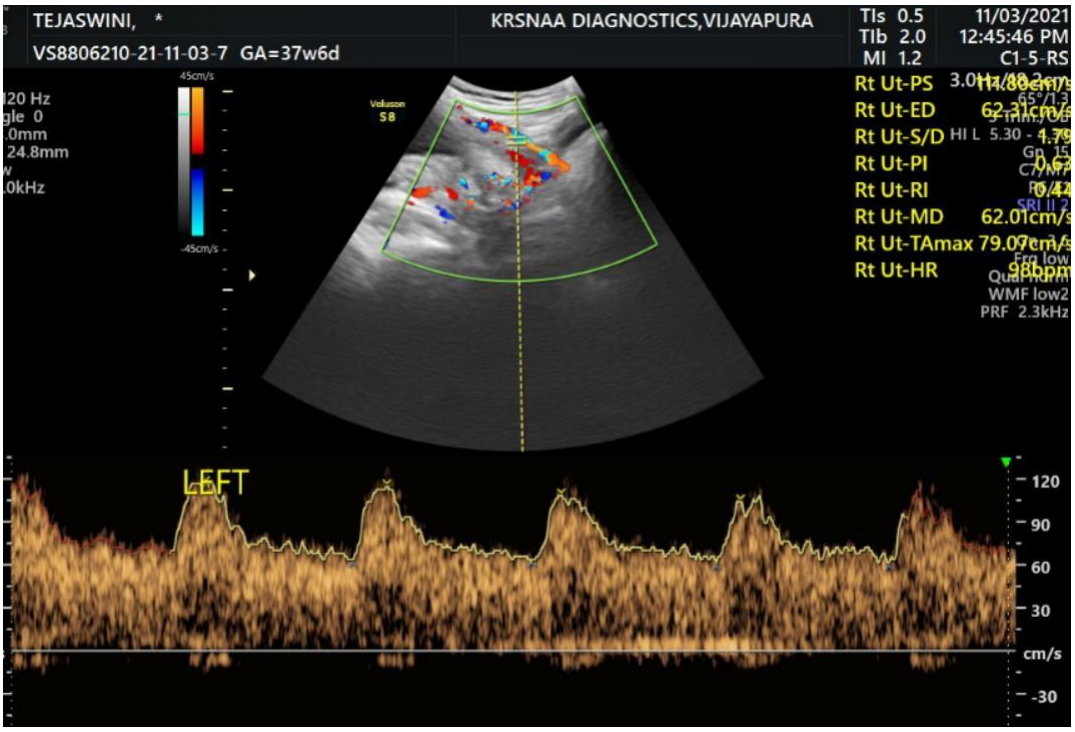


FIG 32: UTERINE ARTERY WITH NORMAL WAVE FORM

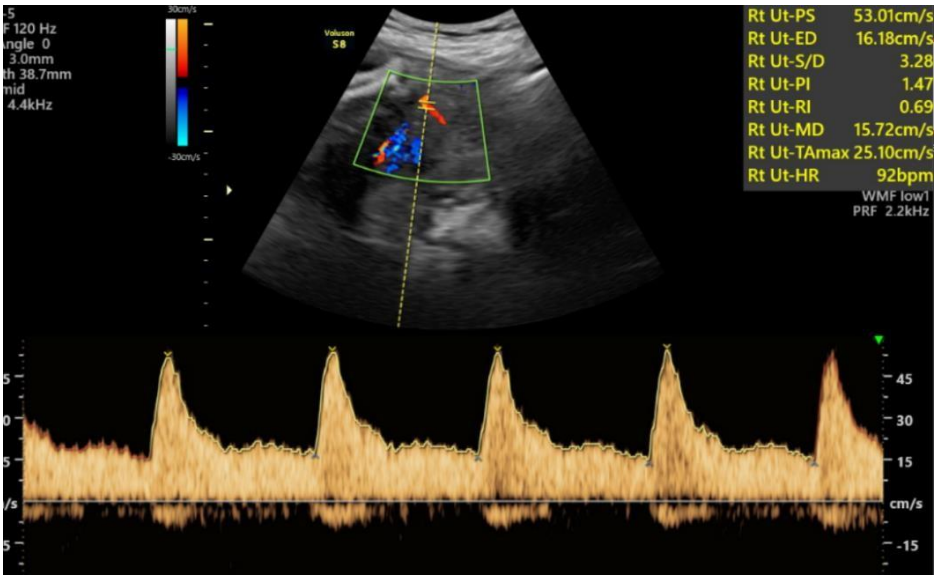


FIG 33: ABNORMAL UTERINE ARTERY WAVEFORM WITH EARLY DIASTOLIC NOTCHING AND RAISED PI 1.47 IN SECOND TRIMESTER

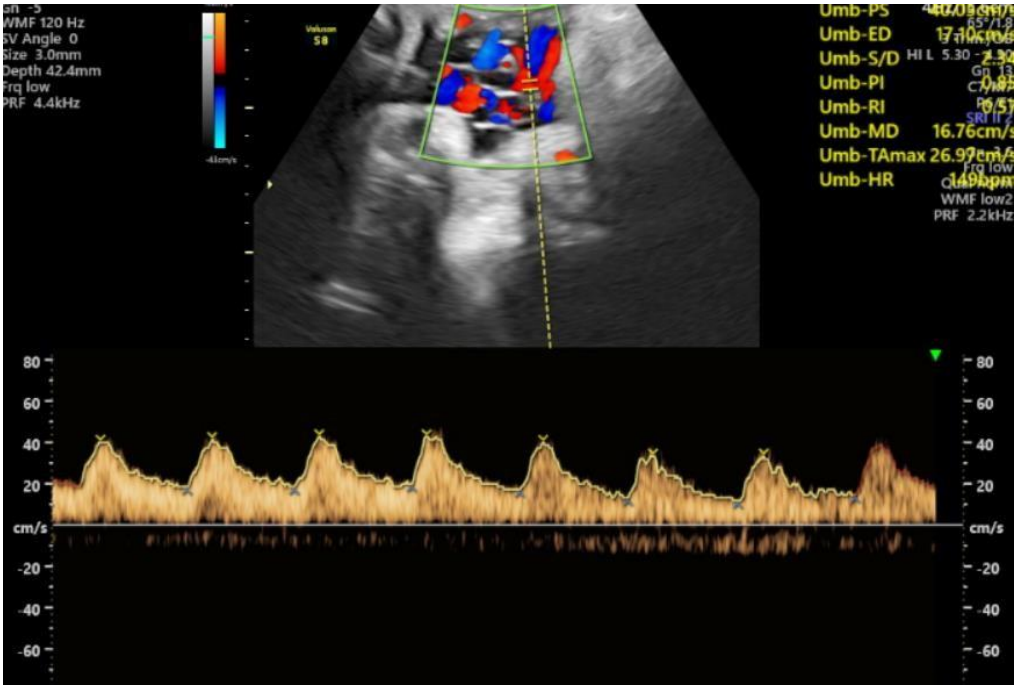


FIG 34: NORMAL UMBLICAL ARTERY WAVEFORM

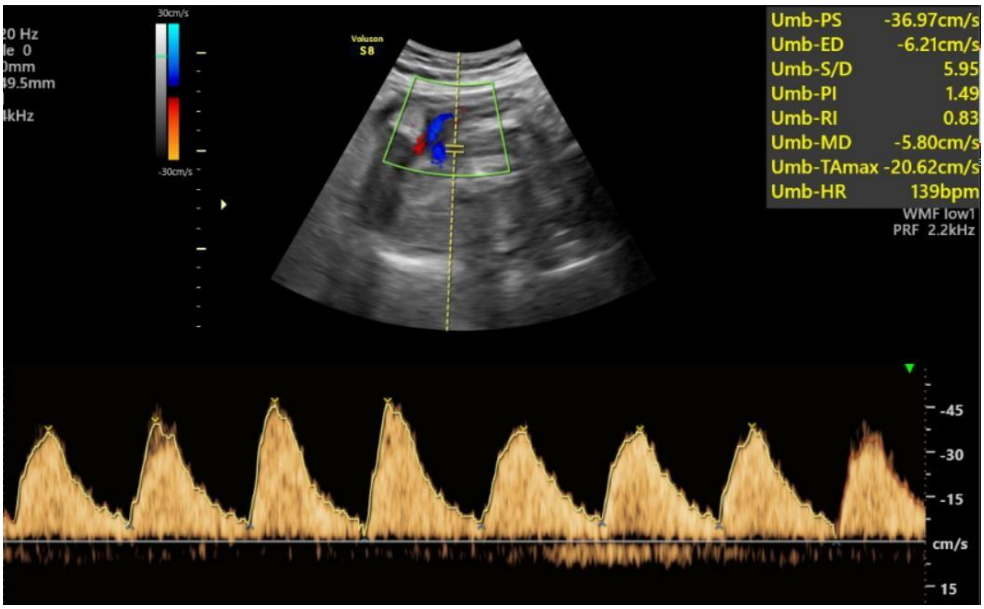


FIG 35: ABNORMAL UMBILICAL ARTERY WAVEFORM WITH SIGNIFICANT REDUCTION IN EDF AND RAISED PI – 1.49

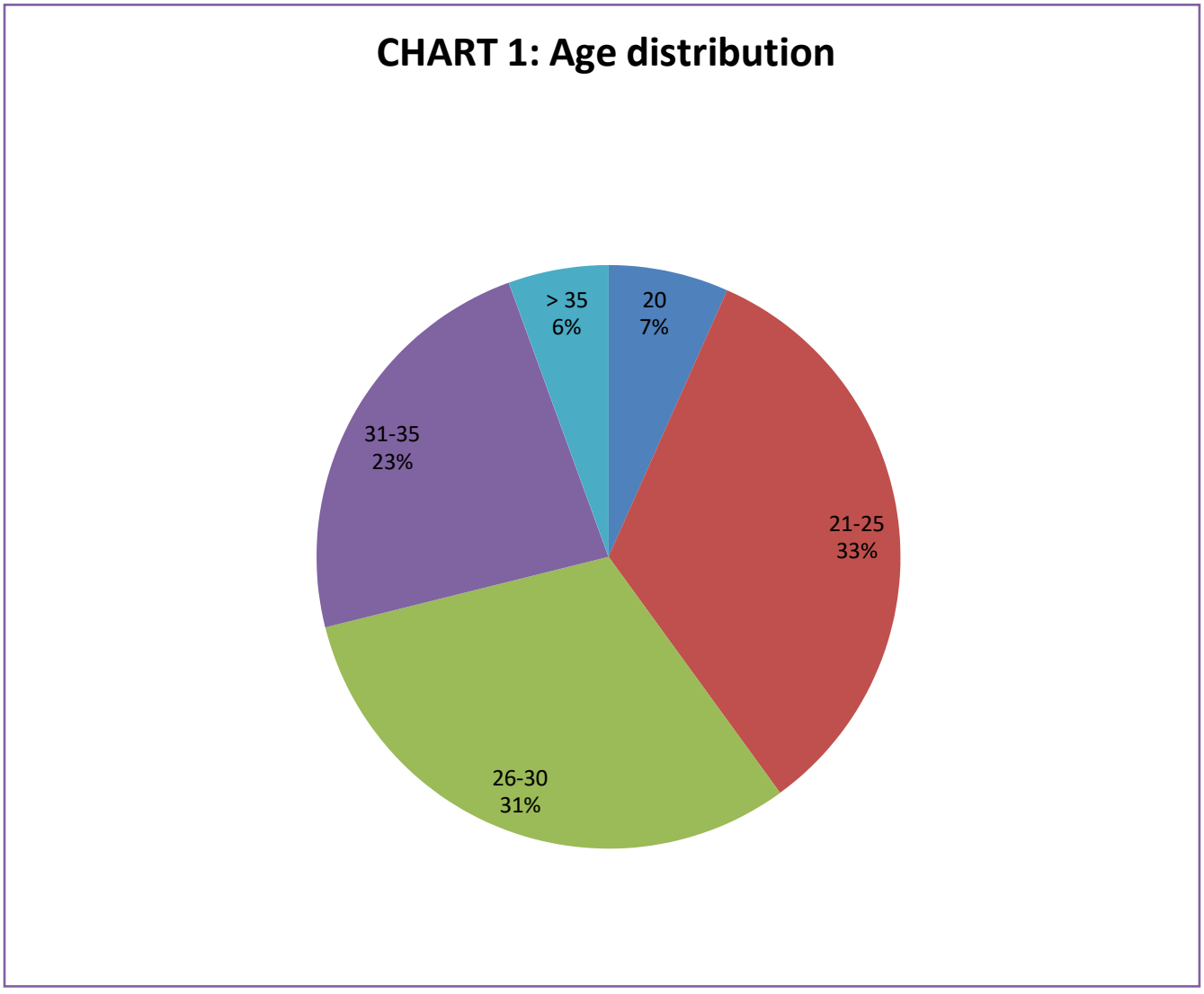
Table 1. Reference cut-off limits for placental pulsatility index from 20 to 40 weeks of gestation age (ga). The 2.5th centile (cent025), 5th centile, the mean, 95th and 97.5th centiles are given as well as the mean +2 SD, +3 SD and +4 SD limits are given.

ga	cent025	cent05	mean	cent95	cent97.5	+2 SD	+3 SD	+4 SD
22.0	0.77	0.81	1.01	1.25	1.30	1.31	1.49	1.68
23.0	0.75	0.78	0.98	1.21	1.26	1.27	1.44	1.63
24.0	0.72	0.75	0.95	1.18	1.23	1.23	1.40	1.58
25.0	0.70	0.73	0.92	1.14	1.19	1.20	1.36	1.54
26.0	0.68	0.71	0.89	1.11	1.16	1.17	1.33	1.50
27.0	0.66	0.69	0.87	1.09	1.13	1.14	1.29	1.47
28.0	0.64	0.67	0.85	1.06	1.10	1.11	1.26	1.43
29.0	0.63	0.65	0.83	1.04	1.08	1.09	1.24	1.40
30.0	0.61	0.64	0.81	1.01	1.06	1.06	1.21	1.37
31.0	0.60	0.62	0.79	0.99	1.03	1.04	1.19	1.35
32.3	0.58	0.61	0.77	0.97	1.01	1.01	1.16	1.31
33.0	0.57	0.60	0.76	0.95	0.99	1.00	1.14	1.30
34.0	0.56	0.59	0.74	0.94	0.98	0.98	1.12	1.28
35.0	0.55	0.57	0.73	0.92	0.96	0.96	1.10	1.25
36.0	0.54	0.56	0.72	0.90	0.94	0.95	1.08	1.23
37.0	0.53	0.55	0.70	0.89	0.93	0.93	1.07	1.21
38.0	0.52	0.54	0.69	0.87	0.91	0.92	1.05	1.20
39.0	0.51	0.53	0.68	0.86	0.90	0.90	1.03	1.18

FIG 36: PPI CUT OFF VALUES REFERRED FROM THE PARENT ARTICLE (ORIGINAL WORK BY GUDMUNDSSON ET.AL)

RESULTS

The study was completed by every person in the study arm, and all participants had access to the results. 90 observations were available, with an average of 2-4 observations per lady. The majority of them fell between the ages of 21 to 25 (33%) and 26 to 30 (31%), with the mean mother age being 27 years (ranging from 20 to 38 years).



The PPI was examined in light of unfavourable outcomes in pregnancies thought to be caused by FGR. PPI that is abnormal is defined as greater than + 2 SD from the mean. Outcomes included SGA, RDS, IUD/Stillborn and motherside.

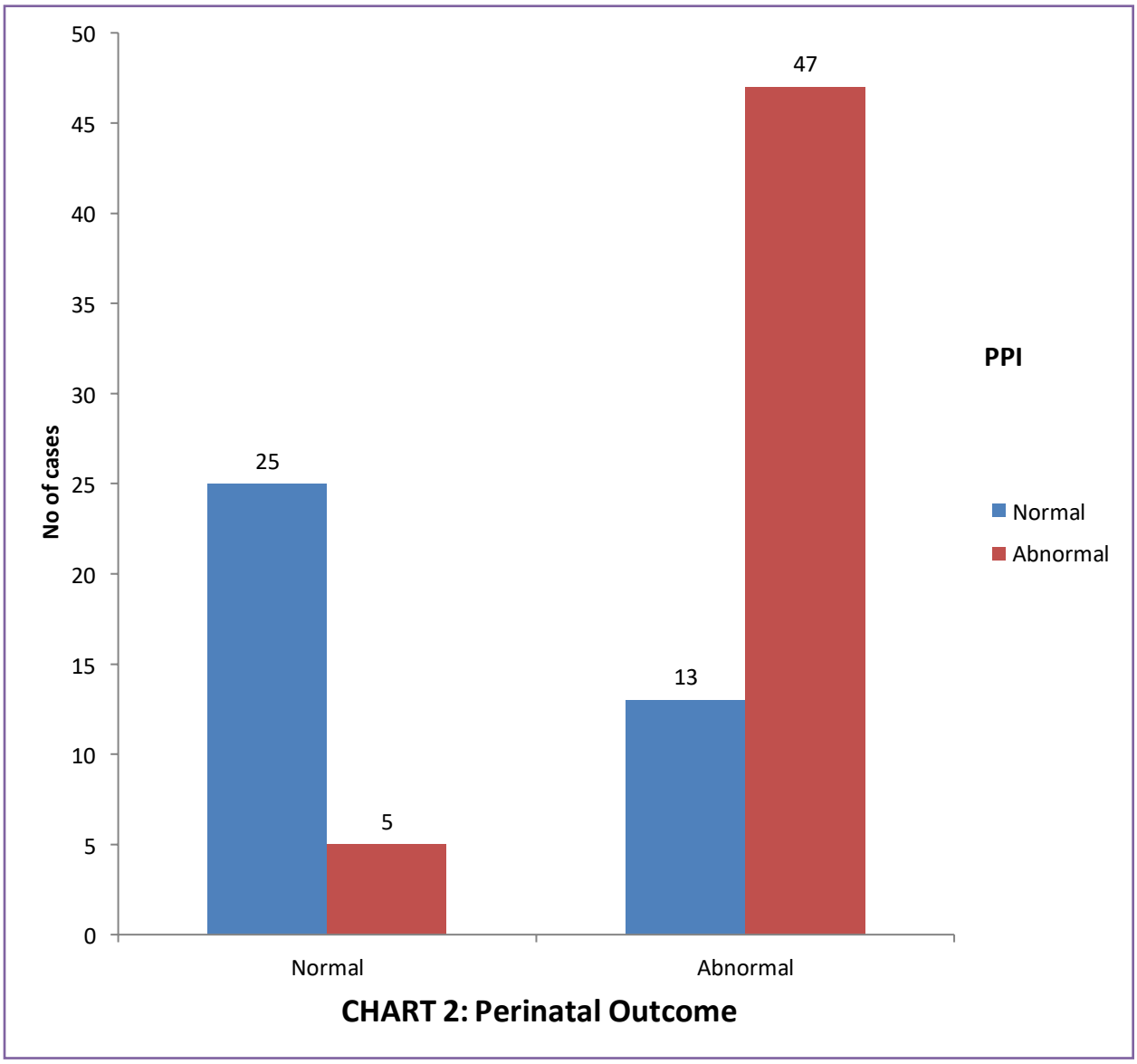


CHART 2: Perinatal Outcome

38 patients with suspected FGR had normal PPI, out of which 25 had normal perinatal outcome and 5 had abnormal perinatal outcome. 52 patients had abnormal PPI, out of which 47 had abnormal perinatal outcome and 5 had normal perinatal outcome.

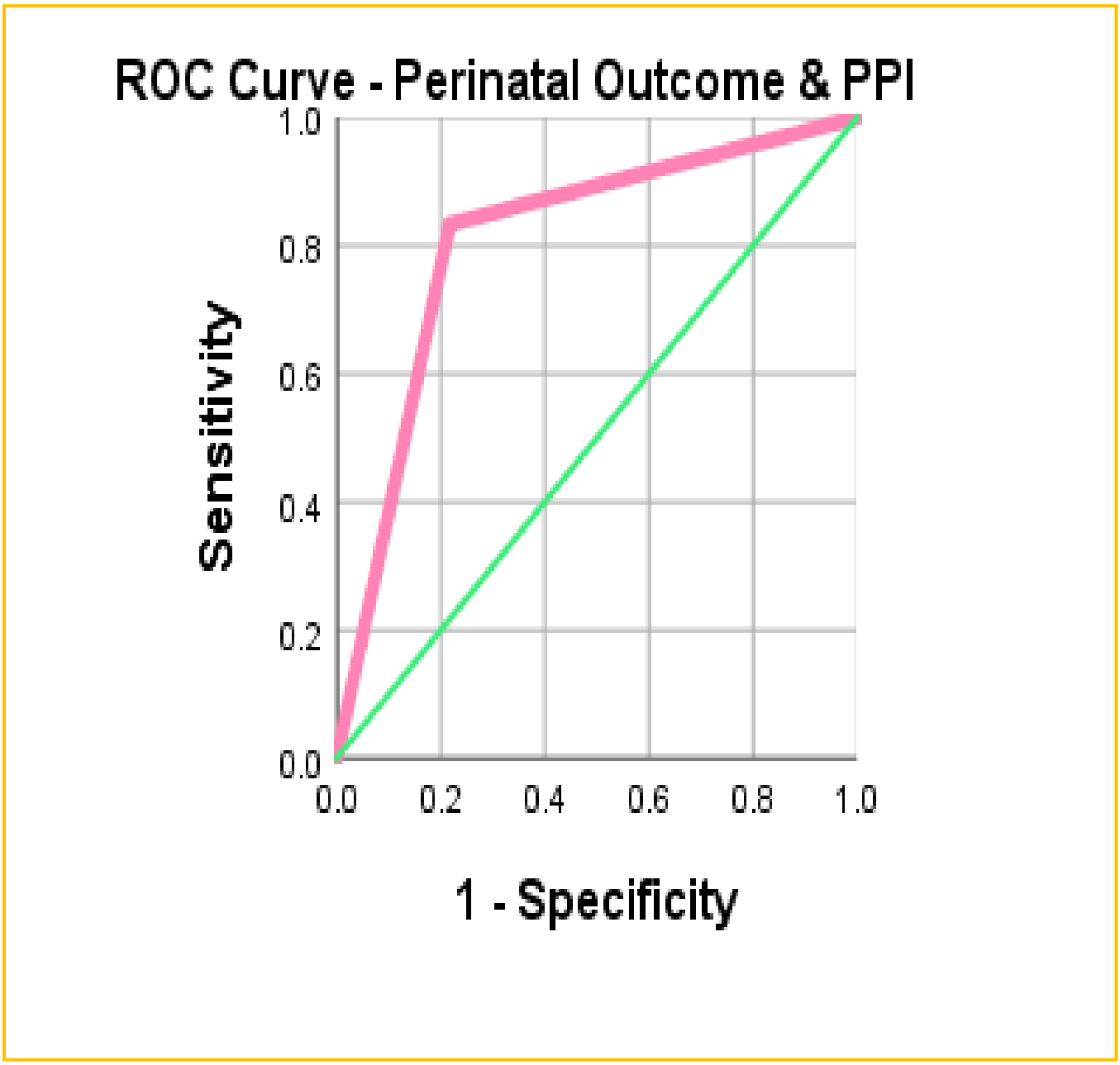
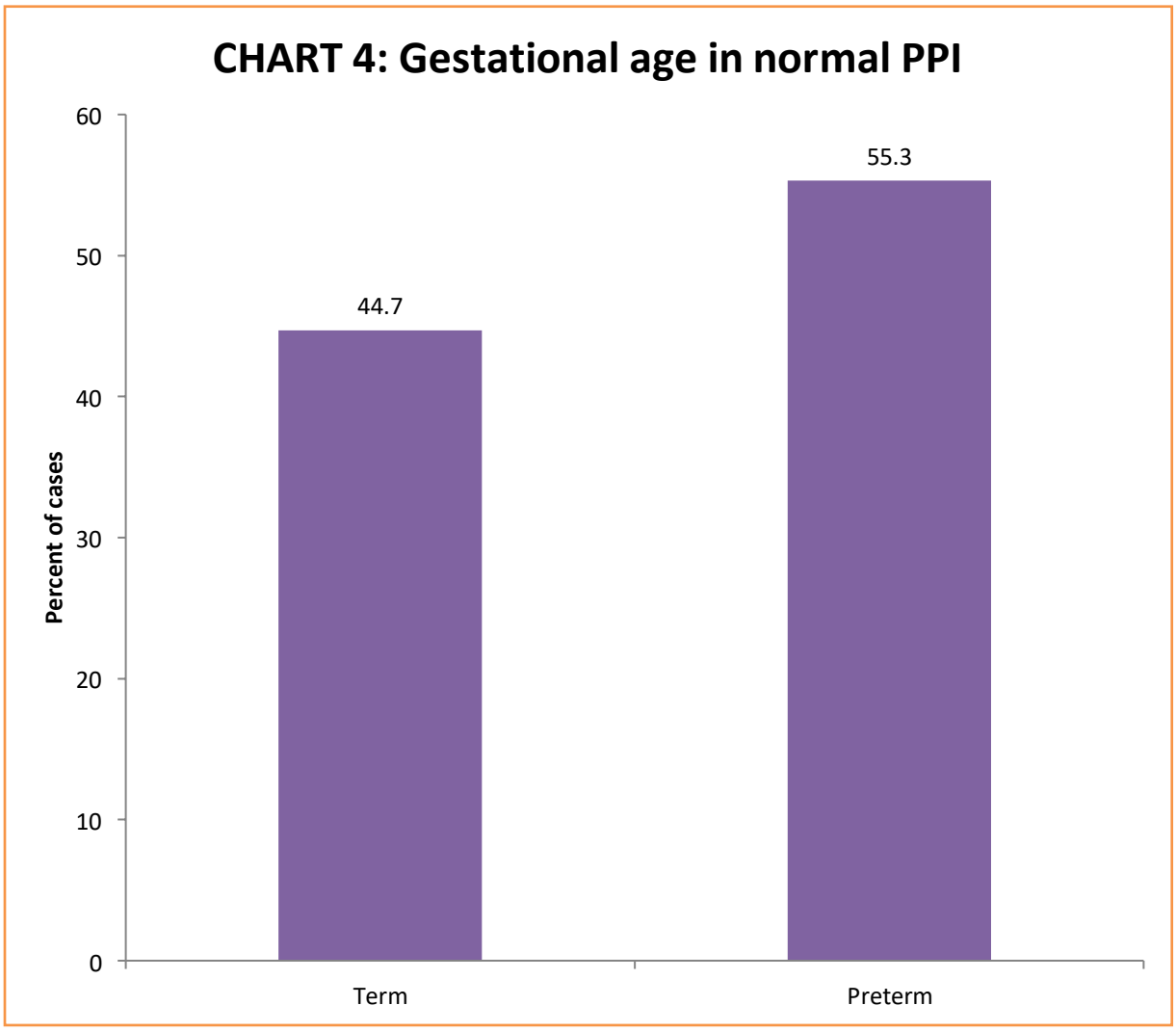


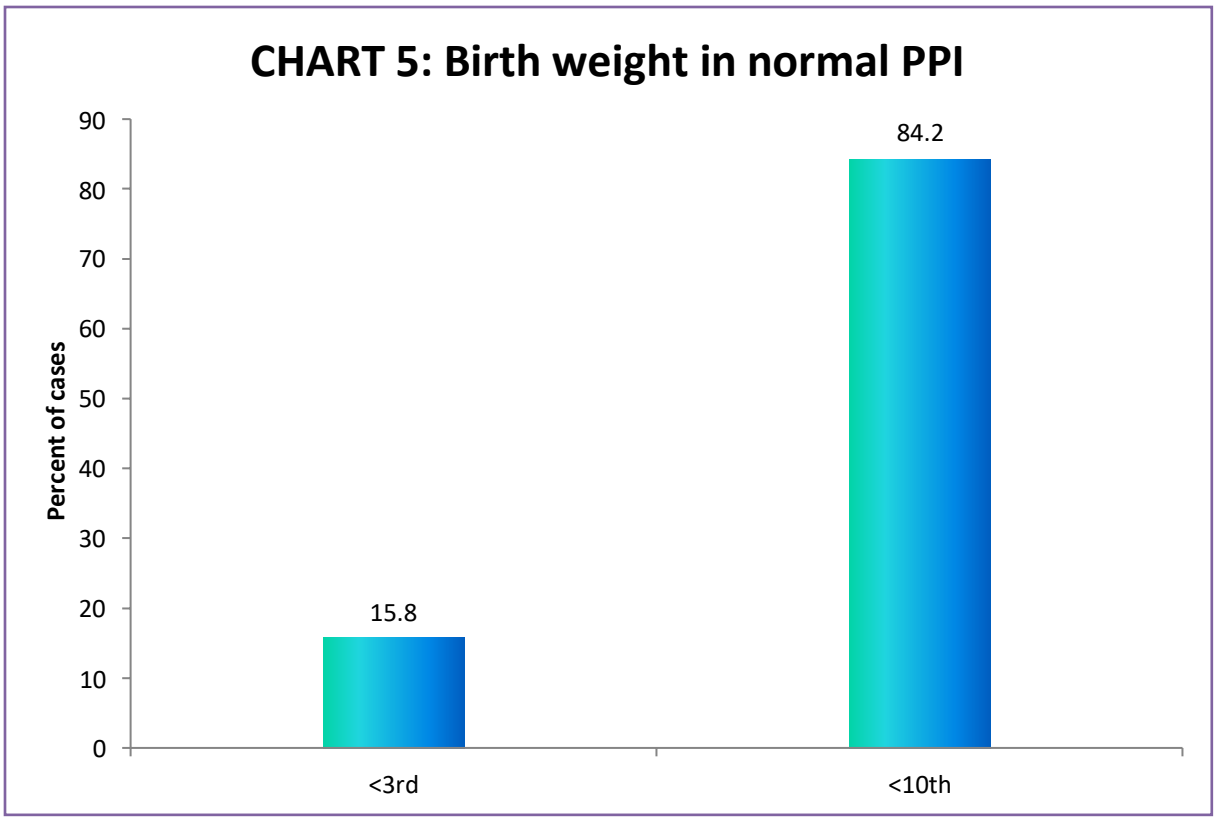
CHART 3

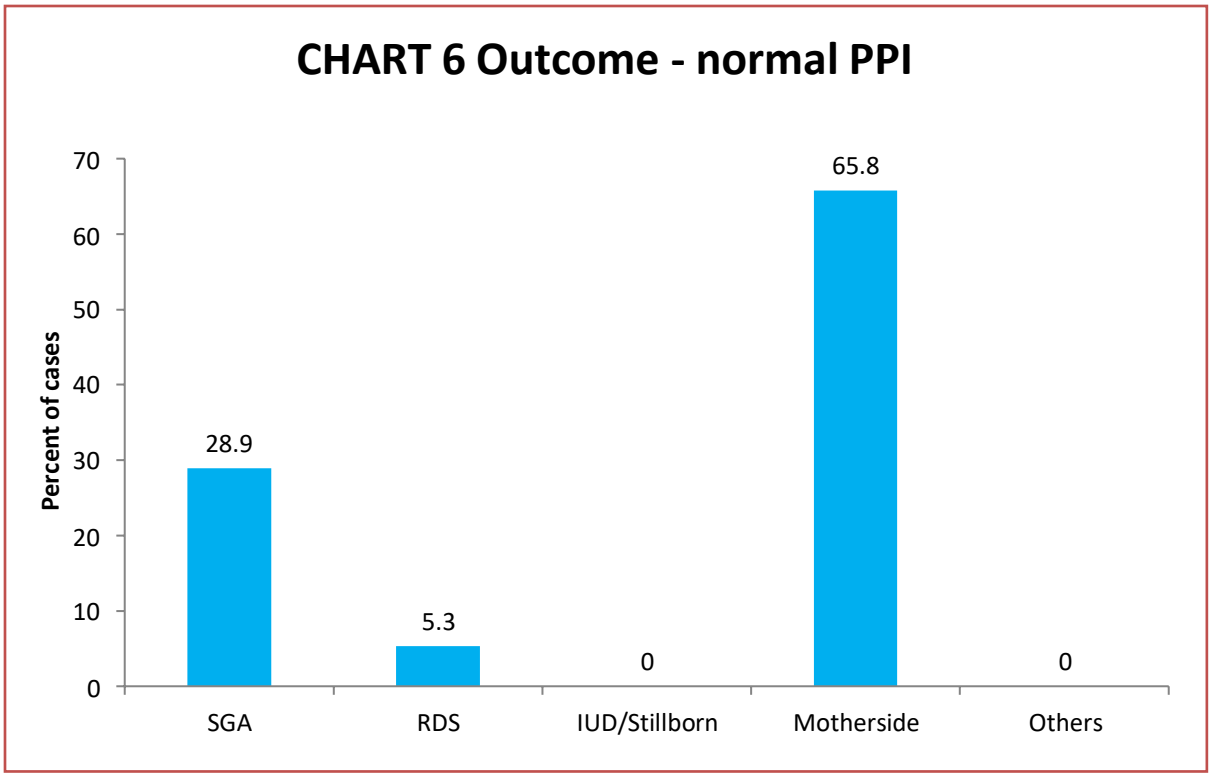
The validity of the PPI in predicting outcome is very high with sensitivity and specificity of 83 and 78%. Diagnostic accuracy is 80%. Area covered under ROC curve is 80%. PPI is a more sensitive indicator of adverse perinatal outcome in FGR suspected pregnancies. The agreement between the two is highly significant (P<0.001).

NORMAL PPI:

Out of 38 pregnancies with normal PPI, 17 were term and 21 were preterm with a birth weight of <3rd percentile in 6 cases and <10th percentile in 32 cases, 11 were Small for gestational age, 2 developed RDS and 25 were healthy and motherside.

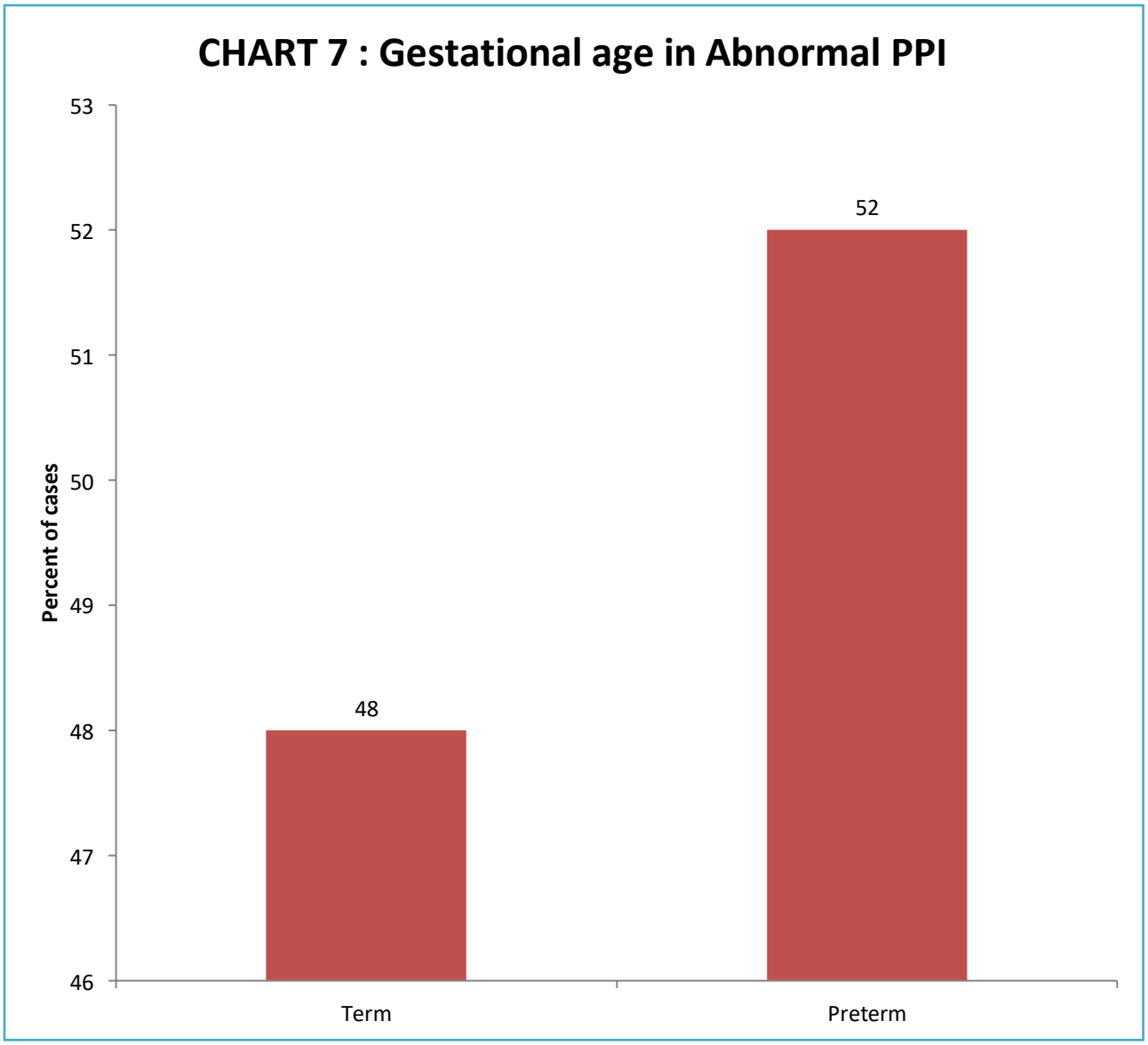


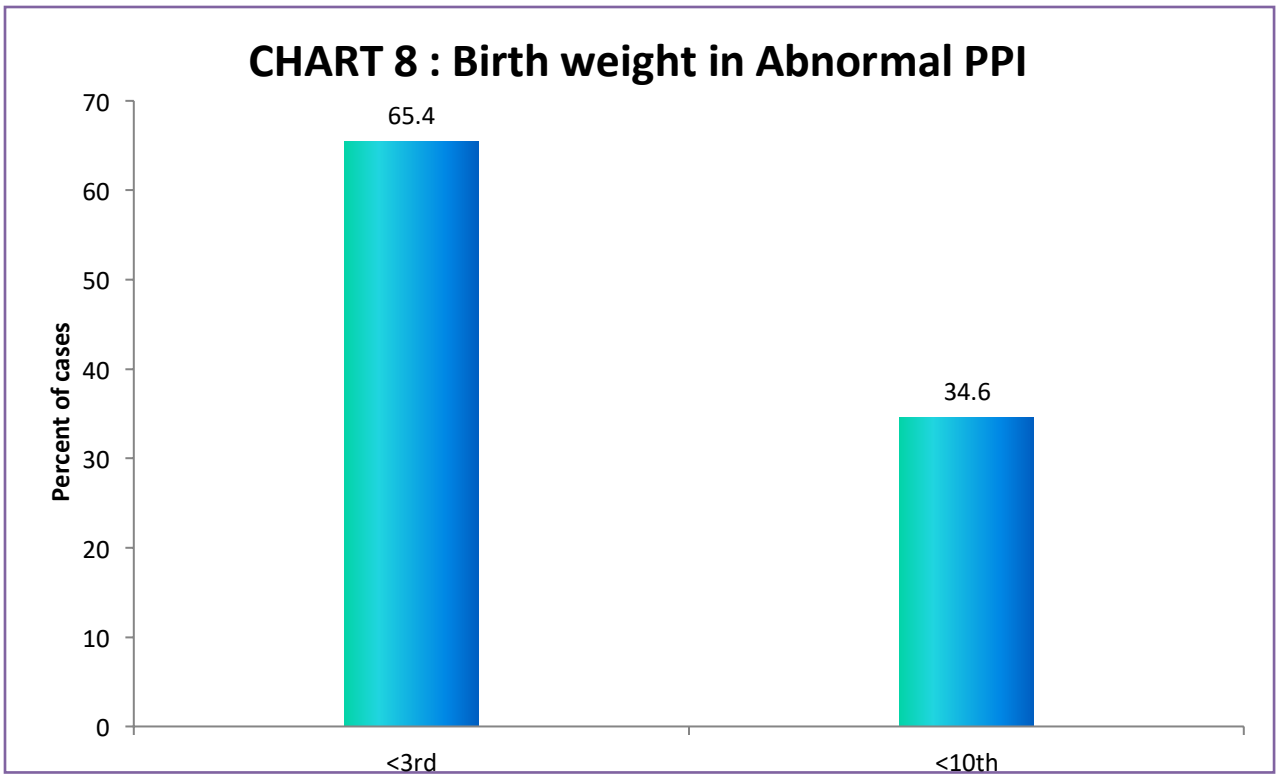


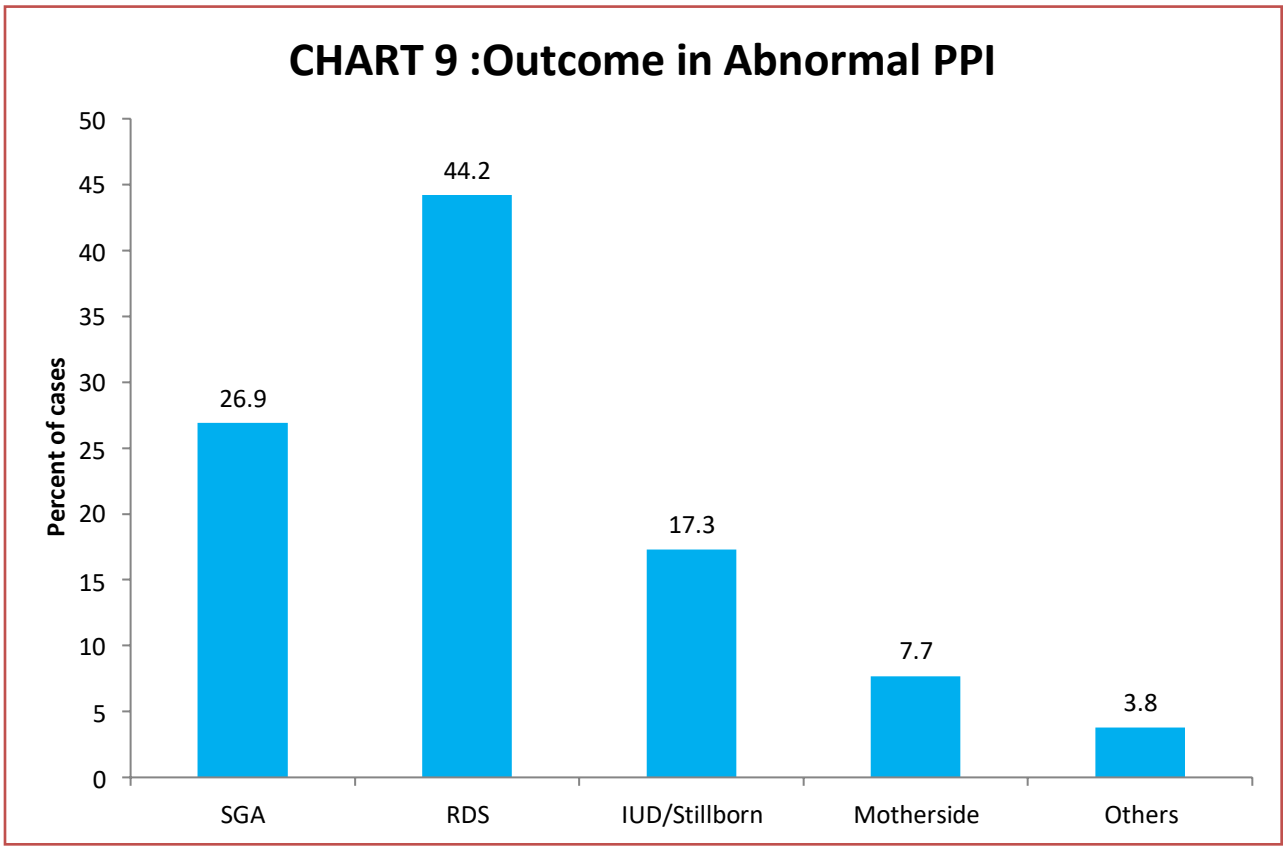


ABNORMAL PPI:

Out of 53 pregnancies with normal PPI, 25 were term and 27 were preterm with a birth weight of <3rd percentile in 34 cases and <10th percentile in 18 cases, 14 were Small for gestational age, 9 WERE IUD/Stillborn, 23 developed RDS, 2 were catergorised under others, 4 were healthy and motherside.

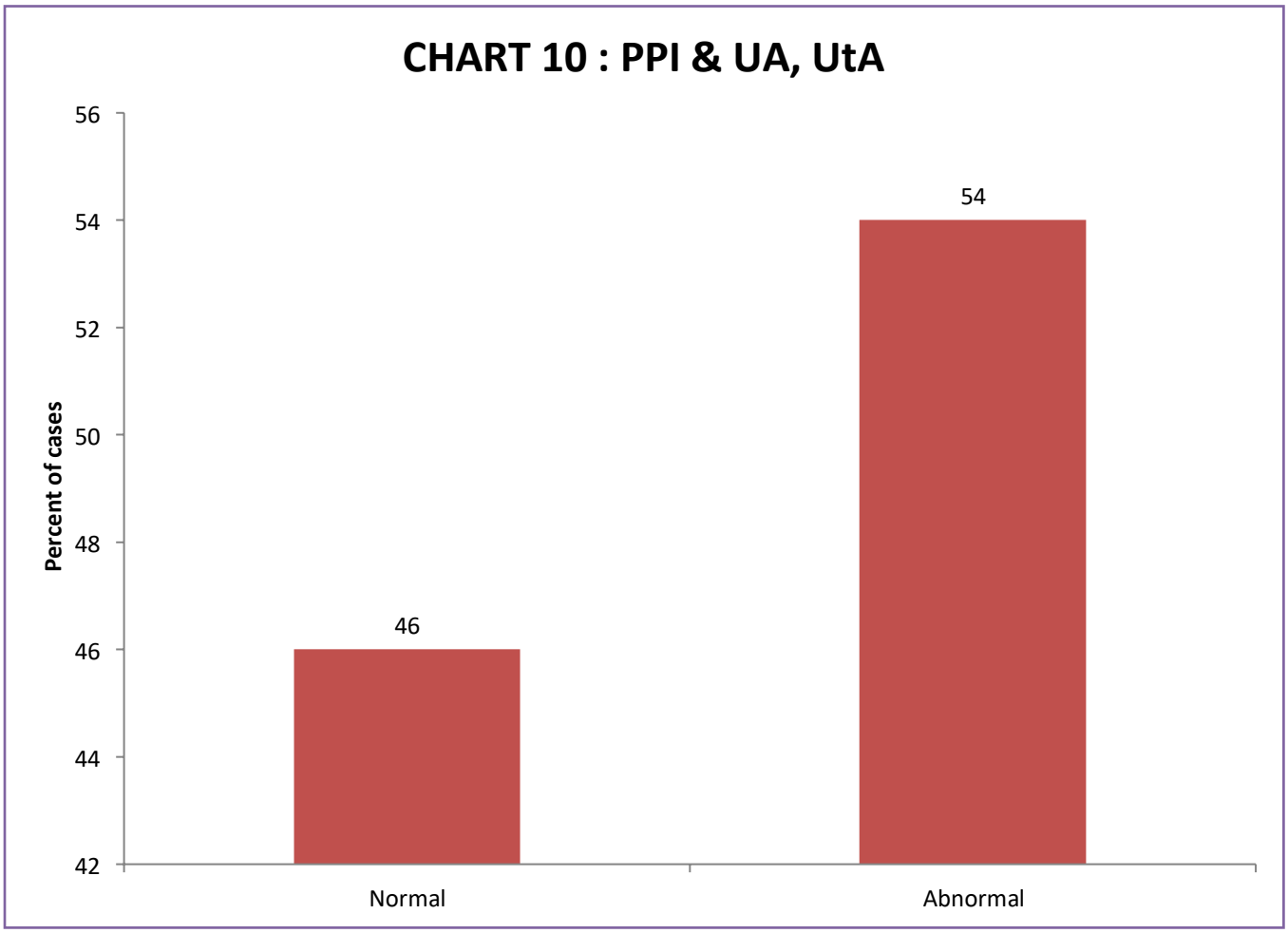






COMPARATIVE STUDY:

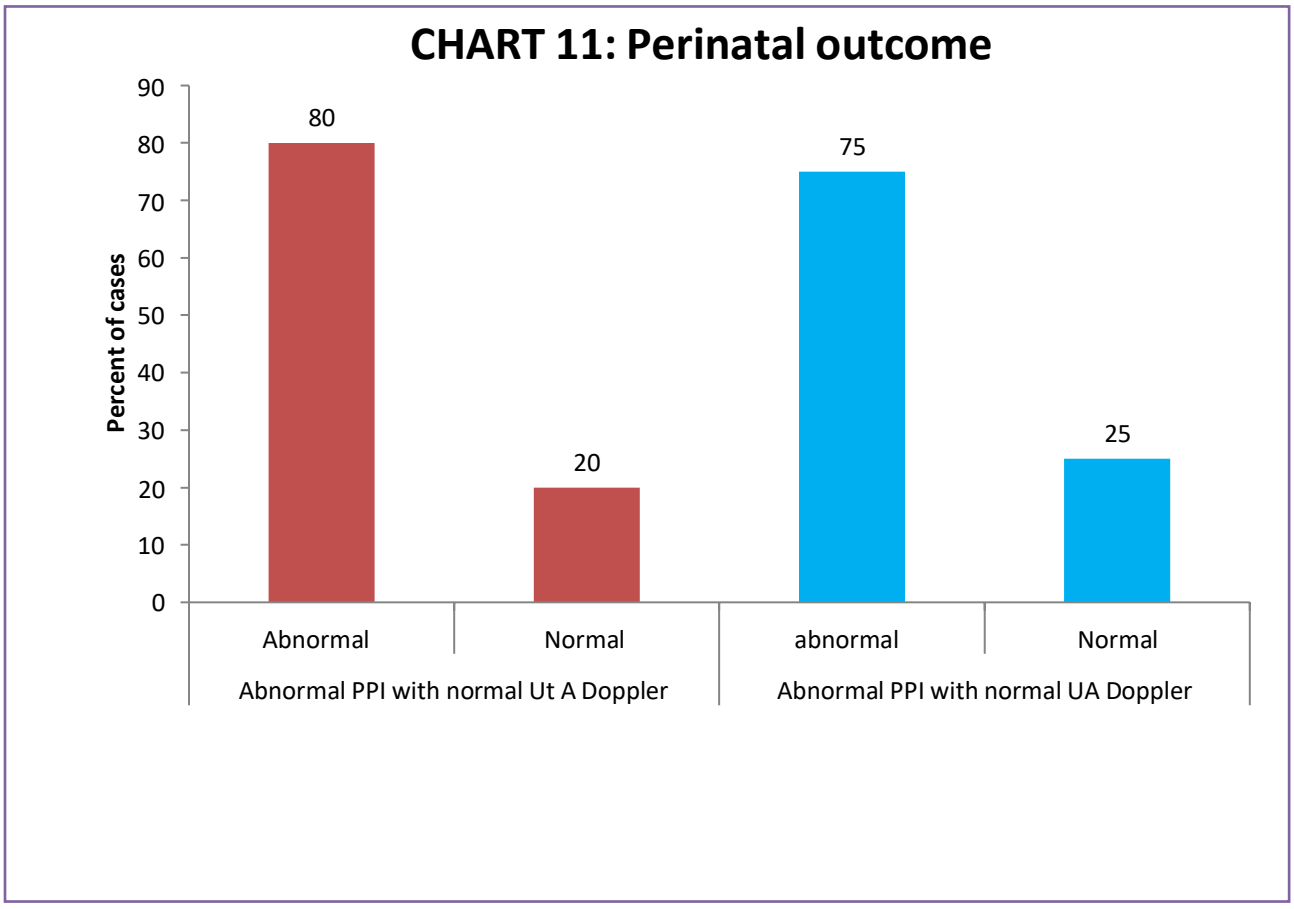
PPI, umbilical artery and uterine artery were normal in 28 cases and abnormal in 33 cases.



5 cases had abnormal PPI and normal uterine artery Doppler, out of which 4 had abnormal perinatal outcome and 1 had normal outcome.

16 cases had abnormal PPI and normal umbilical artery Doppler, out of which 12 cases had abnormal perinatal outcome and 4 had normal outcome.

Finding	N	Perinatal outcome	No of cases	Percent
Abnormal PPI with normal Ut A Doppler	5	Abnormal	4	80
		Normal	1	20
Abnormal PPI with normal UA Doppler	16	abnormal	12	75
		Normal	4	25



PPI	Umbilical artery PI - Inference		Total
	Abnormal	Normal	
Abnormal	36	16	52
Normal	2	36	38
Total	38	52	90
Kappa P<0.001, Sig			

In 52 cases with abnormal PPI, 36 had abnormal and 16 had normal umbilical artery PI. In 38 cases with normal PPI 2 had abnormal and 36 had normal umbilical artery PI.

TABLE 1: STATISTICAL SIGNIFICANCE OF PPI

	Inference
Sensitivity	95%
Specificity	69%
Positive Predictive Value	69%
Negative Predictive Value	95%
Diagnostic accuracy	80%
AUC	82%

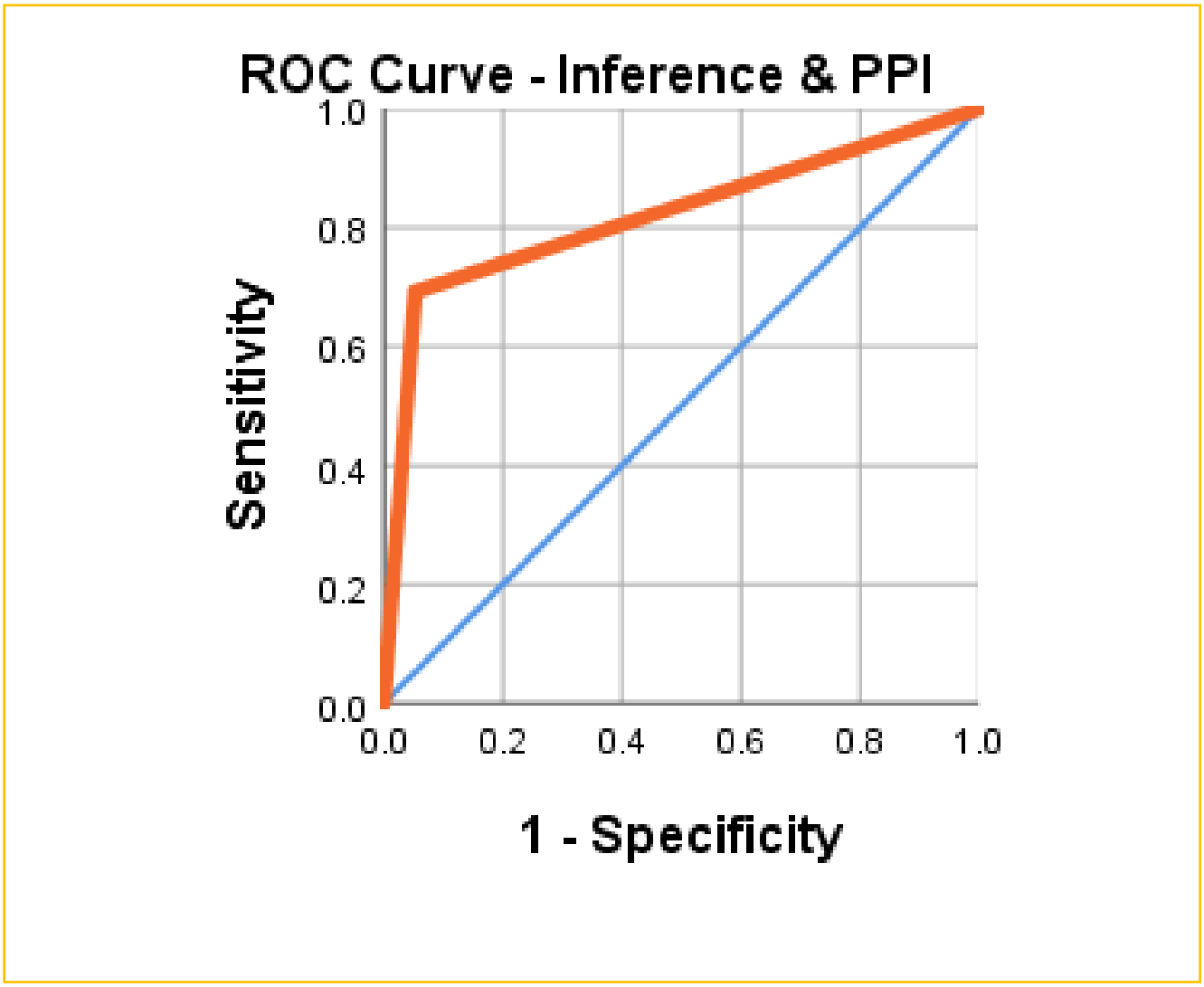


CHART 12:

The validity of the PPI is very high with sensitivity and specificity of 95% and 69%. Diagnostic accuracy is 80%. Area covered under ROC curve is 82%. The PPI had higher sensitivity in comparison to mean UA PI Inference. The agreement between the two is highly significant ($P<0.001$)

DISCUSSION

The Placental Pulsatality Index appears as a helpful predictor of the outcomes of FGR suspected pregnancies, according to this prospective study carried out in B.L.D.E- Deemed to be university's Shri B. M. Patil Medical College Hospital and Research Centre, Vijayapura for 2 years. With advancement gestational age in the late second and third trimester of a typical pregnancy, the PPI values fell. When compared to traditional UA and UtA PIs independently, abnormal PPI in our study appears to be a sensitive indicator of adverse perinatal outcome in FGR suspected pregnancies. By using this index rather than the UA and UtA PIs independently, it may be possible to detect foetal growth restriction linked to increased placental vascular impedance more accurately and help with the planning of follow-up for these pregnancies.

In a study by Hernandez-Andrade E et al., the measurement of vascular impedance on the placenta's maternal side revealed “the presence of a notch in the spectrum of the UtA blood velocity waveform”. Based on the pulsatility index values of uterines and notching whether present or not one or either sides, this has been stated as a UAS of 0–4 (10). The uterine artery score gives clinicians idea on both uterine arteries as a single and simple figure. The sensitivity of Uterine Artery Score was lower than that of PPI. The poor outcome was predicted significantly more accurately by abnormal Uterine Artery Score (greater than 0, which was seen in 97 pregnancies) than by the Umbilical Artery PI and the mean Uterine Artery PI. However, due to issues with the definition of a notch and its inter-observer repeatability, it was thought that the mean UtA PI was a better option than the UAS.

However, we discovered that PPI predicts negative outcomes more accurately than UA PI alone. We discovered that as PPI rose, the likelihood of unfavourable outcomes rose as well. The study's primary

weakness is the issue of how well Hadlock growth charts apply to our study group when taking into account numerous aspects like maternal age, race, parity, etc. This still needs more research. Future standardisation efforts for a population could lead to growth charts that are even more helpful for forecasting negative outcomes in FGR foetuses if they are utilised to diagnose growth restriction based on biometry.

CONCLUSION:

In conclusion, the placental pulsatility index measures the vascular resistance on each side of the placenta. When compared to either UA alone or UtA PI individually in our investigation, The PPI exhibited as a more sensitive predictor of a negative outcome of FGR pregnancies. Therefore, the PPI might make the management of pregnancies suspected of FGR easier and more decision-friendly.

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PROFORMA

PROFORMA

1) Patient's name:

2) Age/Sex:

3) IP No#

4) Obstetric history:

- ✓ **Obstetric score:**
- ✓ **Gestational age**
- ✓ **By LMP:**
- ✓ **By Scan:**

c) Medical history

- ✓ **Hypertensive disorders of pregnancy ------(p)**
- ✓ **Anemia----------(q)**
- ✓ **Others if any-------**

5) Ultrasound findings

- ✓ **EFW:**
  - **<3rd percentile—(r)**
  - **3rd -5th percentile—(s)**
  - **5th-10th percentile—(t)**
- ✓ **AFI----------(2)**
- ✓ **Uterine artery Doppler:**
- ✓ **Placental pulsatality Index:**

6) Perinatal outcome:

- ✓ **Mode of delivery**
  - **Cesarean Section----(x)**
  - **Vaginal delivery-----(y)**
- ✓ **Details of newborn**
  - **Alive----(a)**
  - **Stillborn ---(b)**
  - **IUD----------(c)**
- ✓ **Birth weight**
  - **<1kg----(i)**
  - **1-1.5kg---(ii)**
  - **1.5-2kg---(iii)**

CONSENT FORM

PLACENTAL PULSATILITY INDEX AS A PREDICTOR OF CRITICAL PERINATAL OUTCOMES IN GROWTH RESTRICTED FETUSES.

GUIDE **:** DR. SHIVANAND.V.PATIL

P.G. STUDENT **:** DR. AYESHA.MAHALDAR

PURPOSE OF RESEARCH:

I have been informed that the purpose of this study is to predict the critical perinatal outcomes in growth restricted fetuses using the help of Doppler ultrasound.

PROCEDURE:

I understand that I will undergo history, clinical examination, obstetric ultrasound and Doppler.

RISKS AND DISCOMFORTS:

I understand that there is no risk involved in the above study.

BENEFITS:

I understand that my participation in this study will help to predict critical perinatal outcomes in growth restricted fetuses.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulations of hospital. If the data is used for publications the identity of the patient will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw from study at any time

INJURY STATEMENT:

I understand in the unlikely event of injury to me during the study I will get medical treatment but no further compensations. I will not hold the hospital and its staff responsible for any untoward incidence during the course of study.

Date:

Dr. Shivanand.V.Patil (Guide) Dr. Ayesha.Mahaldar (Investigator)

STUDY SUBJECT CONSENT STATEMENT:

I/my ward confirm that Dr.Ayesha.Mahaldar has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I/my ward have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give my consent to participate as a subject in this project.

_____ _____

(Participant) Date

_____ _____

(Witness to above signature) Date

MASTER CHART

	Age	Gestational Age	Medical history	EFW Percentil	Umbilical artery PI	Inference	Rt uterine artery PI	Lt uterine artery PI	Mean	Placental pulsatility Ind	Mode of Delivery	Outcome	Birth weight
2	30	37 weeks	Anemia	a	0.77	p	0.8	0.9	c	m	Vaginal delivery	e	X
3	28	33 weeks	Severe Preeclamp	a	1.94	q	0.7	1.98	d	n	Vaginal delivery	g	X
4	25	37 weeks	PIH	b	1.31	p	0.81	1.67	d	n	C.section	f	Y
5	27	38 weeks	Anemia	b	0.95	q	0.54	0.63	c	m	Vaginal delivery	h	Y
6	32	36 weeks	Severe Preeclamp	b	1.24	p	0.4	0.53	c	m	C.section	f	Y
7	31	38 weeks	Severe Preeclamp	a	1.56	q	0.9	0.61	c	n	C.section	f	X
8	29	37 weeks	PIH	b	1.15	p	0.9	0.76	c	n	C.section	h	Y
9	32	39 weeks	Severe Preeclamp	b	1.24	p	0.9	1.03	d	n	Vaginal delivery	h	Y
10	34	38 weeks	Severe Preeclamp	a	1.5	q	0.7	0.64	c	n	C.section	f	X
11	24	37 weeks	Not applicable	b	1.64	q	1.75	1.51	d	n	C.section	f	Y
12	22	37 weeks	PIH	a	1.02	p	0.65	0.9	c	m	C.section	e	X
13	30	38 weeks	PIH	a	1.55	q	1.1	1.2	d	n	Vaginal delivery	g	X
14	20	38 weeks	Anemia	a	1.1	p	0.47	0.45	c	m	C.section	h	X
15	26	36 weeks	PIH	a	5.08	q	1.59	1.73	d	n	C.section	f	X
16	26	36 weeks	Anemia	b	1.18	p	0.4	0.75	c	m	C.section	h	Y
17	23	38 weeks	PIH	a	0.8	p	1.03	2.5	d	n	C.section	f	X
18	21	35 weeks	PIH	a	1.49	q	1.47	1.13	d	n	C.section	e	X
19	33	28 weeks	Severe Preeclamp	a	1.6	q	1.2	1.3	d	n	Vaginal delivery	g	X
20	21	32 weeks	PIH	b	0.7	p	1.02	0.75	c	m	Vaginal delivery	e	Y
21	30	29 weeks	Anemia	a	0.77	p	0.8	0.9	c	m	Vaginal delivery	e	X
22	31	30 weeks	Severe Preeclamp	a	1.94	q	0.7	1.98	d	n	Vaginal delivery	g	X
23	36	33 weeks	PIH	b	1.31	p	0.81	1.67	d	n	C.section	f	Y
24	34	35 weeks	Anemia	b	0.95	p	0.54	0.63	c	m	C.section	h	Y
25	38	26 weeks	Anemia	b	1.24	p	0.4	0.53	c	m	C.section	e	Y
26	21	32 weeks	Severe Preeclamp	a	1.96	q	1.1	1.2	d	n	C.section	f	X
27	25	29 weeks	PIH	b	1.9	q	1	0.7	c	n	C.section	e	Y
28	22	30 weeks	Not applicable	b	1.1	p	0.6	0.8	c	m	C.section	e	Y
29	20	36 weeks	Anemia	a	1	p	0.7	0.9	c	m	Vaginal delivery	h	X
30	22	35 weeks	Anemia	b	0.95	p	0.54	0.63	c	m	Vaginal delivery	h	Y
31	22	28 weeks	PIH	b	0.8	p	0.5	0.8	c	m	Vaginal delivery	h	Y
32	34	30 weeks	Anemia	b	1	p	0.7	0.8	c	m	Vaginal delivery	h	Y
33	32	32 weeks	PIH	b	1.01	p	1.4	1.3	d	n	C.section	e	Y
34	31	31 weeks	Severe Preeclamp	a	1.8	q	2	1.6	d	n	Vaginal delivery	g	X
35	33	37 weeks	PIH	b	1.3	p	1.3	1.5	d	n	C.section	e	Y
36	33	38 weeks	PIH	b	1.6	q	1.1	1.2	d	n	C.section	e	Y
37	31	40 weeks	Severe Preeclamp	a	1.6	q	1.8	2	d	n	Vaginal delivery	g	X
38	28	38 weeks	Anemia	b	1.01	p	0.6	0.5	c	m	Vaginal delivery	h	Y
39	27	29 weeks	PIH	b	1	p	1	0.97	c	m	C.section	e	Y
40	26	31 weeks	PIH	a	1.5	q	2.1	1.7	d	n	Vaginal delivery	g	X
41	25	32 weeks	Anemia	b	1	p	0.85	0.95	c	m	Vaginal delivery	h	Y
42	20	37 weeks	PIH	b	1.2	p	1.4	1.5	d	n	C.section	e	Y
43	21	28 weeks	Anemia	b	1.01	p	0.7	0.9	c	m	Vaginal delivery	h	Y
44	19	30 weeks	Severe Preeclamp	a	1.7	q	2	1.8	d	n	Vaginal delivery	g	X
45	28	37 weeks	PIH	b	1.4	p	1.2	1.1	d	n	C.section	e	Y

46	29	36 weeks	Anemia	b	1	p	0.9	1	c	m	Vaginal delivery	h	Y		
47	30	38 weeks	PIH	b	0.9	p	1.3	1.3	d	n	C.section	h	Y		
48	33	39 weeks	Severe Preeclamp	a	1.66	q	1.6	1.5	d	n	C.section	f	X		
49	31	32 weeks	Severe Preeclamp	a	1.8	q	1.8	1.9	d	n	Vaginal delivery	g	X		
50	30	31 weeks	PIH	b	1.01	p	1.2	1.1	d	n	C.section	f	Y		
51	27	38 weeks	Anemia	b	0.9	p	0.7	0.8	c	n	Vaginal delivery	e	Y		
52	29	39 weeks	Anemia	b	1	p	0.8	0.9	c	m	Vaginal delivery	e	Y		
53	28	38 weeks	PIH	b	1	p	0.9	0.9	c	m	Vaginal delivery	f	Y		
54	27	38 weeks	Severe Preeclamp	a	2.3	q	2.4	1.2	d	n	C.section	f	X		
55	24	40 weeks	Anemia	b	1	p	1	1	c	m	Vaginal delivery	h	Y		
56	23	38 weeks	Anemia	b	1	p	1.2	0.8	c	m	Vaginal delivery	e	Y		
57	21	39 weeks	Severe Preeclamp	a	2.3	q	2	2.1	d	n	C.section	f	X		
58	38	39 weeks	Severe Preeclamp	a	2.2	q	2	2.3	d	n	C.section	e	X		
59	36	35 weeks	PIH	b	1.2	p	2	1.5	d	n	C.section	e	Y		
60	34	37 weeks	Severe Preeclamp	a	2.5	q	2	1.3	d	n	C.section	f	X		
61	35	38 weeks	PIH	b	1.3	p	1	1	c	m	C.section	e	Y		
62	27	39 weeks	Severe Preeclamp	a	2.5	q	2	0.6	d	n	C.section	f	X		
63	28	36 weeks	PIH	b	1.2	p	2	0.9	d	n	C.section	e	Y		
64	29	38 weeks	Severe Preeclamp	a	1.8	q	2	1.02	d	n	C.section	f	X		
65	31	38 weeks	Anemia	b	1.1	p	0.9	0.8	c	m	Vaginal delivery	h	Y		
66	37	30 weeks	Severe Preeclamp	a	2.6	q	2	0.9	d	n	C.section	f	X		
67	32	32 weeks	Severe Preeclamp	a	2.4	q	2	1.02	d	n	C.section	e	X		
68	22	37 weeks	Anemia	b	1.1	p	0.7	0.8	c	m	Vaginal delivery	h	Y		
69	35	36 weeks	PIH	b	1	p	1	1.4	d	m	Vaginal delivery	h	Y		
70	20	34 weeks	PIH	b	1.2	p	1	1	c	m	Vaginal delivery	h	Y		
71	21	37 weeks	Severe Preeclamp	a	1.6	q	1.2	1.5	d	n	C.section	f	X		
72	22	35 weeks	PIH	b	0.9	p	1	1.3	d	m	Vaginal delivery	h	Y		
73	22	36 weeks	Severe Preeclamp	a	1.8	q	1.6	1	d	n	C.section	e	X		
74	25	37 weeks	PIH	b	1	p	0.9	0.8	c	m	Vaginal delivery	h	Y		
75	27	29 weeks	Severe Preeclamp	a	2	q	2.2	1.2	d	n	C.section	f	X		
76	26	30 weeks	Severe Preeclamp	a	2.3	q	2	1.4	d	n	C.section	f	X		
77	24	31 weeks	Severe Preeclamp	a	2.5	q	2	1	d	n	C.section	e	X		
78	24	36 weeks	PIH	b	1	p	1.1	1.5	d	m	C.section	h	Y		
79	23	39 weeks	PIH	b	0.8	p	0.9	1	d	m	Vaginal delivery	h	Y		
80	22	37 weeks	PIH	a	1.46	q	0.8	1	c	m	C.section	e	X		
81	21	38 weeks	Anemia	b	0.9	p	0.9	1.6	d	m	Vaginal delivery	h	Y		
82	20	38 weeks	Anemia	b	1	p	0.9	1.7	d	m	Vaginal delivery	h	Y		
83	27	39 weeks	PIH	a	1.9	q	2.1	1	d	n	C.section	f	X		
84	28	39 weeks	PIH	a	1.5	q	1.8	1	d	n	C.section	f	X		
85	21	34 weeks	Anemia	b	0.96	p	0.98	1.3	d	m	Vaginal delivery	h	Y		
86	22	34 weeks	Anemia	b	1	p	0.95	1.3	d	m	Vaginal delivery	h	Y		
87	27	30 weeks	PIH	b	1.1	p	1.77	0.8	d	n	C.section	h	Y		
88	26	33 weeks	PIH	b	1	p	2	1.3	d	n	C.section	h	Y		
89	24	32 weeks	APLA	a	1.5	q	1.7	1.4	d	n	C.section	f	X		
90	23	30 weeks	Severe Preeclamp	a	1.8	q	1.9	1	d	n	C.section	f	X		
91	32	30 weeks	Severe Preeclamp	a	1.9	q	1.9	1	d	n	C.section	f	X		
92				a-<3rd percentile		p-normal			c-normal	m-normal		e-SGA-NICU admission		X-<3rd percentile	
93				b-<10th percentile		q-annormal			d-abnormal	n-abnormal		f-RDS-NICU admission		Y-<10th percentile	
94												g=IUD/Still Born			
95												h=Mothersice			
96															
97															
98															
99															
100															

ETHICAL CLEARANCE CERTIFICATE

IEC/110-09/2021
Date- 22-01-2021

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11-00 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: Placental pulsatility index as a predictor of critical perinatal outcomes in growth restricted fetuses.

Name of PG student: Dr Ayesha Mahaldar, Department of Radiology

Name of Guide/Co-investigator: Dr Shivanand Patil Associate Professor of Radiology

DR .S.V.PATIL
CHAIRMAN, IEC
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.