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Stillbirth Society of India

International Stillbirth Alliance Member

Theme of the Month:
Fetal Growth Restriction

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From the Editor's Desk

Dear Readers,

The much awaited newsletter by the 'Committee for study of stillbirths from Fetal Growth Restriction' is finally released.

It has been an honour edit this e-newsletter of the Stillbirth Society of India. The theme for this e-newsletter is **"Fetal Growth Restriction [FGR]".**

Prevention of stillbirth remains one of the major challenges in obstetrics especially in India. Amongst the various causes of stillbirth, FGR remains important both in prevalence and severity.

One of the major areas of focus in prevention of stillbirth, is earlier detection and appropriate management of pregnancies with FGR. Having a low birth weight for gestational age increases the risk of stillbirth three to four times. Pregnancies diagnosed with FGR need escalated antenatal surveillance to detect foetuses at increased risk of stillbirth. Considering the data on causes of stillbirth, a newsletter on FGR becomes especially relevant.

The first article, **'Optimising Perinatal Outcome in Fetal Growth Restriction'** extensively discusses different aspects of growth restriction starting from the definition of FGR and gradually building up on the clinical scenario to discuss management of both early and late FGR.

The second article '**Doppler in Fetal Growth Restriction: Basics'** discusses the role of fetal Dopplers in management of fetal growth restriction.

The third article, '**FGR in Multifetal Pregnancy: Overview'** discusses lucidly the varied aspects of FGR in multiple gestation. The highlights of this article remain concise and crisp summarisation of the management protocols.

Finally, we have the **'Secretary's Report'** for the webinar conducted by the committee under the aegis of SBSI.

We wish our readers a happy reading!!!

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Optimising Perinatal Outcome in Fetal Growth Restriction

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Introduction

Fetal growth restriction (FGR) has been defined as 'a foetus unable to reach its growth potential'.[1] However, since it is difficult to determine the optimal 'growth potential' of any given foetus, ultrasound criteria including estimated fetal weight (EFW), 'plateauing' in fetal growth accompanied by Doppler abnormalities have been suggested to differentiate small for gestational age (SGA) foetuses from those small foetuses that are at risk of adverse perinatal outcomes and thus truly 'growth restricted'.[2] FGR has also been recategorized as 'early' and 'late' fetal growth restriction when diagnosed before or after 32 weeks of gestation. It is important to note at the outset that a 'discrepancy in weeks' in fetal head circumference (HC) and abdominal circumference (AC) on ultrasound is no longer considered a criteria for defining growth restriction. Also identification of Doppler abnormalities should be based on the Pulsatility index (PI) of the target vessel rather than the traditional 'SD ratio'. Estimated fetal weight should be plotted on a 'growth chart'.

Use of growth charts (irrespective of which chart is used) is essential for noting the degree of smallness ('centile') as well as weight gain over a period of time, typically over 2-3 weeks.

Diagnosis

If a foetus is identified to be small on ultrasound, the first step is to rule out wrong dates. Thus dating should be confirmed, preferably from the early first trimester crown to rump length (CRL). The next step is to differentiate small for gestational age (SGA) foetuses from 'growth restricted' foetuses, ie those small foetuses that are at risk of adverse perinatal outcomes. Thus, newer diagnostic criteria that include both fetal as well as maternal Dopplers have been proposed by a Delphi consensus in 2016 and should be used for diagnosing FGR (table 1).[3]

Very small foetuses, i.e., those with an estimated fetal weight (EFW) of less than 3rd centile would be considered growth restricted even if Dopplers are normal. Foetuses with EFW between 3rd to 10th centile should have a Doppler abnormality before being considered pathologically small.

All growth restricted foetuses may not have EFW below the 10th centile. Use of growth chart helps in identifying a 'plateauing' growth or falling of weight centile which is usually accompanied with cerebral redistribution.

Table 1: Diagnostic criteria for Early and Late Fetal growth restriction (in a structurally normal fetus)	
Early FGR (diagnosed before 32 weeks)	**Late FGR (diagnosed after 32 weeks**
AC*/EFW < 3rd centile **OR**	AC/EFW < 3rd centile **OR**
Umbilical artery – A/REDF# **OR**	
AC/EFW < 10th centile **AND** Uterine artery PI > 95th centile **AND/OR** Umbilical artery PI > 95th centile	Any 2 of the following 3 criteria: AC/EFW < 10th centile **OR** AC/EFW crossing centiles >2 quartiles on growth chart **AND** CPR< 5th centile **OR** Umbilical artery PI > 95th centile

**AC: Abdominal circumference, #A/REDF: Absent or reversed end diastolic flow*

Early fetal growth restriction

Early FGR, diagnosed before 32 weeks, accounts for 1/3rd of antenatally diagnosed FGR and is usually associated with hypertensive disorders of pregnancy. It is easily identified on ultrasound and follows a predictable deterioration in fetal Dopplers: increase in umbilical artery Pulsatility index (PI) followed by decrease in middle cerebral artery (MCA) PI followed by venous Doppler abnormalities. The deterioration in umbilical artery Doppler follows a typical and predictable pattern in early FGR (figure 1). The mean uterine artery PI is usually above the 95th centile in these pregnancies.

Early onset FGR especially those presenting before 22-24 weeks warrant detailed evaluation to rule out fetal structural abnormalities, fetal infections and chromosomal and non-chromosomal genetic abnormalities. Amniocentesis for fetal microarray should be considered in FGR presenting in the second trimester.

Although easier to diagnose, early FGR difficult to manage as the only treatment at present is fetal surveillance and optimal timing of delivery. The perinatal mortality remains high for this subgroup of FGR. Since the underlying pathophysiology seems to involve poor placental implantation and spiral artery abnormalities, this is the type that is amenable to antenatal prediction in the first trimester using the Fetal Medicine Foundation (FMF) algorithm.

The importance of picking up women at risk is the possibility of primary prevention of early preeclampsia (requiring delivery prior to 34 weeks) by giving 150 mg of aspirin to screen positive women – this strategy is proven to prevent 80% of early preeclampsia as well as preterm SGA.[4,5]

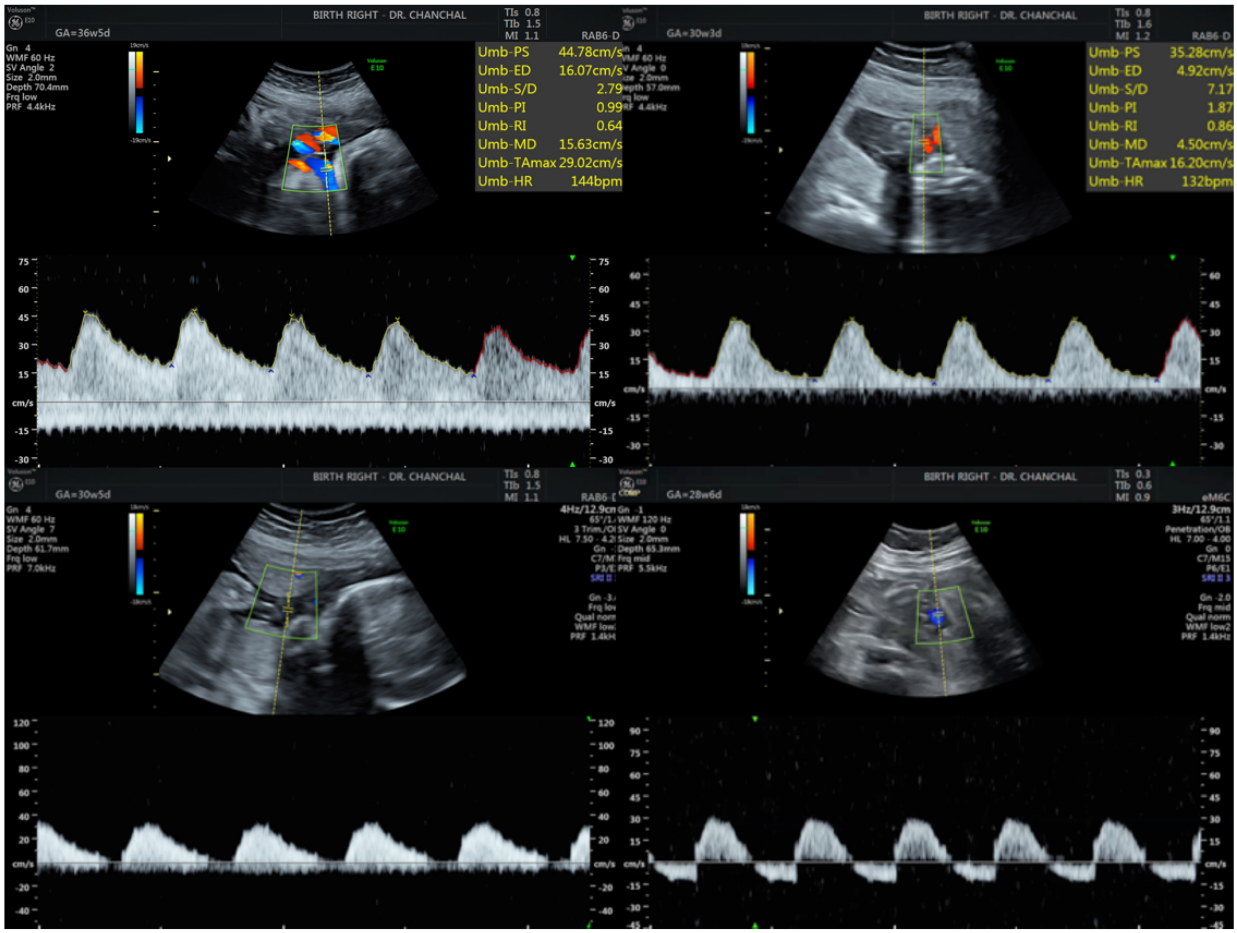

Figure 1: Typical deterioration in umbilical artery Doppler in early FGR (clockwise): normal waveform, increased PI, absent end diastolic flow (AEDF) followed by reversal in end diastolic flow (REDF).

Late fetal growth restriction

Late FGR accounts for 2/3rd of growth restricted foetuses and may be missed as all foetuses may not necessarily be small. In fact the main vessel which is abnormal in early FGR, ie, the umbilical artery waveform may be normal in majority of these foetuses. The main Doppler abnormality in late FGR is cerebral redistribution reflected by a cerebroplacental ratio (CPR) of less than the 5th centile for gestation. Hypertensive disorders are not frequent in this subtype.

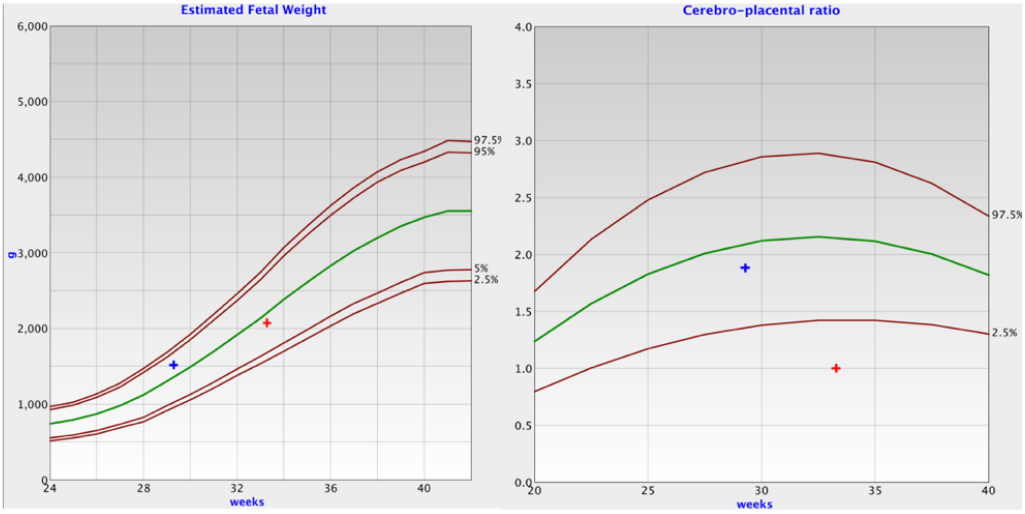

Figure 2: A fall in EFW by 2 quartiles or more than 50 percentile along with a cerebroplacental ratio (CPR) below 5th centile due to cerebral redistribution is typically seen in late FGR.

Management

There is no known treatment for fetal growth restriction at present. The results of the recent STRIDER trial did not show any benefit of Sildenafil either.[6] Thus, current management of fetal growth restriction remains optimizing the surveillance of these high-risk pregnancies and planning delivery at a gestation that provides the best trade-off between iatrogenic prematurity and intrauterine fetal demise. A proposed protocol for evaluation, frequency of surveillance and timing of delivery of 'small' foetuses is given in figure 1.[1,2] Since early and late FGR are two distinct clinical entities, management is discussed separately for each.

Early FGR

Once a diagnosis of early FGR is made, the patient should be managed in a tertiary care centre with maternal-fetal medicine specialists and NICU facilities. The Trial of Randomized Umbilical and Fetal Flow in Europe (TRUFFLE) trial randomised 503 women with early FGR defined as EFW < 10th centile and umbilical artery PI above 95th centile at 26 to 32 weeks' gestation to three arms that would trigger delivery: early DV changes (PI above 95th centile), late DV changes (absent or reversed a wave in DV) and reduced fetal heart rate short term variability (STV) on

82% of children had a normal neurodevelopmental outcome at 2 years – the primary outcome of the trial – which was better than previously reported.[8]

Surveillance

The usual modalities for fetal surveillance of a growth restricted foetus include daily kick count, biophysical profile that includes nonstress test (NST) and assessment of Dopplers. There is no consensus on whether one or all modalities should be used nor how frequently the monitoring should be done. Both would be guided by the gestation at which the diagnosis is made, severity of the condition and presence of maternal preeclampsia. Since cCTG may not be available universally, conventional CTG can be used; however the expected higher baseline fetal heart rate and lower variability of preterm foetuses must be taken into account while interpreting the CTG. 60% of recruited women in TRUFFLE had preeclampsia at study entry; this figure rose to 70% by delivery.[7] Thus, maternal surveillance by BP monitoring, urine protein:creatinine ratio and baseline liver and renal function test is recommended. Foetuses with high PI in umbilical artery with EDF present should be reviewed twice weekly. Foetuses with absent/ reversed EDF should be reviewed daily.

Timing of delivery

The TRUFFLE trial provided the best evidence to guide timing of delivery in early FGR. Foetuses with absent end diastolic flow (AEDF) in umbilical artery should be delivered by 32-34 weeks. Foetuses with reversed end diastolic flow (REDF) should be delivered by 30-32 weeks. Delivery prior to 30 weeks (and after viability) should be based on late ductus venosus (DV) changes. Conventional CTG may be used in place of cCTG as a safety net – however only persistent, repetitive decelerations on NST should be considered an indication for delivery. MCA PI and/or cerebroplacental ratio (CPR) should not be used to time iatrogenic preterm delivery in early FGR. Delivery can be done anytime for maternal indication.

Antenatal steroids

All available guidelines recommend a single course of corticosteroid prophylaxis to prevent neonatal respiratory distress syndrome if birth is anticipated prior to 34 weeks. The Royal College of Obstetricians and Gynecologists' (RCOG) recommends antenatal steroids can be considered upto 35 weeks and 6 days.[1] Since steroids are most effective when delivery occurs within a week after being given, the single course should be timed judiciously to maximise neonatal benefit.

As per Indian guidelines, 4 doses of Dexamethasone 6 mg, 6 hourly is the regime and drug of choice. Administration of steroids may cause a transient improvement in fetal blood flows but it should not affect management as the underlying pathology remains unchanged.

Neuroprotection

Magnesium sulphate for fetal neuroprotection should be given when preterm delivery is anticipated prior to 32 weeks' gestation.[9,10]

Mode of delivery

Fetal indications for elective Cesarean delivery in early FGR include abnormal venous Dopplers, absent or reversed EDF in umbilical artery, deranged biophysical profile and persistently abnormal CTG.[1,2]

Late FGR

As mentioned earlier, the main Doppler abnormality in late FGR is cerebral redistribution. Umbilical artery and ductus venosus are usually normal in these foetuses. Since these abnormalities may be subtle and foetuses near tern have a lower tolerance to hypoxemia, late FGR remains an important cause of unexpected stillbirth in late gestation.

Surveillance

The optimal frequency of ultrasound surveillance in late FGR is not known. Biophysical profile has a poor role in predicting stillbirth in late FGR and hence should not guide frequency of monitoring. In one study, the median interval between low MCA PI and stillbirth as less than 5 days and almost 90% of stillbirths occurred within one week of normal BPP.[12] Thus weekly to twice weekly Doppler surveillance after 34 weeks has been proposed.

Antenatal steroids and magnesium sulphate for neuroprotection

There is lack of consensus amongst various guidelines for giving steroids between 34-36 weeks' gestation though the ROG recommends steroid prophylaxis upto 35 weeks and 6 days. There is no role of magnesium sulphate for neuroprotection after 32 weeks.

Timing of delivery

There is lack of consensus amongst guidelines as to when to offer delivery in late FGR. The RCOG recommends that delivery should be 'offered' after 37 weeks in late FGR.[1] The recent ISUOG guidelines propose that women with late FGR and cerebral redistribution should be delivered at around 38 weeks and not later than 38 weeks and 6 days.[2]

If in addition, umbilical artery is above the 95th centile, delivery can be considered after 36 weeks and no later than 37 weeks and 6 days. Foetuses with birth weight below the 3rd centile have the highest risk of stillbirth, hence these pregnancies should not be allowed to continue beyond 37 weeks and 6 days irrespective of fetal Dopplers.

Mode of delivery

Induction of labour can be done depending on usual obstetric parameters. Continuous intrapartum CTG monitoring is recommended. These foetuses are at higher risk of requiring emergency LSCS for nonreassuring fetal heart rate trace.[2]

Conclusion

Fetal growth restriction should be strictly identified and categorised into early and late on the basis of the revised Delphi consensus. Considering the distinct pathophysiology and clinical phenotypes, management should be tailored to each type as outlined. Since there is no consensus on the modalities and frequency of surveillance, local protocols should be made.

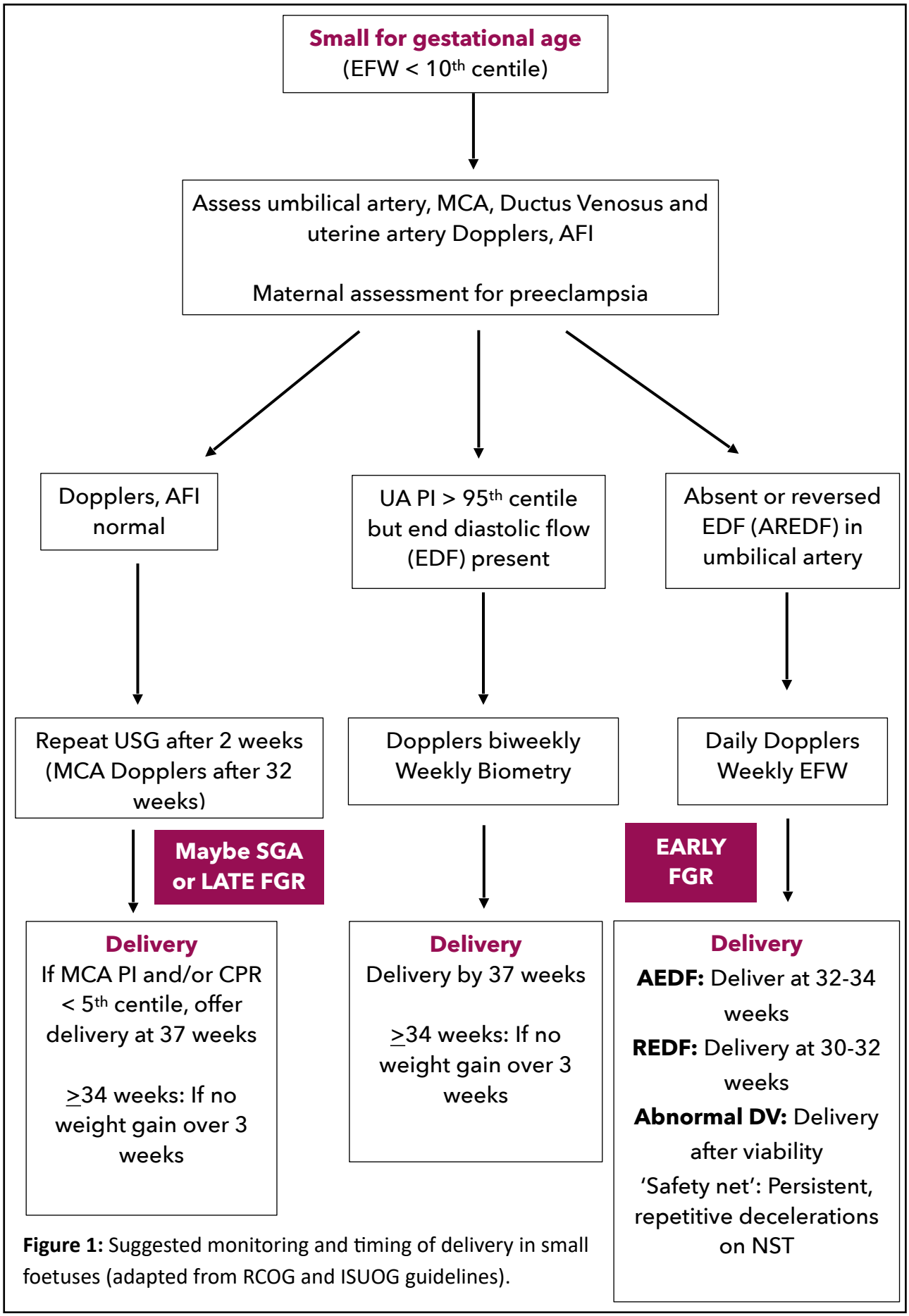

Figure 1: Suggested monitoring and timing of delivery in small foetuses (adapted from RCOG and ISUOG guidelines).

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Doppler in Fetal Growth Restriction: Basics

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Introduction

Doppler ultrasound [US] can be used to assess both fetal and placental circulation in pregnancies affected with fetal growth restriction [FGR].

The Doppler Effect

The Doppler effect is the change in the apparent frequency (or wavelength) of a wave when the observer is moving relative to the source of the waves. It is utilised in Doppler US to interrogate blood flow in vessels. The transducer emits continuous or pulses of US wave which is partly absorbed in tissues and partly reflected back towards the probe. The movement of blood towards or away from the probe results in a shift in frequency of the received signal.

To assess the velocity of blood flow in fetal and placental vessels, the Doppler frequency shift is used; that is, measuring a change in wave frequency that is proportional to the velocity of the blood cells. If the red blood cells are moving towards the beam, the reflected signal will be at a higher frequency than the transmitted wave. Conversely, if the red blood cells are flowing away from the reflected beam, the reflected signal will be at a lower frequency.

By transmitting a pulse of US and comparing the frequencies of received echoes after a chosen time delay, the Doppler shift frequency [and hence, velocity] as well as depth along the beam of the structure can be measured. The Doppler signals are displayed as a frequency spectrum and the technique is known as pulsed Doppler US. Signals from a particular vessel can be isolated and displayed in graphic form with the velocity plotted against time.

The most common index used to quantify umbilical artery [UA] Doppler blood flow velocity is the pulsatility index (PI) being the difference between peak systolic and end diastolic velocity divided by the mean velocity (PI = (Vmax - Vmin) / V mean). PI increases with increased placental resistance.

Factors Affecting the Doppler Indices

Gestational age- As the pregnancy advances there is decline in the impedance to feto-placental blood flow, therefore end-diastolic velocity (D) increases. This is reflected as decline in PI.

Fetal breathing movements and foetal body movements- Changes in intrathoracic pressure and central hemodynamics occuring during foetal breathing, and fetal body movements generated Doppler signals can interfere with the study of UA Doppler. Therefore, Doppler should be done during cycles of foetal apnoea and when the baby is not moving.

Location of the cord studied- The resistance is higher at fetal end of the UA as compared to the placental end. Therefore a mid-level free floating loop of cord is taken to assess the Dopplers. However, the clinical difference between PI at the two ends of the cord is not significant.

Angle of insonation- It is preferable to keep the angle of insonation as close to zero as possible while interrogating the vessel of interest. The angle of insonation affects the Doppler frequency shift and therefore the size of the waveform. The higher the angle, the smaller the waveform. In clinical practice the usage of ratios [RI, PI, S/D] eliminates these problems.

Wall filter setting- The wall filter removes signals generated by the vascular wall but a higher filter setting also removes low frequency UA flow signals during the end diastole. Therefore, the wall filter should be kept as low as achievable for the specific US device.

Which Indices To Use?

Arterial flow velocity waveforms are described in terms of three main indices: S/D ratio, RI and PI. Amongst these, while PI shows a linear correlation with vascular resistance, the S/D ratio and RI show a parabolic relationship with increasing vascular resistance. All the three waveforms are highly correlated and any one may be used for assessment. One advantage offered by PI and RI over S/D ratio is that in the former two instances, the value does not approach infinity with absent or reversed diastolic values. Currently, PI is the most commonly used index in clinical practice. For venous waveforms, pulsatility index for veins [PIV] is commonly used.

DOPPLER US OF MATERNAL VESSELS

Uterine Artery Doppler

It assesses the maternal component of placental blood flow and is a marker of remodelling of spiral arteries by trophoblastic cellular invasion.

In normal pregnancies, spiral artery remodeling results in a low-impedance circulation, which is reflected in the uterine arteries by the presence of high velocity and continuous for- ward flow in diastole. This pregnancy adaptation optimizes the intervillous placental blood flow and delivery of oxygen and nutrients to the foetus. Severe early-onset FGR is characterized by failure of trophoblastic invasion of the myometrial spiral arteries, resulting in reduced utero- placental perfusion. Abnormal uterine artery Doppler, defined as a PI greater than the 95th percentile for gestational age or the presence of a diastolic notch, has been associated with adverse pregnancy outcomes, including preeclampsia, FGR, and perinatal mortality.

Interpretation

In high-risk women, uterine artery Doppler has a moderate predictive value for a small-for-gestational-age neonate and is recommended for use in such situations.

In the first trimester, uterine artery Doppler can predict 81% of women with early-onset pre-eclampsia, 45% with late-onset pre-eclampsia and 50% with gestational hypertension, with a false positive rate of 10%. This detection rate increases to 96% for early pre-eclampsia and to 54% for all pre-eclampsia, with a false positive rate of 10% with the addition of biomarkers, mean arterial blood pressure and maternal history.

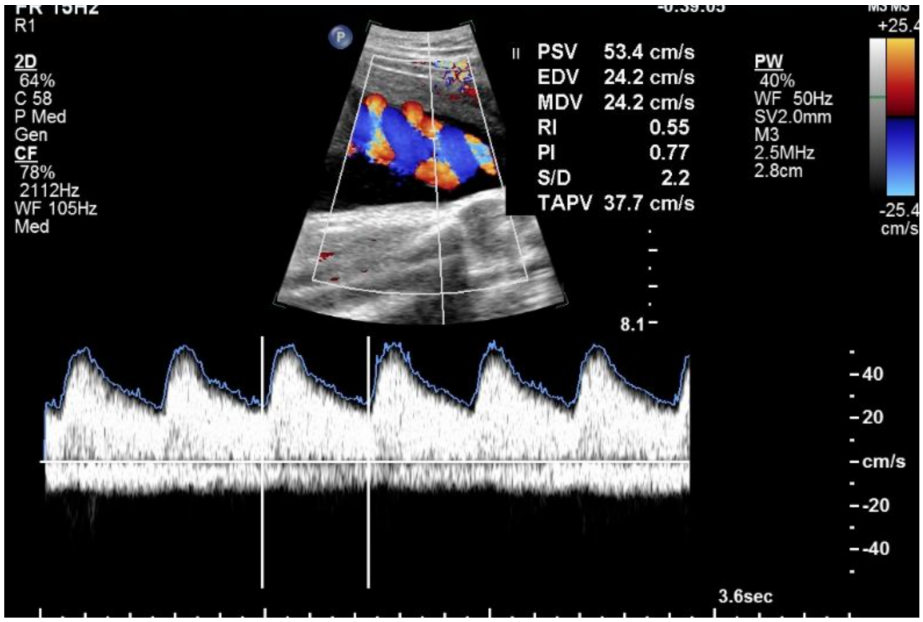
DOPPLER US OF FETAL VESSELS

Doppler investigation of fetal vessels including the aorta, ductus venosus [DV] and middle cerebral artery [MCA] can provide information about fetal wellbeing in the presence of FGR. With hypoxia, there is reduced resistance and increased diastolic flow (decreased PI) in the MCA, reduced or absent diastolic flow in the fetal aorta and, as a consequence of hypoxic myocardial insufficiency, increased pulsatility in the central veins supplying the heart such as the DV and inferior vena cava with absent or reversed late diastolic flow in the DV.

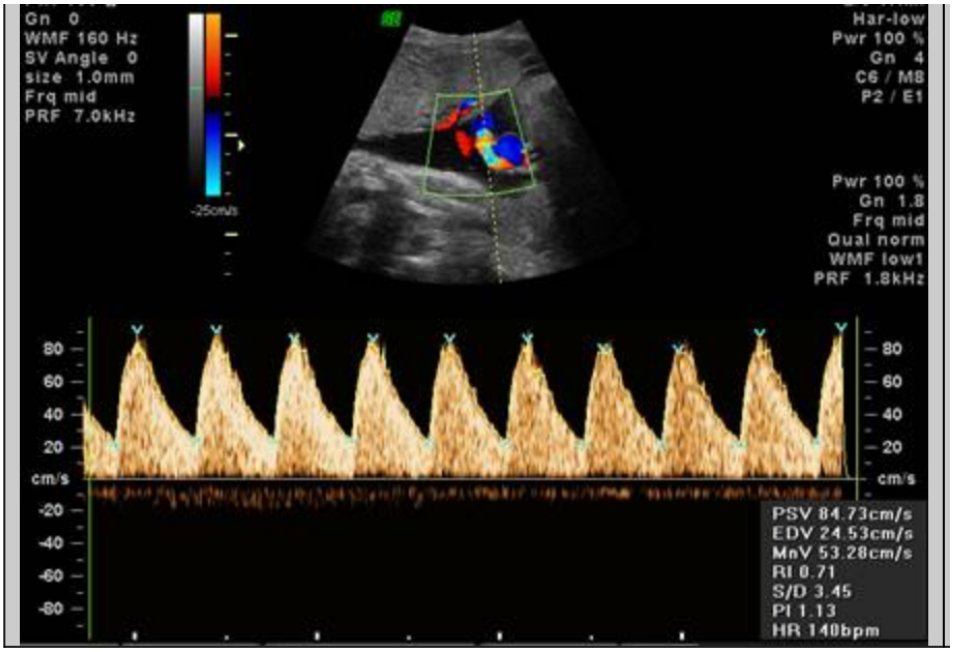
Umbilical artery [UA] Doppler

UA Doppler is an essential component of fetal surveillance in FGR. It has been shown to significantly reduce the risk of perinatal death, induction of labor, and cesarean delivery.

The UA Doppler assesses impedance to blood flow along the fetal component of the placental unit. As early as 14 weeks of gestation, low impedance of the fetal placental circulation permits continuous forward flow in the UA throughout the cardiac cycle.



NORMAL UMBILICAL ARTERY DOPPLER



INCREASED RESISTANCE IN UMBILICAL ARTERY

As placental resistance increases, UA Doppler waveform changes with an increase in PI corresponding to a progressive reduction in placental surface area available for gas and nutrient exchange and increased fetal afterload resistance. Maternal or placental conditions that obliterate small muscular arteries in the placental villi [e.g. hypertension, diabetes, thrombophilia and confined placental mosaicism] result in a progressive increase in placental resistance, visible as a decreased end-diastolic flow in UA waveform. Therefore, placental resistance to blood flow is an indirect measure of its function with increased resistance being found in FGR. An abnormal UA Doppler waveform is a predictor of fetal compromise and appears to be present 12 days preceding acute fetal deterioration.

Measurement

Doppler waveforms of the UA can be obtained from any segment along the umbilical cord. Waveforms obtained near the placental end of the cord reflect downstream impedance and show higher end-diastolic blood flow velocity than waveforms obtained near the fetal cord insertion. In general, this variation in UA Doppler end-diastolic flow along the umbilical cord is minimal and not significant enough to affect clinical decision-making. The waveforms should be obtained in the absence of fetal breathing movements which are visualised as episodic and irregular movements in between episodes of quiescence.

Interpretation

An abnormal UA Doppler waveform reflects the presence of placental insufficiency and can help differentiate FGR foetus from constitutionally SGA foetus. It is defined as a PI, RI, or S/D ratio greater than the 95th percentile for gestational age or an absent or reversed end-diastolic velocity (AEDV or REDV). AEDV/REDV in the UA reflects the presence of significant placental deterioration and is associated with high perinatal mortality. These findings may initially be intermittent, gradually progressing to become persistent.

Middle Cerebral Artery [MCA] Doppler

MCA is the largest vessel of the fetal cerebral circulation and carries about 80% of cerebral blood flow. The blood flow through MCA is measured by using PI or cerebroplacental ratio [CPR]. CPR is a ratio of MCA PI with UA PI. In hypoxemia associated with growth restriction there is redistribution of blood flow in the foetus, with increased flow to essential organs like brain, heart, liver and adrenals and vasoconstriction in other fetal vessels. Thus there is cerebral vasodilatation which results in reduced resistance and increased diastolic flow (decreased PI) in the MCA on Doppler studies. This is an early adaptive mechanism and is called the 'brain sparing effect'.

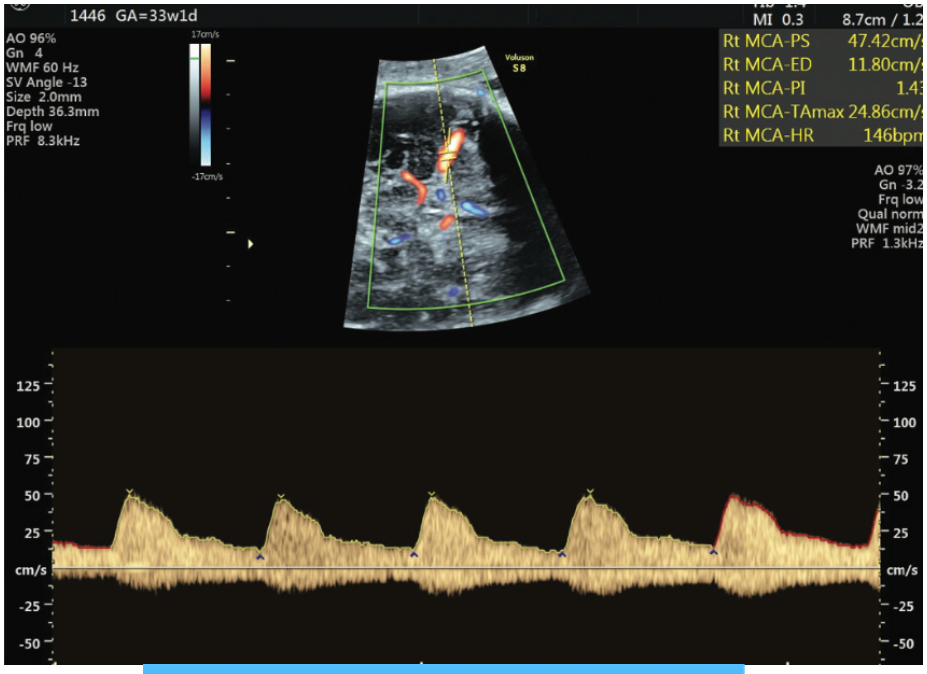
Measurement

An axial image of the fetal skull is obtained at the level of the sphenoid bone wings and thalami is taken and magnified. Color flow mapping is used to identify circle of Willis and the proximal MCA. A 2-mm pulsed wave Doppler gate is placed at the proximal third of the MCA, close to its origin in the internal carotid artery. The angle of insonation between US beam and MCA is kept as close to 0° as possible and care taken to avoid any unnecessary pressure on the fetal head. An average of three or more consecutive waveforms is taken and peak systolic velocity [PSV] calculated from the highest point of excursion of Doppler waveform. This is converted into multiple of the median [MoM]. An MCA PSV greater than 1.5 MoM is used to flag a foetus at risk for fetal anemia. MCA PSV is used instead of PI values as the former has been found to be a better predictor of perinatal mortality in FGR.

Interpretation

MCA PSV values are used to assess fetal anemia and determine need for intrauterine blood transfusion. It can predict the existence of moderate-to-severe fetal anaemia with a sensitivity of 100% and a false positive rate of 12%. The MCA Doppler is currently the main tool for surveillance for fetal anaemia in cases of red cell alloimmunisation disease. Presently, we do not have enough evidence to utilise the values

of MCA as a standalone in informing decisions about timing of delivery in FGR.



MCA DOPPLER

Cerebroplacental Ratio [CPR]

This is calculated by dividing the MCA PI by the UA PI. It has been investigated as a predictor of adverse pregnancy outcomes in FGR babies. The CPR represents the interaction of alterations in blood flow to the brain caused by increased diastolic flow due to hypoxia-induced cerebrovascular dilatation and increased placental resistance, resulting in decreased diastolic flow of the UA. It is therefore, used to assess fetal brain sparing. A foetus is considered to have brain sparing when this ratio is less than the fifth percentile for gestational age.

Ductus venosus [DV] Doppler

Blood flow in DV primarily reflects central venous pressure, indirectly measuring right ventricular end-diastolic pressure and cardiac muscle compliance. Doppler abnormalities of DV reflect an advanced stage of fetal compromise, central cardiac failure and are associated with increased perinatal morbidity and mortality.

The normal Doppler waveform is characteristically biphasic. The first peak is the highest and corresponds to ventricular systole (S wave). The second peak is the second highest and corresponds to early ventricular diastole (D wave), which is followed by a nadir in late diastole that corresponds to the atrial contraction (A wave).

In normal foetuses, flow in the venosus circulation is forward and uniform (toward the fetal heart) throughout the cardiac cycle. Decreased, absent, or reversed flow in the A wave may represent increased end-diastolic pressure from increased right ventricular afterload.

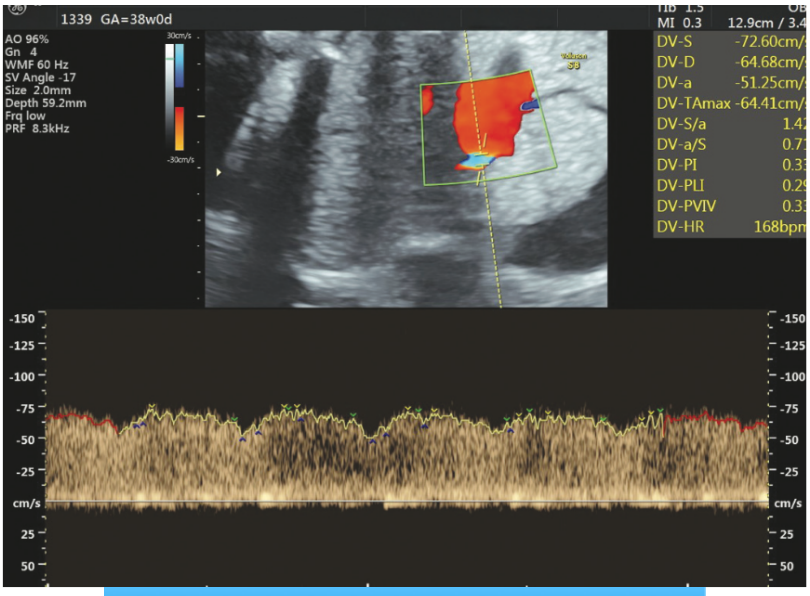
The reversal of a-wave in DV Doppler pattern signifies significant cardiac compromise. An absent or reversed DV A wave is a late finding and a sign of impending acidemia or death, usually within 7 days.

Abnormal DV correlates with reduced fetal heart rate variability on cardiotocogram and abnormalities in the fetal biophysical profile score. It is to be noted that Doppler abnormalities of DV in the setting of

possibly related to the presence of fetal cardiac, vascular, or genetic abnormalities, and thus are most often not reflective of significant placental disease.

Measurement

DV Doppler best obtained in sagittal plane from the anterior lower fetal abdomen. The velocities are relatively high, between 55 and 90 cm/s for most of the second half of pregnancy, but lower in early pregnancy.



DV DOPPLER

Interpretation

The DV Doppler is recommended for surveillance and timing of delivery of a preterm growth-restricted foetus with an abnormal UA Doppler, provided that the foetus is viable and steroids have been administered.

Suggested Reading:

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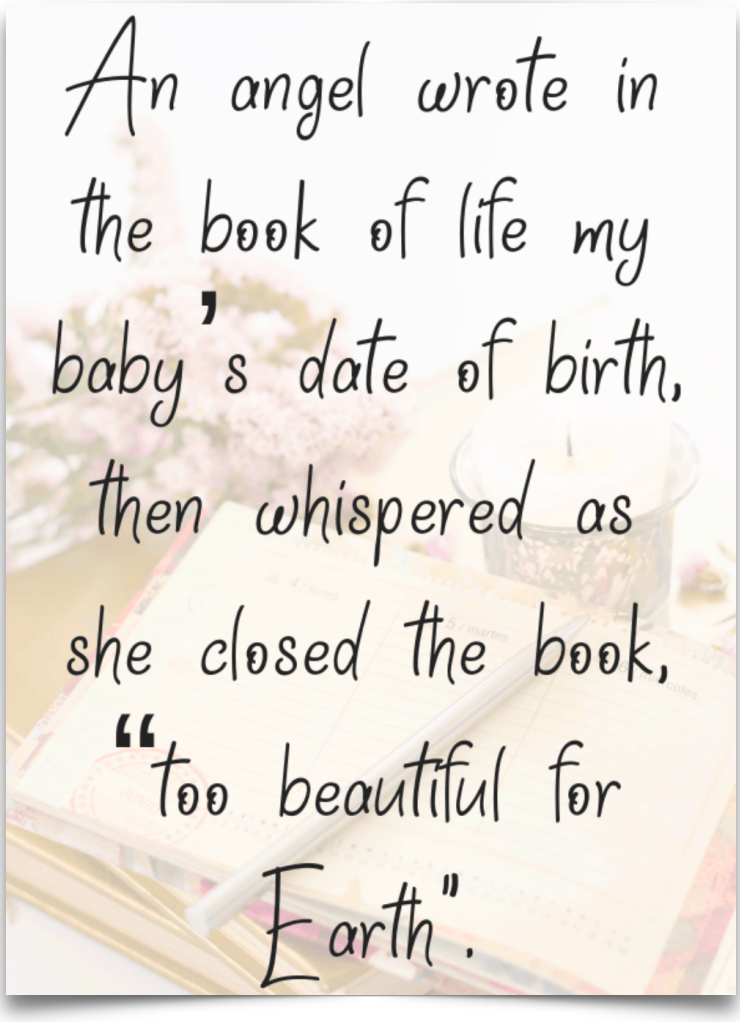

Fetal Growth Restriction in Multifetal Pregnancy: Overview

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Member, FGR Committee, SBSI

Introduction:

There has been an exponential rise in the incidence of multifetal pregnancies, especially attributed to the rise in usage of fertility therapies. The management of these pregnancies involves multidisciplinary care due to increased feto-maternal complications such as anaemia, pre-eclampsia, antepartum haemorrhage, malpresentation, preterm birth, discordant growth, twin-twin transfusion syndrome and twin reversed arterial perfusion.

Fetal growth restriction [FGR] complicates nearly 25-47% of twin as compared to 8% of singleton pregnancies. The risk of neonatal morbidity is seven times higher in growth restricted or discordant twins. Obstetricians are often confronted with the double challenge of balancing the risks of continuing a pregnancy risking intrauterine fetal death vis-a-vis a premature delivery and the associated risks.

Definition

The definition of selective FGR [sFGR] is inconsistent with international societies laying down different criteria for discordant growth. These range from 15-30% estimated difference between weight of the foetuses. [Table 1] *[Ref: Dagmara Filipecka Tyczka,2020]*

Discordant growth is calculated by the following formula:

[(EFW larger foetus – EFW smaller foetus) ÷ EFW larger foetus]* 100

Table 1- Definition of sFGR by Different Guidelines

Society	Date	Definition of sFGR	Growth charts	Other twins recommendation
NICE	2019	≥25% EFW discordance and EFW of one foetus <10th centile for GA	Undefined	
ACOG	2019	One foetus has EFW <10th centile and disproportion between EFW >20%	Undefined	
ISUOG	2016	One foetus has EFW <10th centile and the intertwin weight discordance >25%	Singleton	
RANZOG	2017	Undefined	Undefined	Recommendation about MC twins but without definitions of FGR
SOGC	2017	AC and/or EFW of one or both twins are <10th centile or when growth discordance is identified	Singleton	
ACR	2017	One foetus EFW <10th centile and the intertwin EFW discordance >25%	Singleton	
FIGO	2019	One foetus EFW <10th centile and the intertwin EFW discordance >25%	Twin	

AC, abdominal circumference; ACOG, American College of Gynecologists; ACR, American College of Radiology; DC, dichorionic; EFW, estimated foetal weight; GA, gestational age; FIGO, International Federation of Gynecology and Obstetrics; ISUOG, International Society of Ultrasound in Obstetrics and Gynecology; MC, monochorionic; NICE, National Institute for Health and Care Excellence; RANZOG, Royal Australian and New Zealand College of Obstetricians and Gynaecologists; SOGC, Society of Obstetricians and Gynaecologists of Canada. [Ref: Dagmara Filipecka Tyczka,2020]

The growth rate in third trimester is slower in multiple as compared to singleton pregnancy, being more prominent in monochorionic [MC] twins. Thus, one must exercise caution in labelling physiologically growth restricted babies from pathological ones. Stillbirth is higher in multiple as compared to singleton pregnancies. Therefore, one cannot solely rely on foetal size and better markers such as Doppler parameters should be used to distinguish growth restricted foetuses from small for gestational [SGA] babies. In an attempt to unify definition among societies for sFGR, an expert consensus was conducted using the Delphi procedure. [Table 2] *[Ref: Dagmara Filipecka Tyczka,2020]*

Table 2- sFGR Definition by Expert Consensus: a Delphi Procedure

EFW <3rd centile or

DC twins (2/3 criteria have to be present to recognise sFGR)	**MC twins** (2/4 criteria have to be present to recognise sFGR)
EFW of one foetus <10th centile	EFW of one foetus <10th centile
AC is not taken into account	AC of one foetus <10th centile
The disproportion between foetal weight ≥25%	The disproportion between foetal weight ≥25%
UAPI of smaller foetus >95th centile	UAPI of smaller foetus >95th centile

AC, abdominal circumference; DC, dichorionic; EFW, estimated foetal weight; MC, monochorionic; sFGR, selective FGR; UAPI, umbilical artery pulsatility index.

[Ref: Dagmara Filipecka Tyczka,2020]

Aetiology

The leading cause of sFGR is thought to be of placental origin.

- **DCDA twins-** placental insufficiency and other causes affecting singleton pregnancy like hypertension
- **MCDA twins-** discordance in placental sharing amongst the twins, total placental mass and interdependent feto-placental circulation.
- Intrauterine infections caused by TORCH group, Zika virus, parvovirus etc.
- Discordancy for chromosomal and congenital anomalies (higher in MC twins).

Screening of pregnancies in which sFGR is likely helps in counselling, timely intervention and treatment. In the first trimester crown rump length [CRL] discordance of 7% has a sensitivity of 92% and specificity of 76%. It is associated with higher rates of adverse pregnancy outcomes, preterm delivery and pregnancy loss. Isolated abnormal cord insertion has been found to be associated with sFGR although it remains a poor predictor for the same. In the second trimester, concordant growth at 21-24 weeks is more predictive of sFGR not developing later on and frequency of monitoring.

Follow-up in twins involves 4 weekly ultrasound from 24 weeks of gestation, Doppler evaluation and biophysical profile in case of suspected sFGR. Doppler classification is based on singleton pregnancy guidelines. *[Ref: Figueras]*

- **Type I –** PI of UA above 95th centile and positive end diastolic flow [EDF]OR cerebro-placental ratio [CPR] below 5th centile.
- **Type II –** absent EDF [AEDF]
- **Type III –** reverse EDF and or PI of ductus venosus [DV] above 95th centile.
- **Type IV –** reversed DV or abnormal CTG.

In MC twin, surveillance for sFGR begins from 16 weeks of gestation along with Doppler. Pregnancy outcome prognostication is done depending on severity of Doppler changes:

- **Type I -** positive EDF has good prognosis.
- **Type II -** absent/ reverse EDF [AREDF] has poor prognosis.
- **Type III -** intermittent AREDF (iAREDF) is unique for MC pregnancies. In a shared placenta, large-diameter anastomoses in shared placenta allow cyclical compensatory flow between foetuses making prognostication unreliable.

Management: *[Dagmara Filipecka Tyczka,2020; Townsend R, 2018)*

For DCDA with sFGR, management is similar to singleton pregnancy with an aim to continue pregnancy as long as it favours the appropriately growing co-twin. Foetal growth is monitored biweekly with Doppler monitoring advised biweekly or more frequently if required. Selective reduction maybe considered in growth retarded foetus of women with severe preeclampsia which may result in resolution of preeclampsia and permitting continuation of pregnancy for optimal outcome. Specific treatment of intrauterine infection should be done after amniocentesis to optimise outcome.

Suspected chromosomal or congenital anomaly in the growth restricted foetus requires detailed assessment for counselling, prognosis and management. In the event of intrauterine demise of one twin, the prognosis of the co-twin remains unaffected. Should the parents decide on foeticide, early decision is preferred to decrease the risk of preterm delivery.

In MC twins with sFGR, Doppler is done weekly or more frequently and fetal growth assessment done biweekly. Complications arise in case of demise of the affected twin as it is associated with a 15% risk of IUFD and 25% risk of neuro-developmental impairment of the surviving co-twin owing to acute feto-fetal transfusion.

Therefore in order to minimise complications, the ability to predict deterioration and IUFD and intervene accordingly is critical for managing these pregnancies. The umbilical artery [UA] Doppler findings do not prognosticate like singleton or DC twin pregnancies due to changes in vascular dynamics owing to placental anastomoses. Whereas, type I have good prognosis with regular monitoring and elective delivery at 34-36 weeks of gestation, problems arise in managing Type II and III. The other two require intervention and isolated UA Doppler has poor predictive value.

Management depends on the severity of sFGR, gestational age, DV Doppler, oligohydramnios, technical capabilities and parents' preferences and it may vary from expectant management, cord occlusion of smaller twin, selective laser photocoagulation of placental connecting vessels [SLPCV] or termination of pregnancy. After 26-28 weeks gestation, these procedures reduce the risk of preterm delivery. Selective reduction of smaller twin in these two types has an overall survival rate of 46.6% and survival of larger twin at 93.3%.

Whilst SLPCV is a standard treatment protocol for twin-twin transfusion syndrome [TTTS], in sFGR, the root cause may not be anastomotic connection and also more difficult to perform. It may hasten the process of IUFD of the smaller twin and increases the risk of preterm delivery, preterm prelabour rupture of membranes and chorioamnionitis.

Studies have found that it contributed to slightly higher rates of overall survival but the survival of larger twin decreased to 67.7-73.3% and rose for smaller twin to 30.4-38.7%. Type III sFGR with large arterio-arterial [AA] anastomoses are at maximum risk of feto-foetal transfusion causing neurological damage in surviving co-twin in a short while after IUFD of affected twin.

Post SLPCV in these twins resulted IUFD of smaller twin with improved prognosis of surviving larger twin. Table 3 elaborates the gestational age of delivery based on sFGR.

In case of IUFD of one twin, co-twin should be managed with MCA-PSV assessment. Conservative management in case of prematurity, ultrasound monitoring with Doppler and fetal neurosonography after 4-6 weeks to predict intracranial damage in surviving twin. In preterm, after corticosteroid coverage in uncomplicated cases, delivery at 34 weeks is recommended and immediate delivery in term pregnancies.

Table 3- Recommended GA at delivery in stable twins pregnancies complicated by sFGR according to Doppler assessment compared with FGR singleton pregnancies.

Chorionicity	sFGR Type I	sFGR TypeII	sFGR Type III	sFGR Type IV
DC	UAPI >95th centile CPR <5th centile	AEDF	REDF, DV PI >95th centile	DV a wave reversed
MC	I	II	III	
	UAPI >95th	AREDF	iAREDF	DV a wave reversed (it is not stage IV in MC)
Recommended GA at delivery (weeks)				
DC	34–36	30–32	30–32	>26 <26 expectant management or selective termination*
MC	34–36	30–32	30–32	>26 <26 SLPCV, selective termination (RFA, cord occlusion)
Singletons	37	34	30	26 <26 expectant management

Data reproduced from Figueras and Gratacós, Gratacós et al., ISUOG guideline and Khalil et al. AEDF, absent EDF; AREDF, absent/reverse EDF; DC, dichorionic; DV, ductus venosus; DV PI, ductus venosus pulsatility index; EDF, end-diastolic flow; FGR, foetal growth restriction; GA, gestational age; iAREDF, intermittent AREDF; MC, monochorionic; REDF, reverse EDF; sFGR, selective FGR; SLPCV, selective laser photocoagulation of placental connecting vessels; RFA, radiofrequency ablation; UAPI, umbilical artery pulsatility index.

**This is the UK-recommended treatment. In Poland, it is not legally possible to terminate a pregnancy or perform selective termination after the end of 22 weeks.*

*** [Ref: Dagmara Filipecka Tyczka,2020]*

Conclusion:

Multiple pregnancies with sFGR pose challenge in timing of delivery and optimising fetal outcome. It poses greater risk in MC pregnancy and one must aim at balancing the competing interests of the twins. Based on regular monitoring, the Doppler classification, laser interventions, corticosteroid therapy and individualising delivery optimal outcome can be achieved.

Suggested Reading

1. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins – Obstetrics and the Society for Maternal-Fetal Medicine. ACOG practice bulletin no. 204: fetal growth restriction. Obstet Gynecol. 2019;133(2):e97–109. doi: 10.1097/AOG.0000000000003070.
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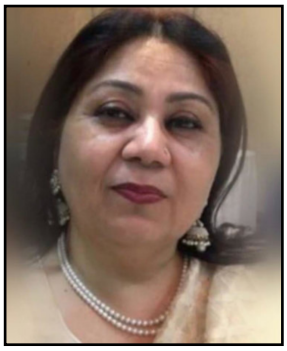
Secretary's Report



Tamkin Khan
Professor & Unit Head, ObGyn, JN Medical College, Aligarh
Founder Secretary, SBSI

The Chair, Dr Chanchal Singh and Secretary Dr Ayesha Ahmad of the SBSI Committee for Prevention of Stillbirths from FGR organised a webinar on 8th January 2022.

It was a very well planned session- the topics were very relevant to SBSI's mission. Dr Chanchal gave a very crisp, to the point introduction to the topic: Current Definition of FGR–the Delphi Consensus explaining the details in a very lucid manner.

The well organised webinar included eminent International speaker Professor Arjit Biswas Senior Consultant, Division of MFM, NUH and President, College of Obstetrics & Gynaecology Singapore. He talked on FGR and Dopplers–Preventing Stillbirths. Prof. Biswas had pulse on the audience , cleared the basics and then gave us food for thought - FRGP (Failure to reach Growth Potential) foetuses.

Professor Asma Khalil gave a talk on FGR in Twins–Newer Concepts. It was a treat to listen to a world renowned figure. It was a great initiation for further reading on sFGR in twins. The talks generated numerous questions which were moderated by Dr Ayesha Ahmad. We were honoured to have Professor Ashok Khurana, Director and Consultant, The Ultrasound Lab , New Delhi as the Chairperson for the session.

The Webinar was the most well-attended till date. SBSI is indeed fortunate to have Dr Chanchal Singh on the team.

Stillbirth Society of India

www.stillbirthindia.org

FGR Committee Webinar

Date: 8th January 2022
Time: 06:30 pm - 08:00 pm

Chair of Committee : Dr Chanchal Singh
Secretary of Committee : Dr Ayesha Ahmad

International Speakers

Prof. Arijit Biswas
Senior Consultant, Division of MFM, NUH
President, College of Obstetrics & Gynaecology Singapore

Prof. Asma Khalil
Professor
St George's Medical School
University of London

Chairperson

Prof. Ashok Khurana
Director, Senior Fetustician and Consultant The Ultrasound Lab
New Delhi

Programme

1. Welcome: Dr Neelam Aggarwal	6.30-6.32 pm
2. Introduction to FGR Committee: Dr Tamkin Khan	6.32-6.35 pm
3. Current definition of FGR- The Delphi Consensus: Dr Chanchal singh	6.35-6.45 pm
4. Introduction to International expert: Dr Nuzhat Aziz	6.45-6.50 pm
5. FGR & Dopplers-Preventing Stillbirths: Dr Arijit Biswas	6.50-7.15 pm
6. Q & A: Dr Ayesha Ahmad	7.15-7.25 pm
7. Introduction to International expert: Dr Nuzhat Aziz	7.25- 7.30 pm
8. FGR in Twins—Newer Concepts: Dr Asma Khalil	7.30-7.50 pm
9. Q & A: Dr Ayesha Ahmad	7.50-8.00 pm

Dr Neelam Agarwal
President
SBSI, India

Dr Nuzhat Aziz
Vice President
SBSI, India

Dr Tamkin Khan
Secretary
SBSI, India

Dr Asna Ashraf
Joint Secretary,
SBSI, India

Dr Ayesha Ahmad
Joint Secretary,
SBSI, India

Dr Neetika Garg
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BirthRight by Rainbow Children's Hospital, New Delhi
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JNMCH, AMU, Aligarh
Member

January 2022

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26	27	28	29	30	31	1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
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23	24	25	26	27	28	29
30	31	1	2	3	4	5

Webinar by Committee for Study of Stillbirths from Rh-sensitisation