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Review Article

Colour Doppler in IUGR- Where are we and where do we go?

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Abstract

Intra-uterine growth restriction (IUGR) is an important perinatal problem giving rise to increased morbidity and mortality in the growth restricted fetus. The aim of fetal medicine today, is to prevent the mere occurrence of IUGR in high risk pregnancies and to deliver the fetuses already afflicted with growth restriction, before they have suffered from the effects of hypoxia. The use of Doppler provides this information, which is not readily obtained from the other conventional tests of fetal well being. The Doppler patterns follow a longitudinal trend in the arterial and venous circulation of the fetus as well as the placental vasculature guiding management decisions regarding the appropriate time of delivery. Progressive knowledge of the fetal circulation and its adaptation when the fetus is subjected to hypoxia, has helped us recognize the early signs of IUGR thereby improving the prognosis of these complicated pregnancies. It has therefore become the gold standard in the management of the growth-restricted fetus.

Key words: Intra uterine growth restriction, Fetal circulatory changes in IUGR, Doppler based management in IUGR Aortic Isthmus

Introduction

Intrauterine growth restriction (IUGR) is a term used to describe the fetus with a birth weight at or below the 10th percentile for gestational age and sex. The IUGR fetus is a fetus that does not reach its growth potential.

The two components that are necessary to define an IUGR fetus are:

a) birth weight < 10th percentile; b) Inadequate interval growth in sequential screening

The placenta is the lifeline of the fetus and, when challenged, it has a remarkable ability to adapt. Developmental problems can occur from the maternal side, the fetal side, or both [1].

The development of a good utero-placental circulation is essential for the achievement of a normal pregnancy. To facilitate this, remarkable changes occur in the maternal, placental and fetal vasculatures [2]. When this mechanism fails, abnormal vascular resistance patterns develop which lead to compromise of fetal well-being with a 6 to 10 times higher risk of perinatal mortality,

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morbidity, and impaired neurodevelopment [3, 34].

Kingdom et al demonstrated that maldevelopment of the villous tree in pregnancies complicated by fetal growth restriction is associated with abnormal uterine artery waveforms, indicating abnormal uteroplacental blood flow. In pregnancies also complicated by absent end-diastolic umbilical flow, the placental villi are elongated, and the capillary loops are uncoiled and sparse. These findings are correlated with an increase in fetal-placental vascular impedance and impaired gas and nutrient exchange. An enhanced branching angiogenesis represents an adaptive response to impaired uteroplacental blood flow [4].

The introduction of color Doppler technology has provided the first opportunity for repetitive noninvasive haemodynamic monitoring in pregnancy. There is ample evidence that Doppler indices from the fetal circulation can reliably predict adverse perinatal outcome in an intrauterine growth restricted (IUGR) pregnancy. Compared to other methods of fetal monitoring, Doppler has proved to be more sensitive in detecting fetal compromise early and aids in the guiding and making of decisions regarding the appropriate timing of delivery [5]. The Doppler patterns follow a longitudinal trend with early changes in the middle cerebral artery and umbilical artery followed by other peripheral arteries. These indicate the occurrence of redistribution of blood flow in growth restricted fetuses and therefore caution us to closely monitor the fetus and intervene before the situation becomes unsalvageable. If adequate measures are not taken at this point, venous changes appear in the severely compromised fetus. These are strong predictors of poor perinatal outcome and indicate impending irreversible damage.

Doppler reveals changes of hypoxia at least a week before the non-stress test or the biophysical profile. It has therefore become the gold standard in the management of the growth-restricted fetus [6, 7].

Technique of Color Doppler ultrasound

The patients are first scanned in the routine fashion using B-mode with a 3.5- or 5-MHz curved-array transducer. The vessel of interest is located by color Doppler. The spectral Doppler waveform is then obtained by placing the Doppler gate directly over the vessel of interest. The spectral recordings should ideally be obtained in the absence of fetal breathing movements and fetal heart rate between 120 and 160 bpm. . The best waveform will be obtained when the angle of insonation is between 30 to 60 degrees. Difficulty maybe encountered when studying fetal vessels that move with fetal movements and that are non-linear, e.g. the umbilical artery. The pulse repetition frequency and wall filter is kept to a minimum in order to not obscure minimal end-diastolic flow when present. However, it should not be set inappropriately low to avoid eliminating valuable high frequency information in a high velocity circulation such as that in the fetal aorta [8].

Normal Fetal circulation

Blood with the highest concentration of oxygen and substrates enters the fetus via the umbilical vein and reaches the liver as the first major organ. The umbilical vein delivering oxygenated blood from the maternal placenta to the fetus distributes 18-25% of its supply to the right atrium, 55% to the dominant left hepatic lobe and 20% to the right hepatic lobe. The ductus venosus is the first shunt that determines the proportional distribution of these nutrients between the liver and the central circulation [2]. The watershed area associated with the ductal shunt is the left portal vein, where umbilical venous blood that continues to the liver comes in contact with depleted portal blood that drains the splanchnic circulation.

The heart is the next major organ receiving blood with a range of nutritional content from different sources. Among the right atrial tributaries, the ductus venosus and the left hepatic vein carry blood with higher nutritional content than do the other venous tributaries viz. inferior and superior vena cavae, right and the middle hepatic veins and the coronary sinus. On the left side, the pulmonary veins return depleted blood to the left atrium. The foramen ovale is the second shunt partitioning these incoming bloodstreams. Due to their different directionality and velocities, the position of the crista dividens and valve of the foramen ovale, saturated blood from the ductus venosus reaches the left ventricle preferentially, while the relatively depleted blood enters the right ventricle.

The preductal aorta delivers nutrient rich blood to the myocardium and brain (via the brachiocephalic circulation), while less saturated blood from the right ventricle enters the lungs and ductus arteriosus. The ductus arteriosus serves as a conduit that unites these two bloodstreams through its insertion in to the aorta distal

to the left subclavian artery. The aortic isthmus is the associated watershed area where the shunting between the bloodstreams originating from the left and the right ventricle occurs. Downstream of the ductus arteriosus, the descending aorta carries the blood with the nutritional content that results from the mixture of these two bloodstreams.

The umbilical artery provides the fourth shunt where depleted blood is channeled to the placenta for gas, nutrient and food exchange.

Fetal Haemodynamics in IUGR

IUGR in a majority of the cases is secondary to uteroplacental insufficiency.

Doppler ultrasound gives us information on the uteroplacental vascular resistance and, indirectly on the blood flow. Analyses of the Doppler waveforms are made by measuring the peak systolic (S) and end diastolic (D) velocities. Three indices are considered related to the vascular resistance: S/D ratio (systolic/diastolic ratio), resistive index (RI = systolic velocity - diastolic velocity/systolic velocity), and pulsatility index (systolic velocity - diastolic velocity/mean velocity). Gestational age based normative data have been established for all measurements. Flow changes can be observed in both the arterial and venous system of the fetus and in the uterine arteries.

Changes in the Arterial Circulation

Uterine circulation

The uterine artery Doppler waveform is best obtained by first identifying the maternal internal iliac artery. The transducer is then moved slightly cephalad and medial until a vessel is noted running perpendicular to the internal iliac artery, going into the myometrium. The Doppler gate is then placed over the artery to obtain the Doppler waveform, which is easily recognized by its shape and the slower rate consistent with maternal pulse (Figure 1).

Uterine Artery Doppler correlates well with hemodynamic changes in the placental circulation. As the fetoplacental compartment develops and gestational age advances, there is an increase in the number of tertiary stem villi and arterial channels, and hence the impedance in the uterine artery decreases. A diastolic component in the uterine artery flow velocity waveform appears during the early second trimester, i.e., at 14 weeks' gestation, and progressively increases up to 20 to 24 weeks (Figure 2).

Pregnancies that are destined to result in normal term deliveries show increased diastolic blood flow velocity and loss of the early diastolic notch by 22 weeks of gestation, whereas pregnancies that show persistent high-resistance waveforms with early diastolic notches are at risk of preterm delivery from pre-eclampsia, abruption, intrauterine growth restriction and overall higher morbidity as well as mortality [9].

An abnormal flow velocity waveform in the uterine arteries demonstrating a persistent diastolic notch and low diastolic flow beyond 24 weeks gestation reflects abnormal resistance downstream in the uteroplacental vascular bed (Figure 3). Fleischer and Schulman have found that in IUGR complicated by pregnancy-induced hypertension, there is inadequate trophoblastic invasion of the spiral arteries, leading to increased resistance in the spiral arteries (Figure 4) and decreased blood flow in the placental vascular bed and in the uterine artery, thereby resulting in an increase in the uterine artery PI and bilateral notching [10]. This is described as uteroplacental insufficiency and leads to the delivery of neonates who are small for gestational age [9].

A combined Doppler and hormonal profile of placental function may be of value to screen for pregnancies that are at increased risk of pre-eclampsia, fetal death, and IUGR even as early as the first trimester [11, 12].

Umbilical artery

The umbilical artery is the signature vessel in the Doppler study of the fetus as it is a direct reflection of the flow within the placenta. It is usually the first vessel to be studied when suspecting an IUGR fetus.

The umbilical artery is assessed at three sites, the placental origin, fetal abdominal insertion site and in the mid free floating loop. Resistances at the abdominal cord insertion tend to be higher and those at the placental insertion tend to be lower than those at the midcord [13] (Figure 5).

In the normal fetus, the pulsatility index decreases with advancing gestation. This reflects a decrease of the placental vascular resistance (Figure 6). In fetuses with

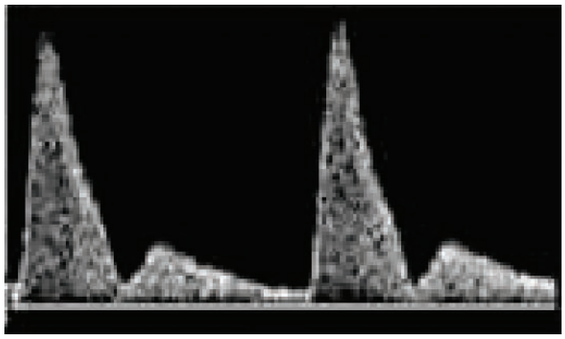

Figure 1: Abnormal uterine artery waveform seen in pre-eclampsia showing persistent pre-diastolic notch.

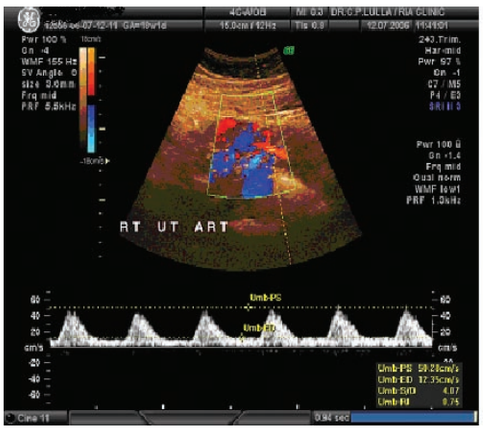

Figure 2: Increased resistance wave pattern in the uterine arteries seen in uteroplacental insufficiency

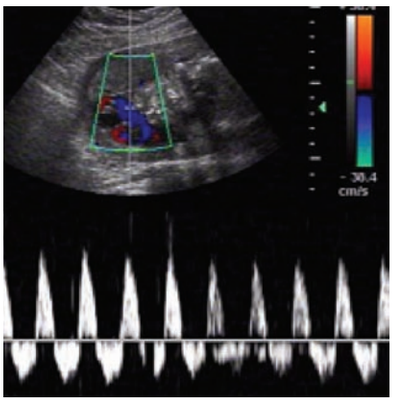

Figure 3: Reversal of diastolic flow

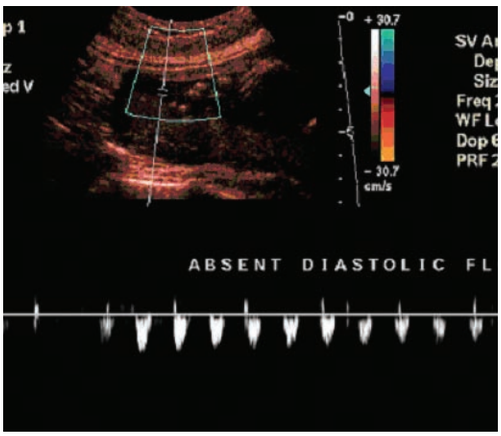

Figure 4: Absent end diastolic flow

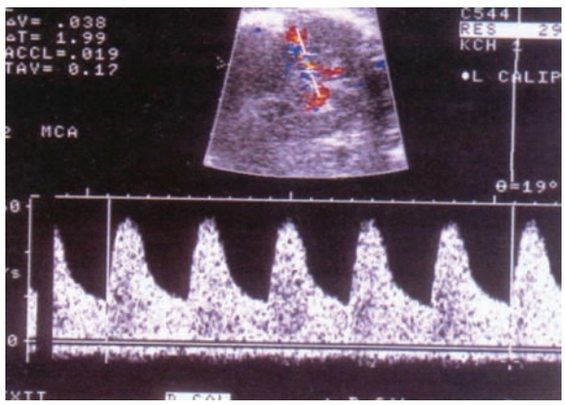

Figure 5 : Brain- sparing effect seen in MCA- Increased end diastolic flow and decreased P.I.

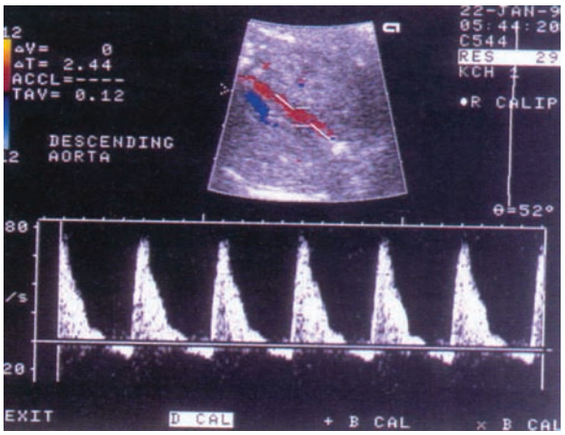

Figure 6: Reversal of diastolic flow in the aorta suggestive of severe hypoxia, predictor of academia and neonatal necrotizing enterocolitis.

IUGR there is an increase of the pulsatility index secondary to the decrease, absence or reversal of end- diastolic flow. The changes of these waveforms are thought to be indicative of increased placental resistance. The absent or reversed end-diastolic flows are strongly associated with ,an abnormal course of pregnancy and a higher incidence of perinatal complications, when compared to fetuses with IUGR characterized by the presence of end-diastolic flow [14].

The prevalence of perinatal death in fetuses with absent or reversed end diastolic flow velocity is reported to be over 40%. Yoon et al demonstrated in their study that AEDF is a strong and independent predictor of adverse perinatal outcome [15].

Some fetuses have decreased diastolic flow that remains constant with advancing gestation and never becomes absent or reversed which may be due to a milder form of placental insufficiency.

In some IUGR fetuses, the fetus maintains a normal diastolic flow velocity in the umbilical artery by altering the fetal cardiac output in an attempt to conserve placental oxygenation and hence function. This suggests that the umbilical artery functions as a shunt to maintain placental oxygenation.

Although the umbilical artery waveform is a good reflector of placental resistance it has lost its status as the key vessel as it does not give any information as to how the fetus is coping with the compromised blood supply and hence does not help to determine optimum time of delivery.

Fetal cerebral circulation

The middle cerebral artery is the vessel of choice to assess the fetal cerebral circulation because it is easy to identify and has a high reproducibility. Fetal middle cerebral artery waveforms are best obtained with the cranium in a transverse position as the angle of insonation would be as close to 0 degrees as possible , and therefore, information on the true velocity of the blood flow may be obtained. During normal pregnancy, the MCA shows high resistance and low diastolic flow pattern with continuous forward flow throughout the cardiac cycle.

In mild cases of fetal hypoxia when the resistance of the umbilical artery is increased, no change maybe demonstrated in the flow pattern of the MCA due to the adaptation of the fetal circulation in maintaining the after load of the left ventricle [16]. An increase in the MCA PSV maybe the only perceivable finding at this early stage [17]. However, if there is continued and progressive fetal hypoxia, a phenomenon known as "brain sparing effect" is seen with dilation of the fetal intracranial vessels, which provides increased blood flow to the brain at the expense of other organs. The Doppler waveform depicts this as increase in diastolic flow with decreased pulsatility index . The presence of such compensation suggests a compromised fetus [18]. In pregnancies with chronic fetal hypoxia, the blood volume in the fetal circulation is redistributed in favor of vitally important organs, i.e., the heart, kidneys and brain [(2)]. With continuing hypoxia, the overstressed fetus loses the brain sparing effect and the diastolic flow returns to the normal level. Presumably, this reflects a terminal decompensation in the setting of acidemia or brain edema. When brain edema becomes severe, reversal of diastolic flow maybe seen due to the raised intracranial tension, which suggests grave and irreversible fetal neurological outcome [16].

To describe the correlation of placental resistance and cerebral adaptation Arbeille et al described the cerebral placental ratio .This is constant during pregnancy especially after 30 weeks and suggested 1 as the cut off value; all values less than 1 is considered abnormal [(19)]. This ratio is shown to have higher sensitivity (100%) in predicting adverse perinatal outcome and fetal hypoxia when compared to pulsatility index of MCA or umbilical artery alone (50%) according to study by T. Ozcan et al [17].

Fetal Aorta

The fetal aorta provides a direct reflection of the cardiac output and the peripheral resistance of the systemic circulation. It gives the summation of blood flow information to the kidneys, abdominal organs, lower limbs and placenta.

Normal blood flow in the fetal descending aorta is highly pulsatile with a minimal end diastolic component. The diastolic velocities start to present during the second and third trimesters, however the PI remains constant [24]. Wladimiroff et al in their study got a normal pulsatility index of 1.7-1.8 in the descending aorta [20]. In the hypoxic fetus, due to redistribution of flow to the brain, there is peripheral vasoconstrictions, which is re-

flected in the rising RI and PI values. In presence of severe hypoxia, the diastolic flow reverses and this strongly correlates with gross acidemia and impending neonatal necrotizing enterocolitis due to severe mesenteric ischemia [21].

Changes in the Venous Circulation

Doppler waveforms obtained from the central venous system of the fetus reflect the physiologic status of the right ventricle giving specific information regarding the ventricular preload, myocardial compliance and right ventricular end-diastolic pressure. The vessels that give us invaluable Doppler information regarding the adaptation to fetal hypoxia are the inferior vena cava, the ductus venosus and the umbilical vein.

Ductus venosus

The ductus venosus can best be identified in a sagittal section or an oblique section through the upper fetal abdomen. It is seen as a continuation of the intraabdominal umbilical vein with a narrow inlet and a wider outlet and connects to the IVC. On colour Doppler, it usually stands out due to the turbulent flow seen through its narrow lumen and resultant aliasing of colour signals seen within it.

The spectral waveform seen in this vessel can be described as a classic 'M' pattern characterized by a first and second peak coinciding with ventricular systole and early diastole when there is passive filling of the ventricles. Following this second peak is the nadir before the onset of the next systole. This nadir of brief diminished forward flow coincides with atrial contractions during late diastole.

In IUGR when there is progressive hypoxia and worsening contractility of the ventricles and atria secondary to myocardial ischemia, the ductus venosus shows a progressive decrease in forward flow due to an increasing pressure gradient in the right atrium. In such cases, tricuspid regurgitation causes a reversal of flow in the inferior vena cava, which eventually leads to reversal of flow in the ductus venosus. Abnormalities in this waveform have been associated with worsening fetal hypoxemia and acidemia, which may precede abnormalities in the fetal heart rate [17]. Gonzalez et al observed 5 fetuses with reverse flow velocity waveforms at the ductus venosus and all the fetuses died in utero. In 18 other fetuses with abnormal umbilical and middle cerebral artery waveforms, but without reverse flow in the ductus venosus, no deaths occurred [(6)].

Umbilical Vein

The umbilical vein carries oxygenated blood from the maternal side of the placenta to the fetus. This blood is then carried via the ductus venosus into the right side of the heart. It can be assessed either within its entrance into the fetal abdomen at the site of umbilical cord insertion, further up near the liver or in the free floating loops in the amniotic fluid.

The normal Doppler waveform reveals a monophasic waveform with continuous forward flow throughout the cardiac cycle. This continuous diastolic flow, gradually increases from the 20th wk of gestation up to the 38th week. The umbilical vein is probably one of the last vessels to change its flow pattern in the setting of fetal hypoxia. In severe cases, when there is reversal of flow in the IVC and ductus venosus due to right heart failure, a pulsatile flow pattern begins to appear due to the high resistance to forward flow. The presence of umbilical vein pulsations is associated with an increased risk of adverse perinatal outcome.

Changes in the Fetal Heart in IUGR

IUGR is associated with several changes at the level of the fetal heart as it plays a central role in the adaptive mechanisms for hypoxemia and fetal insufficiency. In order to understand these changes, it is imperative to know the basics of the fetal circulation

- Two ventricular pumps perfuse the same systemic circulation in a parallel fashion with the right ventricular output being greater than the left [22].
- 85 to 90 % of the Right ventricular output supplies the sub diaphragmatic organs and carcass via the blood going into the descending aorta from the pulmonary artery via the ductus arteriosus, and10–15% goes into the pulmonary circulation.
- The dormant pulmonary circulation (due to physiologic non-functioning of the lungs) maintains a high pulmonary vascular resistance, which is almost equal to the systemic side. Hence there is small left to right shunt across the foramen ovale. The flow to the pulmonary vascular bed gradually increases towards the end of gestation With advancing gestation the R>L shunting across the foramen ovale decreases by 45% due to corresponding increase in the

pulmonary blood flow.
- Cephalic part of the fetus gets perfused by the left ventricular output [2].
- Aortic Isthmus establishes communication between the two arterial outlets that perfuse in parallel the upper and lower body of the fetus namely the right and left ventricular output [2].

The changes seen in an adapting IUGR fetal heart involve preload, after load, ventricular compliance, and myocardial contractility. Longitudinal data on the haemodynamic sequence of the natural history of fetal growth restriction show that the umbilical artery and the MCA are the first variables to become abnormal. These arterial Doppler abnormalities are followed by abnormalities in the right cardiac diastolic indices, followed by right cardiac systolic indices, and finally, by both left diastolic and systolic cardiac indices. Preserving the left systolic function as the last variable to become abnormal ensures an adequate left ventricular output, which supplies the left cerebral and coronary circulation.

Changes in the right heart: An increase in after load is seen at the level of the right ventricle owing to increased placental impedance. This in turn causes increased systemic venous pressure and increase in venous shunting through the ductus which leads to a concomitant reduction in umbilical flow to the liver [2]. There is also increased shunting from the left to the right heart through the foramen ovale. With further deterioration, these adaptive mechanisms are overwhelmed, and there is a high incidence of tricuspid regurgitation followed by reversal of flow in the IVC and ductus venosus. These Doppler abnormalities are strong predictors of myocardial cell damage [23].

Changes in the left heart: A decrease in the after load is noted at the level of the left ventricle owing to decreased cerebral impedance associated with the brain sparing reflex. These changes in the after load result in a redistribution of the cardiac output from the right to left ventricle in order to maintain an adequate supply to the brain, heart and the adrenals [24]. This is known as 'arterialization of the circulation'.

Changes on both sides: Preload is reduced at both atrioventricular valves owing to hypovolemia and decreased filling associated with IUGR. Evidence of reduced myocardial contractility has also been reported in the presence of IUGR. Ventricular ejection force, an index of ventricular systolic function that is independent of preload and afterload is decreased at the level of the right and left ventricle in fetal growth restriction. IUGR fetuses with reduced ventricular ejection force have a shorter time to delivery, a higher incidence of non- reassuring fetal heart tracing and a lower pH at birth. A significant correlation between the severity of the fetal acidosis and cordocentesis and ventricular ejection force values validates the association of this index and severity of fetal compromise.

Doppler based management in IUGR
Severe Uteropla cental insufficiency

A) The cause for the development of uteroplacental insufficiency may begin as early as the time of the implantation. However, no effect is seen on growth or Doppler until 20-24 weeks gestation. These fetuses do not have signs of growth restriction or abnormal Doppler ultrasound prior to this period

B) At 22-24 weeks gestation if the fetus is measurably small by ultrasound, several Doppler patterns may occur. 1) The umbilical artery may still have a normal pulsatility index (resistance index or S/D ratio); the middle cerebral artery may have either a normal or abnormal pulsatility index. 2) The umbilical artery has an abnormal pulsatility index; the middle cerebral artery has either a normal or abnormal value of pulsatility index. 3) The umbilical artery and the middle cerebral artery have both an abnormal value of pulsatility index. The fetus needs to be monitored very closely. Bed rest and oxygen therapy may be useful; however, if both vessels have an abnormal value at this early gestational age, it is very likely that the fetus will continue to deteriorate and the chance of a delivery at term is remote.

C) The pulsatility index of the umbilical artery may increase while that of the middle cerebral artery may decrease. The other fetal vessels may still appear normal and the only Doppler abnormalities are the umbilical artery and middle cerebral artery. The fetus starts to show signs of IUGR. The biophysical profile is normal. At this time the lack of fetal growth, and/or the development of pre-eclampsia/ eclampsia, or a persistent abnormal biophysical profile may interrupt the process with delivery of the fetus. These fetuses are at lower risk for the development of respiratory distress syndrome and intraventricular hemorrhage. The reason is not

completely understood. However, production of steroids with stress may play an important role in this process. If the fetus is not delivered, the process continues.

D) At this time tricuspid regurgitation may appear, ductus venosus reverse flow and umbilical vein pulsations may be present intermittently. The biophysical profile may still appear normal [36].

E) Ductus venosus reverse flow and umbilical vein pulsations are present continuously. The fetus starts to lose the brain sparing effect. The biophysical profile becomes abnormal [38].

F) Fetal demise. The time interval between E and F is variable (from 6-12 hours to 2 weeks). Oligohydramnios may be present at any stage of the above process.

Muld uteroplacental insufficiency

In mild Uteroplacental insufficiency no effect may be seen on Doppler and growth until 26-32 weeks gestation. The umbilical artery and the middle cerebral artery waveforms may be abnormal. However, the process is not severe enough to stop fetal growth completely or to deteriorate as above. These cases may be followed with outpatient monitoring and they often deliver at term [(39)].

Changing trends in Doppler assessment of IUGR fetuses

There has been a dramatic shift in the role and goals of the Doppler study from its advent in the early 80's when it was used to recognize the presence of IUGR by assaying the umbilical artery and MCA, which in turn led to the understanding of management protocols in the 90's by diagnosing adverse fetal outcome in utero. However, there remained a large gap as we continued to produce fetuses afflicted with different manifestations of hypoxia in the postnatal period. We have surely come a long way since then and now in the twenty-first century, the main focus has been to devise techniques to predict the 'likelihood' of fetal morbidity in the setting of IUGR and avert the occurrence of fetal compromise. The aim is to identify those pregnancies 'at risk' of IUGR before the fetus has actually become growth restricted and to prevent the occurrence of fetal decompensation if growth restriction has already occurred. Hence the role of Doppler is shifting from curative to preventive medicine.

1. First trimester uterine artery screening: The maternal adaptation to pregnancy is thought to result from the trophoblastic invasion of the maternal spiral arterioles in the first half of pregnancy. The invaded arterioles are rendered maximally dilated and minimally responsive to the sympathetic and parasympathetic systems. This adaptation is intended to ensure a sustained increase in the blood flow to the uterus during the pregnancy [2]. Numerous studies have shown that late first trimester screening of the uterine artery in high-risk women can accurately identify a subset of women who are destined for major complications that will be attributable to placental disease. Serial Doppler assessment of the uterine artery is performed from the 16th wk onwards in these high risk women who may have history of factors known to cause IUGR [25, 26]. The persistence of the pre-diastolic notch and gradually increasing impedance indices suggest an abnormal uterine circulation and hence is an indicator to treat these women with bed rest, antihypertensives and oxygen therapy right from the onset of the pathology. This has helped in completely averting serious pregnancy complications including IUGR itself, pre-eclampsia, preterm delivery and poor postnatal fetal outcome [27].
2. New vessels giving new hope- The Aortic Isthmus
   The Aortic Isthmus (AoI) is the only arterial shunt between the right and left ventricular output (Figure 26,27). It is located between the Left Subclavian artery and aortic insertion of the ductus arteriosus [(28)]. The ductus arteriosus is a physiologic shunt and hence blood flow through it is considered physiological in fetal life and not as a pathologic diversion from the right circulation to the left. The aortic isthmus, on the other hand is the link between the parallel vascular systems perfused by the left and right ventricle [29]. As a consequence, AoI blood flow velocity patterns reflect the balance between left and right ventricular outputs and are influenced by differences in the impedance to flow in the placental and cerebral vascular systems [30].

When the net peripheral resistance is low (as is seen in a normal fetus with normal S/D ratio in the umbilical artery) blood flow in the aortic isthmus is forward directed throughout the cardiac cycle. In the advent of fetal hypoxia, when the placental resistance becomes high causing a fall in umbilical blood flow of approxi-

mately 50%, there is diastolic reversal of flow seen even though the diastolic flow in the umbilical artery remains forward. However, because of the systolic predominance, the net flow in the isthmus is forward. When there is more severe increase in placental resistance corresponding to a decrease of 75% in umbilical blood flow, the net flow through the isthmus becomes retrograde. Retrograde blood flow in the aortic isthmus represents abnormal flow ejected by RV into a vascular territory usually perfused by the left ventricle. When the net flow in the aortic isthmus becomes retrograde, nutrient and O2 content of the left ventricle drops and there is markedly increased risk for adverse childhood neurodevelopment in fetuses. The study of AoI velocity waveform is a promising tool allowing a comprehensive study of the fetal circulation when peripheral resistances to ventricular output are changed. Studies have conclusively proved that Aortic Isthmus velocity waveforms become abnormal at an earlier stage of fetal compromise than Ductus Venosus [31].

In order to objectively gauge the flow through the aortic isthmus, the Isthmic Flow Index (IFI) was proposed. The circulatory indices that are clinically used thus far are useful for indirect assessment of the impedance of vascular networks. They however, do not give any information about the direction of flow. Hence, for clinical purposes, the IFI is used which reflects both the amount and the direction of blood flow through the fetal isthmus and is particularly sensitive to the change in direction of the diastolic flow. IFI is equal to the Systolic velocity + Diastolic velocity / Systolic velocity [28]. Positive and negative signs are assigned to antegrade and retrograde velocity values, respectively.

To summarize, greater the reverse isthmic flow, lower is the IFI and higher risk of cerebral damage. This index has implications in understanding and grading the left ventricular dysfunction in a hypoxemic fetus. Reversal of flow in the isthmus (IFI < 1) indicates a significant fall in left ventricular output causing compensatory perfusion of the upper body circulation by the right ventricle. This suggests that the left ventricle will not be able to take charge of the postnatal systemic circulation which will continue to be ductus dependent.

Conclusion

Placental insufficiency is the most common cause of intrauterine growth restriction (IUGR) and Pregnancy induced Hypertension (PIH). It is an important obstetric problem on account of the high associated perinatal mortality and morbidity. Uterine artery Doppler has important role to play in predicting the onset of PIH and IUGR at 20-24 weeks There seems to be a need to recognize placental insufficiency early so that its hazards can be reduced, if not averted. The preventive role of uterine artery Doppler is hence shifting to the first trimester [32].

Fetuses with IUGR show evident modifications of Doppler parameters in the uteroplacental and fetal circulation. Sequential studies enable us to determine the condition of these fetuses by observing the Doppler changes in different vascular territories. The delivery of the sick fetus can hence be appropriately timed to prevent the associated complications [33, 34].

In the past the focus has been to reduce near term mortality and morbidity, but recent studies have documented adverse long term neurological sequelae even in those fetuses subjected to hypoxia for a short duration [37]. Hence the role of Doppler has shifted from a curative to a preventive one with truly informed and meaningful brain-oriented fetal care becoming a clinical reality .The advent of the aortic isthmus as the new vessel of hope in analyzing early disruption in the cerebral perfusion, is in this direction [35].

There are, however, still many uncertainties concerning the relationships between the Doppler changes and the metabolic situation of the fetus and therefore, on the optimal timing of delivery in order to completely prevent the occurrence of any intrauterine injury.

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