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Ultrasound evaluation of multiple gestation anomalies

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Background

Through advances in ultrasound technology we have been able to better understand and document the physiology of normal and abnormal multiple pregnancy. Twin to twin transfusion syndrome was once a diagnosis made at delivery and hence was more of interest to paediatricians. Fetal medicine specialists and obstetricians have a window to in-utero events so that now TTTS is an ultrasound-based diagnosis. Multiple pregnancies account for a disproportionate share of major adverse perinatal outcomes. In addition to the increased rates of perinatal mortality and morbidity attributed to preterm delivery, multiple pregnancies are also at higher risk of miscarriage, fetal abnormality, stillbirth, fetal growth restriction, delivery complications and neurodevelopmental impairment. The rates of multiple pregnancy vary worldwide with dizygous twinning and high order multiple rates affected by maternal age, parity, ethnicity and the use of assisted reproductive techniques. The incidence of monozygous twinning is relatively constant. In developed countries, multiple gestation rates have increased over the last 40 years and account for up to 2% of all births.

Zygosity, chorionicity and amnionicity

Zygosity describes the number of separate fertilised ova. Chorionicity refers to the number of chorions which corresponds to the number of placentae. Amnionicity refers to the number of amniotic sacs. Multiple pregnancies are normally classified by the number of placentas and the number of amniotic sacs. A multiple pregnancy may arise through the fertilization of : more than one oocyte (multizygotic) or from the spontaneous splitting of a single zygote (monozygotic). One third of twins are monozygotic and two-thirds are dizygotic. Higher order multiples usually arise from multiple ovum but very rarely can arise from zygotic splitting and then re-splitting. If Multizygotic or monozygotic division occurs before implantation they will have separate placentas (i.e., dichorionic) and separate amniotic cavities.If the division occurs after implantation then they will share the placenta (i.e., monochorionic) and either share the amniotic cavity (i.e., monoamniotic) or have their own (i.e., diamniotic). The

majority of monozygotic twins will be monochorionic-diamniotic (MCDA). Some monozygotic twins (approx 1 in 7) will have separate placentae and be dichorionic-diamniotic (DCDA). Hence, in same sex dichorionic-diamniotic twins. zygosity cannot be determined without DNA testing. Chorionicity and amnionicity can be accurately established in the first trimester using ultrasound. It is important to establish chorionicity to enable the risk stratification of a multiple pregnany.

Monoamniotic pregnancies

Approximately 1% of twins, on ultrasound when there is a single placenta, two fetuses and no inter-twin dividing membrane. Umbilical cord entanglement is a major complication.The majority of fetal deaths in monoamniotic twins are due to cord entanglement. The risk of fetal death increases by 2-5% every week from 15 weeks gestation and totals 30-40% by 30 weeks gestation.

Twin-to-twin transfusion syndrome(TTTS)

TTTS is the major complication of MC pregnancies where twins share a single placenta.

It is characterised by the development of polyhydramnios in one twin sac, whilst the other develops oligohydramnios. Untreated, the polyhydramnios usually results in premature delivery and the loss of both twins.

Pathophysiology

MC twins have a shared placenta and have anastomoses on the surface that join the two twin's circulations. These anastomotic patterns are generally balanced, but in about 10-15% of MC there is an unbalanced transfusion of blood from one twin to the other resulting in the development of TTTS .The donor twin loses its blood volume and decreases its urine output which results in the development of oligohydramnios. The recipient twin increases its urine production resulting in the development of polyhydramnios . TTTS is diagnosed on ultrasound when the deepest pocket of amniotic fluid around the donor twin is $\leq$2 cm and the deepest pocket around the recipient is $\geq$8 cm. There can be abnormalities in fetal Doppler flow patterns with absent or reversed flow in the umbilical arteries. In the more severe form of TTTS : hydrops can develop in the recipient with cardiomegaly, ascites, oedema and abnormal Doppler flow patterns

in the ductusvenosus TTTS is the commonest cause of increased mortality and morbidity in MC twin pregnancies. Untreated, TTTS will result in up to 80% perinatal mortality, with major risk of preterm delivery and long term morbidity in survivors

Associated complications

1. Fetal growth restriction (FGR) can occur in up to 20% of twins with TTTS , but FGR or fetal size discordance is not part of the diagnosis nor Staging criteria for TTTS. 2. Brain injuries can be detected in severe cases, with ventriculomegaly at the time of presentation occasionally being seen. 3. Death of one MC twin in utero may occur with TTTS. If this occurs prior to intervention, the loss of one twin may result in an acute transfusion from one twin to the other, 1/2 of these transfusions will be minor with survival of the co-twin., ½ will have a major transfusion : leading to either loss of the co-twin (about 25%). in the remaining 25% the twin survives but with significant long term neurodevelopmental disability.

Management

Pregnancies with TTTS managed conservatively have a very poor outcome, apart from mild (stage 1) TTTS, when the condition may stabilise and resolve. Serial amnioreduction of the polyhydramniotic sac has been used but is associated with poorer short and long term outcomes in comparison to fetoscopic laser ablation which is now the treatment of choice. .Fetoscopic laser ablation of the placental communicating vessels interrupts the TTTS process and allows the twins to recover, with urine production recommencing in the donor twin and both the oligo- and polyhydramnios normalising after the procedure. Laser ablation may be performed from 16 weeks gestation up until 28 weeks. In cases of hydrops : the cardiac failure generally resolves over the course of a few weeks following laser ablation. Long term cardiac function normalises although there are cases of pulmonary stenosis described. Once fetal laser ablation is performed and the TTTSprocess resolves, the twins may progress normally. However, there is still the risk of intrauterine growth restriction (if there is unequal placental sharing). There is also the risk that neurological damage may have occurred either before or about the time of surgery and so close surveillance of the brain of both twins is indicated and fetal magnetic resonance imaging (MRI) may be considered. If the recipient was hydropic, assessment of the fetal heart of the recipient is indicated post-delivery. Laser ablation is not an indication, for delivery by Caesarean

section. However, there needs to be close monitoring and management as for other multiple pregnancies.

Selective fetal growth restriction(sFGR)

sFGR complicates 10-15% of MC pregnancies. The underlying cause of sFGR is unequal placental sharing . often associated with a velamentous cord insertion. Three different types on the basis of the umbilical artery Doppler waveforms: type 1 - normal umbilical artery Doppler waveform. type 2 - persistent absent or reversed end-diastolic flow. type 3 - intermittent absent or reversed end-diastolic flow. In most cases these Doppler types do not change once the diagnosis is established. Type 1 is associated with a good prognosis. Type 2 is associated with a greater risk of fetal death (30-40%) of the smaller twin and the mean gestation at delivery is 30 weeks. For type 2, the overall risk of neurological injury for survivors (either small or normal size) is 15%. Type 3 is associated with a risk of unexpected fetal death of the smaller twin of 10-20% and there is an increased risk of neurological injury for the normally grown twin (10-20%).The mainstay of management of sFGR in MC twins is appropriately timed delivery balancing the risks of fetal death and its co-twin consequences with the risks of prematurity if delivered. Ultrasound assessment and monitoring of twin pregnancies with sFGR should be undertaken in tertiary facilities with appropriate multidisciplinary support.

Twin anaemia-polycythaemia sequence (TAPs)

TAPs is characterised by large inter-twin haemoglobin differences in the absence of amniotic fluid discordance. TAPs may occur spontaneously in up to 5% of MC twins and in 2-13% of cases of TTTS treated by laser photocoagulation The underlying cause of TAPs is the presence of small arteriovenous vascular anastomoses which allow a slow transfusion of blood over time from the donor to the recipient twin. The antenatal diagnosis of TAPs is based on discordant Doppler ultrasound velocities of the middle cerebral artery (MCA) flows in each twin.For timely diagnosis of TAPs ,routine middle cerebral artery Doppler ultrasound surveillance is recommended in all MC twins, and in particular in those following laser surgery for TTTS. Postnatal diagnosis of TAPs is based on a haemoglobin discordance between twins (<11 g/dl in the anaemic twin and >20 g/dl in the polycythaemic twin). Reports on the management and perinatal outcome in TAPs are limited. The incidence of neurodevelopmental

impairment is unknown. Treatment options for TAPs include : expectant management, intrauterine transfusion, delivery, fetoscopic laser surgery or selective fetocide via an occlusive cord procedure.

Discordant fetal abnormality.

Multiple pregnancy is associated with an increased incidence of structural and chromosomal abnormalities compared to singleton pregnancies (although in dizygotic twins the rate of abnormalities is not increased per twin). Anomaly rates are higher in monozygotic twins compared with dizygotic twins. Discordant fetal abnormality increases the likelihood of an adverse outcome for the normal co-twin. Detection rates of fetal abnormalities in twins are similar to those reported in singleton pregnancies.

Twin reversed arterial perfusion sequence (TRAPs) Twin reversed arterial perfusion sequence (TRAPs)

TRAPs, or acardiac twinning, occurs in 1% of MC pregnancies. The acardiac twin is haemodynamically dependent on the co-twin which is designated as the 'pump twin'. The growth of the acardiac twin threatens the pump twin exposing it to the risk of cardiac failure, polyhydramnios, ruptured membranes, preterm delivery, hydrops and death. Perinatal mortality rates for the pump twin of 35-55% have been reported. The acardiac twin is usually severely malformed to the extent that it may not resemble a fetus. Management strategies for TRAPs include expectant observation with planned; preterm delivery, termination and surgical interventions aimed at inteAdverse neurological outcomes have been reported in the surviving twins of pregnancies with TRAPs but the true risk of this outcome has not been defined. Further studies are needed to define optimal management strategies to reduce perinatal mortality and morbidity in the pump twin. Interrupting the blood flow to the acardiac twin.

Single twin death

The death of one of the twins occurs in up to 6.2% of all twin pregnancies. Risks to the co-twin include :fetal death, preterm delivery and neurodevelopmental impairment .outcome influenced by the underlying cause and gestational age at delivery. Causes of single fetal death in a multiple pregnancy include:The surviving co-twin is potentially at risk from the same condition

that led to the death of the other twin. The main features that affect outcome are the chorionicity and the timing of fetal death. MC pregnancies are at greater risk due to shared placental vessels. Following the death of one twin : the risk of death to the co-twin is 12% in MC and 4% in DC pregnancies. First trimester loss does not usually impact on the surviving co-twin. Fetal loss in the 2nd and 3rd trimester can cause preterm delivery in both DC and MC pregnancies. Management of the surviving co-twin following single twin demise depends upon the gestation and the chorionicity of the pregnancy: In MC , conservative management to 34 weeks to avoid additional risks of prematurity. Doppler ultrasound assessment of the MCA velocity to examine for fetal anaemia in the surviving twin should be done as soon as possible after the death of a twin is noted. Fetal brain MRI should be considered following single twin death in MC twins with an interval of at least three weeks from the event. In DC , with single twin death, delivery is not indicated to term unless indicated for obstetric reasons.

Conjoined twins

Conjoined twins are a rare complication of multiple pregnancy. The classification of conjoined twins is typically based on the description of the fused anatomical region (e.g., craniopagus twins are joined at the head).

Conjoined twins can be reliably diagnosed on routine antenatal ultrasound in the late first and early second trimester. Fetal MRI can also be used to more precisely determine the extent of fusion and to assist with counselling of the parents about prognosis. Survival after birth is difficult to predict antenatally and each set of conjoined twins is unique.

Preterm birth and multiple pregnancy

The association between multiple pregnancy and spontaneous preterm birth is well established. Preterm birth in multiple pregnancy may also may result from obstetric intervention for maternal medical reasons. About 60% of twin pregnancies deliver <37 weeks gestation and 10% deliver before 32 weeks. The rate of preterm delivery in triplet and higher order multiples is almost 100%. The neonatal mortality rate of twins is 6-7 times that of singletons at 18 per 1000 live births. For triplets and higher order multiples the neonatal mortality rate reaches 40 per 1000 births. More than 50% of neonatal deaths among multiple births are attributable to prematurity.

Fetal growth restriction and multiple pregnancy

Fetal growth discordance of at least 20% affects approximately 16% of all twin pregnancies. Discordance is defined as using the larger twin as the standard of growth. Due to lack of international consensus the range of 15-25% difference in weight between the twins is considered significant and associated with an increased risk of morbidity and mortality

Antenatal management

Early ultrasound assessment to establish chorionicity is essential for the management of multiple pregnancy so as to permit identification and treatment of certain complications. First trimester NT assessment can be used for aneuploidy risk assessment in multiple pregnancies. Discordant NT in MC twins can predict an increased risk of TTTS. First trimester serum markers can be combined with NT assessment in DC twins but they do not improve screening performance in MC twins. Detailed morphology ultrasound is recommended at 20 weeks gestation. Ultrasound surveillance of MC twins every 2 weeks from 16 gestation is recommended for early recognition of TTTS. Regular fetal growth assessment every 4 weeks from 24 weeks gestation is recommended in both MC and DC twins. Cervical length as measured by TV shows a correlation with risk of preterm birth with the shorter the cervix, the higher the risk. The clinical usefulness of cervical length assessment however is predominantly associated with its negative predictive value so as to avoid unnecessary hospitalisation and intervention. There are no proven treatments to prevent preterm delivery in multiple pregnancy. Randomised trials showing antenatal progesterone therapy may prevent preterm birth in singleton pregnancies have not demonstrated similar benefits in multiple pregnancies. Cervical cerclage for cervical shortening has also been found to have no beneficial effect on rates of preterm birth in multiple pregnancy. The type and frequency of fetal monitoring in monoamniotic twins remains controversial with cardiotocography and ultrasound imaging used variably.

Labour and delivery

Consideration of early delivery in multiple pregnancies occurs commonly because one or more of the fetuses may be at risk if they remain in utero. Usually the options to be considered are either do nothing (i.e., continue the pregnancy), or deliver early: Each option should be