Sustainable Practices on Aquaculture 1

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Content

CHAPTER I

Approach To Multiple Gestations

Dilara DUYGULU BULAN[1]

1.İntroduction

Multiple pregnancies, which account for approximately 1-3% of all pregnancies, are an obstetric condition that requires special attention due to their significant impact on both the mother and the fetus. The frequency of multiple pregnancies has increased significantly in recent years with the increasing use of assisted reproductive technologies. Compared to singleton pregnancies, multiple pregnancies have a higher complication rate. In multiple pregnancies, the risk of premature birth before 37 weeks of gestation is around 60%, a situation that is responsible for a large proportion of perinatal mortality, neonatal morbidity and long-term morbidity. (Tucker & McGuire, 2004) In addition, fetal growth retardation and congenital anomalies contribute to the poor outcomes. Specific

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complications unique to multiple pregnancies, such as abnormal placental anastomoses in monochorionic twins, twin-to-twin transfusion syndrome (TTTS), twin anemia polycythemia sequence (TAPS), and selective fetal growth restriction, pose additional risks to these pregnancies. This book aims to comprehensively cover the obstetric management, clinical diagnostic methods, complications and treatment options in twin pregnancies. A thorough examination of the subject will improve understanding of the risks associated with twin pregnancies and guide healthcare professionals in the management of the pregnancy process.

2.Epidemiology

Spontaneous pregnancies account for 70% of dichorionic twin pregnancies and 30% of monochorionic twin pregnancies, while the majority of multiple pregnancies resulting from assisted reproductive technologies (ART) are dichorionic. The prevalence of monozygotic twins is not influenced by patient-specific factors. However, ART has led to a significant increase in monochorionic pregnancies, although the mechanism behind this increase remains unclear. Monochorionic monoamniotic pregnancies are extremely rare and account for less than 1% of all pregnancies. (Paladini & Volpe, 2024) Factors influencing the prevalence of dizygotic twins include assisted reproductive techniques, maternal age, geographic region/race, parity, family history, nutrition, maternal weight and height. In the United States, before the widespread use of ART in 1980, the rate of twin births was 1 in 53 births. However, in 2019-2021, this rate dropped to 1 in 32 births due to strategies to reduce the number of embryos transferred.(Osterman vd., 2023) Maternal age is an important factor influencing the prevalence of multiple pregnancies. The incidence of dizygotic twins increases significantly with advanced maternal age.

After the age of 35, increased levels of follicle stimulating hormone (FSH) lead to multiple ovulation of the egg cells and thus increase the probability of dizygotic twin pregnancies. In addition, the use of ART increases the risk of multiple pregnancies in women over 35. The risk of dizygotic twin births is higher in obese (body mass index [BMI] ≥30 kg/m²) and tall women.(Reddy vd., 2005)

3.Embryology

Dizygotic twins result from the fertilization of two separate ovum by separate sperm, either spontaneously or with the help of reproductive technologies. Each fertilized ovum develops into its own chorion, amnion and embryo. Dichorionic twins can result from either dizygotic (fertilization of two separate ovum) or monozygotic (a single fertilized ovum divides into two embryos) pregnancies. In these pregnancies, each embryo forms its own chorion and its own amniotic sac. Monochorionic twins share a single chorion and generally develop from a single fertilized ovum (monozygotic). Monochorionic twins can develop in different ways depending on when the embryo divides after fertilization. If the inner cell mass divides between the 4th and 8th day of development, monochorionic diamniotic twin formation occurs, in which both embryos share a single chorion but develop in separate amniotic sacs. In monochorionic monoamniotic twins, the embryo divides after day 8 so that both embryos develop in the same chorion and in the same amniotic sac. Siamese twins occur when the embryo divides later, usually after day 13, and incomplete division results in the embryos remaining physically connected.(Woodward vd., 2021)

4.Determination of chorionicity and amnionicity in twin pregnancies

Chorionicity and amnionicity are decisive parameters in the diagnosis and treatment of multiple pregnancies. High perinatal morbidity and mortality are strongly associated with preterm births, which are related to chorionicity. Accurate determination of these parameters plays an important role in monitoring the pregnancy and preventing complications. The optimal time to determine chorionicity is in the first trimester.(Emery vd., 2015)

Transvaginal ultrasound (TVUS) is often used due to its high resolution. First, the number of chorions is determined, followed by the identification of amniotic sacs and embryos.

The presence of two separate placentas is a reliable indicator of dichorionic twins, which is particularly useful in early pregnancy as separate placentas may appear fused later. In very early stages, yolk sacs can sometimes be counted instead of amniotic sacs, but this should be rechecked as the pregnancy progresses. In monochorionic monoamniotic pregnancies, the absence of the membrane between the twins is an important diagnostic feature. At the beginning of the pregnancy, the membrane may not be recognizable, which can lead to a misdiagnosis of a monoamniotic pregnancy. In such cases, the number of yolk sacs can be helpful, as monochorionic monoamniotic twins usually only have one yolk sac. The "twin peak" or "lambda (λ)" sign" is an important finding in the diagnosis of dichorionic diamniotic pregnancies. This sign represents a triangular protrusion of tissue between the layers of the fused dichorionic placenta.(Wood vd., 1996) This sign is best seen between the 10th and 14th week of pregnancy, but becomes less obvious after the 20th week. The "T" sign is seen in monochorionic diamniotic pregnancies, where the membrane formed by two amniotic layers emerges from the placenta

at a 90° angle. Fetal sex differentiation, typically performed in the second trimester, can help confirm the chorionicity of multiple pregnancies.

5.The role of Doppler in multiple pregnancies

Doppler ultrasound is an important tool in the management of multiple pregnancies. It is particularly valuable in high-risk pregnancies, such as monochorionic twins, for early detection and treatment of complications. Color Doppler is used to determine the location of the placental insertion. Marginal or velamentous cord insertion increases the risk of growth restriction and may indicate an uneven distribution of the placenta, especially in monochorionic pregnancies. Color Doppler is also the most effective method for detecting vasa previa. In the second and third trimester, Doppler ultrasound is used to examine the umbilical artery (UA) and middle cerebral artery (MCA) to detect complications such as TAPS and TTTS.(Mulcahy & McAuliffe, 2022)

6.Labeling of twin fetuses

The position of the fetuses may change over the course of the pregnancy, but accurately tracking the growth of each fetus is critical for early diagnosis and management of complications. Therefore, a consistent labeling strategy should be used. The most common strategy is labeling based on fetal position (right, left; top, bottom).

In the first trimester, labeling can also be based on the position of the umbilical cord. The designated fetal positions should be clearly documented in the pregnancy record.(National Collaborating Centre for Women's and Children's Health (UK), 2011a) To avoid confusion, each fetus should ideally be identified with as many features as possible. The phenomenon of fetal displacement, where fetuses move or change position during the course of pregnancy, is

common in multiple pregnancies, especially monoamniotic twins.(Khalil vd., 2016) This can pose a challenge for accurate labeling and tracking during diagnostic procedures such as chorionic villus sampling (CVS). Correct labeling is crucial to avoid confusion during procedures such as selective reduction.

7.Sonographic Diagnostic Evaluation

In multiple pregnancies, the gestational age should ideally be determined when the crown-rump distance (CRL) measurement is between 45 and 84 mm. In spontaneous pregnancies, the greater of the two CRLs should be used to estimate gestational age.(Khalil vd., 2016) For uncomplicated dichorionic twin pregnancies, a detailed anatomical examination should be performed in the second trimester after the first trimester ultrasound. Monitoring should be carried out every four weeks. However, in complicated cases, the monitoring frequency should be adapted to the maternal and fetal condition and the severity of the situation. For uncomplicated monochorionic twins, an ultrasound examination should be performed every two weeks from the 16th week. Frequent monitoring helps to prevent delayed diagnosis of TTTS and TAPS. Fetal biometry, amniotic fluid volume and umbilical artery Doppler measurements should be assessed at every ultrasound scan from 20 weeks onwards. In monochorionic pregnancies, measurement of the peak systolic velocity of the middle cerebral artery (PSV) for TAPS screening should be performed at 20 weeks. In monochorionic diamniotic pregnancies, amniotic fluid volume should be assessed at every ultrasound scan to detect early signs of TTTS. In order to assess the risk of a premature birth, the length of the cervix should also be measured during the second trimester ultrasound.(Khalil vd., 2016)

Screening for chromosomal abnormalities

In twin pregnancy, trisomy 21 screening can be done in the first trimester using the combined test, which includes maternal age, NT measurement, and serum β-hCG and PAPP-A levels. Alternatively, maternal age and NT measured between 11+0 and 13+6 weeks can be used for risk assessment.

In monochorionic pregnancies, the risk calculations are performed per pregnancy, whereas in dichorionic pregnancies, a separate risk assessment is performed for each fetus. However, the accuracy of these tests in twin pregnancies may be lower for twin pregnancies than for singleton pregnancies, and the results should be evaluated separately for each fetus. (National Collaborating Centre for Women's and Children's Health (UK), 2011b) In the case of a vanished twin, if a measurable fetal pole remains, β-hCG and PAPP-A levels may be inaccurate, and therefore, NT should be used alone for risk assessment.

Non-invasive prenatal testing (cfDNA), which analyzes fetal genetic material from maternal blood samples, can also be used to detect chromosomal abnormalities. Cell-free DNA (cfDNA) testing of maternal blood for assessing the risk of fetal trisomy 21 is becoming increasingly common in clinical practice. It offers advantages over the combined test due to its higher detection rate (DR) and lower false positive rate (FPR). However, as each fetus in a twin pregnancy may have different genetic material, interpreting and ensuring the accuracy of the test is more complex than in singleton pregnancies.(Hui, 2013)

8.Maternal Complications

In twin pregnancies, maternal complications are more frequent and often more severe compared to singleton pregnancies. These

complications can occur both during pregnancy and in the postpartum period, and may significantly affect maternal health. Common maternal complications in twin pregnancies include preeclampsia, postpartum hemorrhage, maternal death, placenta accreta spectrum, and hypertensive disorders of pregnancy.

Gestational hypertension and preeclampsia are more common in women with twin pregnancies, occurring in 13% of twin pregnancies compared to 5-6% in singleton pregnancies. The more severe forms of these conditions, such as early-onset severe preeclampsia and HELLP syndrome (Hemolysis, Elevated Liver Enzymes, Low Platelets), are also seen more frequently in multiple pregnancies than in singleton pregnancies.(Francisco vd., 2017)(Sibai vd., 2000)

It is unclear whether gestational diabetes is more common in twin pregnancies. However, screening, diagnosis, and management of gestational diabetes in twin pregnancies are similar to those in singleton pregnancies. (Schwartz vd., 1999)(Roach vd., 1998) Interestingly, large-for-gestational-age (LGA) newborns are less common in twin pregnancies complicated by gestational diabetes compared to singleton pregnancies affected by the same condition.(Ashwal vd., 2021)

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CHAPTER II

Dichorionic Diamniotic Twins

Aziz KINDAN[2]

1.Introduction

Twin pregnancies are slightly more risky than singleton pregnancies, except for those that are very late or very big. The greatest risk is that of premature birth.. This is the primary cause of the elevated mortality, morbidity, and long-term complications observed in twins. Furthermore, the increased likelihood of fetal growth restriction and congenital anomalies associated with twin pregnancies elevates the inherent risksIt's thought that monochorionic twins may share their placenta unevenly, which could unfortunately lead to some pretty serious complications. These can include twin-twin transfusion syndrome, twin anemia polycythemia sequence, and selective fetal growth restriction. Similarly, there is a possibility that monoamniotic twins may also be susceptible to complications resulting from the umbilical cord becoming entangled.. About 2.9% of live newborns are twins, with most multiple pregnancies being twins..(Cameron, Edwards, Derom, Thiery, & Boelaert, 1983)

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It would seem that there is a greater prevalence of dizygotic twins in some populations. Monozygotic twins are less common. It is estimated that they occur in three to five out of every 1,000 births worldwide. It should be noted that patient-specific factors do not appear to affect them, except in patients undergoing IVF..(Osterman, Hamilton, Martin, Driscoll, & Valenzuela, 2023)

2. Risk factors

The primary factors influencing the incidence of dizygotic twins can be classified as follows.(Adashi, 2016)

2.1 Assisted Reproductive Techniques

Twin pregnancies are more common with fertility treatments than with natural conception. Over a third of all twin babies born in the United States of America are the result of fertility treatments. Twin births in the United States increased from 1 in 53 babies in 1980 to 1 in 29 babies in 2014. Then it decreased to 1 in 32 babies between 2019 and 2021.(Lisonkova, Joseph, Bell, & Glinianaia, 2013)

The occurrence of dizygotic twins is more prevalent in pregnancies resulting from in vitro fertilisation (IVF) than in those occurring naturally. This is due to the fact that, in some cases, two embryos are transferred to the uterus.. However, IVF also makes it more likely that twins will be monozygotic. IVF is the only known cause of monozygotic twins.(Cameron et al., 1983)

2.2 Age of Mother

Approximately one-third of the observed increase in multiple births in recent years can be attributed to older maternal age. The chance of having dizygotic twins naturally increases two to three times between the ages of 14 and 45.It might be the case that the hormone follicle-stimulating hormone increases with age. It is possible that this is due to the hormone follicle-stimulating hormone increasing with age. It is also worth noting that older people are more likely to use fertility treatments.(Cameron et al., 1983)

2.3. Geography

The number of naturally conceived dizygotic twins varies around the world. One report suggests that in Japan, there may be as many as 1.3 out of every 1,000 babies born as dizygotic twins. In the United States and Europe, the figure is 8 out of every 1,000. In Nigeria, the figure is thought to be around 50 out of every 1,000.(Mullins & Kumar, 2012)

It would appear that twins occur with greater frequency in the Black population (Adashi, 2016).

2.4 Family history

It seems that there may be a genetic component involved in dizygotic twinning, which can be inherited from either the mother or father. It is thought that if a mother has a family history of twins, there is a greater chance that she will have twins herself. It would appear that the father's family history has little or no effect on his partner's risk of having twins. Pregnant women who are obese or tall are more likely to give birth to dizygotic twins than those who are thin or short.(Adashi & Gutman, 2018)

2.5 Diet

Diet may affect the rate of dizygotic twins in some places, among certain races, and in people with certain body habits. Some studies have indicated that there may be a correlation between folic acid supplements and an increased twinning rate. It is possible, however, that these studies may be biased..(Adashi & Gutman, 2018)

3. Diagnosis

In order to diagnose a twin pregnancy, it would be advisable to conduct an ultrasound examination. It would be advisable to have an ultrasound scan to diagnose a twin pregnancy.(Fox, Rebarber, Dunham, & Saltzman, 2009)

A study of over 15,000 pregnancies revealed that in some cases, twin pregnancies were not diagnosed until after 26 weeks, and

in a few instances, not until delivery. This suggests that without a routine ultrasound in the second trimester, there may be instances where a twin pregnancy goes undiagnosed.(McLennan et al., 2017)

In studies, it would appear that no twin pregnancies were overlooked when the ultrasound was conducted between 15 and 22 weeks (Shields, 1970).

3.1 Determination of gestational age

If there is a difference in measurements between the twins, it is suggested that the estimated date of birth should be based on the older twin's measurements. This will help to avoid missing growth restriction, which is common in multiple pregnancies, because of an incorrect estimate of the due date.(“Multiple Gestation Associated with Infertility Therapy: A Committee Opinion,” 2022)

An ultrasound before 22 weeks helps to work out the right time for birth. This is important for all pregnancies, but especially for twins because there are more complications. It is important to know the correct gestational age for various tests during pregnancy, to check the baby is growing normally, and to know when to deliver. (Lisonkova et al., 2013)

3.2. Evaluation of chorionicity and amnionicity

It might be helpful to find out whether the twins are monochorionic or dichorionic, as monochorionic twins have a shared fetoplacental circulation, which could potentially lead to certain complications. It is also worth noting that monochorionic twins are at risk of complications such as cord entanglement and conjoined twins. It would seem that there may be a higher risk involved with monochorionic twins compared to dichorionic twins. It is worth noting that monochorionic and monoamniotic twin pregnancies are monitored more closely than dichorionic twin pregnancies, for a very good reason.(Palomaki et al., 2021)

Chorionicity and amnionicity are best determined by ultrasound in the first trimester, around 7 weeks. In the second trimester, accuracy is lower but still good (sensitivity ≥ 90%). It is

harder and less accurate to assess the fetal membranes in the third trimester, especially if there is oligohydramnios.

Two separate placentas show that you are carrying dichorionic twins. This indicator is only useful in early pregnancy. It is not reliable later on as separate placentas often appear fused. A single placental mass does not necessarily indicate a monochorionic pregnancy. The placentas may appear fused early in pregnancy. Sometimes, a monochorionic placenta with two lumps looks like two separate placentas.(Kathiresan et al., 2011; Mullins & Kumar, 2012)

In dichorionic/diamniotic twin pregnancies, an intertwin membrane with a 'twin peak' or 'lambda (λ)' sign shows that the twins are separate. This sign is a triangular piece of tissue that sticks out from a fused placenta between the layers of the membrane. You can see it at 10 to 14 weeks, but it gets less obvious after 20 weeks.(Hoekstra et al., 2008)

It would appear that the intertwin membrane is thicker in dichorionic twins than in monochorionic twins.. This is due to the fact that the dichorionic/diamniotic membrane comprises four layers, whereas the monochorionic/diamniotic membrane has only two. There is no consensus regarding the optimal thickness of the membranes. The range of suggested measurements for the first trimester is between 1.5 and 2 mm. The disparity in membrane thickness is less discernible as gestation progresses. Following the initial trimester, it is relatively straightforward to ascertain the sex of the foetus. This is a good way to confirm that they are both pregnancies. So, doctors look at the genitals when they see twins.(Fox et al., 2009)

If you know if the twins are monochorionic or dichorionic, monochorionic twins are almost always identical. In 18% of twin pregnancies, the twins are dichorionic and identical. (Nylander, 1981)

I believe it would be helpful to note that these rates do not apply to IVF pregnancies, where dichorionic twins are usually formed by double embryo transfer and are therefore dizygoticI wonder if I might suggest that a transferred embryo has the potential to divide after transfer, which could result in monozygotic dichorionic twins. It is possible that a transferred embryo may divide after transfer, which could result in monozygotic dichorionic twins. It would appear that in IVF pregnancies, there is a higher incidence of monozygotic twins than in natural pregnancies.. (Delbaere et al., 2008)

Some dizygotic twins have monochorionic placentation. Blood tests show that these twins have mixed blood. We don't know how monochorionic dizygotic twins are formed. It might be related to assisted reproductive technology, but this condition has also been reported in naturally occurring pregnancies. (Basso, Nohr, Christensen, & Olsen, 2004)

In counselling parents of monochorionic twins, it is important to consider the possibility of the Y chromosome being lost in one twin, resulting in a 45,X and a 46,XY twin. Additionally, rare cases of dizygotic twins with chimerism and a disorder of sexual differentiation in one twin should be taken into account. Many cases of monochorionic dizygotic twins go unnoticed because the babies are the same sex. It is important to be careful when checking for an intertwin membrane in the early first trimester (around 7 to 9 weeks). The amnion may not be easy to find, which could lead to mistakes in diagnosing monoamniotic twins. If there are two yolk sacs, the twins are diamniotic. If there is one yolk sac, the twins are monoamniotic. (Suzuki, 2007)

Dizygotic twins come from two eggs being fertilised. This results in two placentas. Some dizygotic twins have been born after assisted reproduction. The reason is unknown. Dizygotic twins have also been reported after a single embryo transfer.(Steinman, 2006)

NIPT can also tell the zygosity. You can find out the zygosity of a baby using a test called NIPT. This test can help to assess

chorionicity when ultrasound findings are unclear. A study to validate single nucleotide polymorphism-based NIPT reported 100% accuracy for zygosity in 29 monozygotic and 64 dizygotic twin samples. The other two samples were inconclusive. Monozygotic twins have the same number of amnion and chorion, while dizygotic twins are usually dichorionic. However, there are very rare cases of monochorionic dizygotic twins, so dizygoticism alone rarely confirms dichorionicity in NIPT. ("Practice Bulletin No. 175: Ultrasound in Pregnancy," 2016)

The first trimester ultrasound can also find problems that could lead to a bad outcome. These include head-leg length discrepancy (associated with aneuploidy), enlarged nuchal translucency (which associated with aneuploidy, congenital anomalies,) and some congenital abnormalities.(McLennan et al., 2017)

In the second and third trimesters, ultrasound is used to screen for abnormalities. Screening for short cervix is also done. There are two main treatments for short cervical length: vaginal progesterone or cerclage. Studies have had different results. ("Multifetal Gestations: Twin, Triplet, and Higher-Order Multifetal Pregnancies," 2021)

It is important to use the same method to identify and label each twin during second and third trimester exams. It is important to know which twin is leading and which is the other. For same-sex twins, each twin can be identified by its position: left or right for laterally positioned twins and superior or inferior for vertically positioned twins. In laterally positioned twins, the leading twin may change. In vertically positioned twins, the lower twin is likely to remain the leading twin. It is also useful to note where the placenta is implanted and where the cord is attached.("Multiple Gestation Associated with Infertility Therapy: A Committee Opinion," 2022)

4. Fetal complications

Multiple pregnancies have more complications than singleton pregnancies.

4.1. Vanishing Twins

Sometimes twins disappear and become a single baby. Some studies say that vanishing twins are more likely to be low birth weight and small for their gestational age than singleton pregnancies. (Hack et al., 2008)Others say the risks are similar. This could be because vanishing twins are born at different stages of pregnancy and because of different IVF techniques. The risk of losing a twin is lower than the risk of having twins. (Ortibus et al., 2009)

The phenomenon of the lost twin has no impact on the surviving twin. Nevertheless, the results of the DNA test used to screen for common aneuploidies may be affected by the deceased twin.(Dias et al., 2011)

4.2. Growth Restriction

In dichorionic twins, there is a higher risk of fetal death in those with selective growth restriction. The risk of fetal death increases with increasing non-compliance . The smaller twin was more likely to die or have health problems after birth than the larger twin.(Hoekstra et al., 2008; Monni, Iuculano, Peddes, & Monni, 2021; Reddy, Branum, & Klebanoff, 2005)

4.3. Fetal Anomaly

It is hard to diagnose a foetal abnormality in a twin because the process affects both foetuses. How you treat a baby with a birth defect depends on the type of defect and how far along the pregnancy is. Patients who choose to continue the pregnancy should be told how the other twin may be affected It can be particularly challenging to make decisions regarding monitoring, therapy and delivery when a congenital anomaly has been diagnosed in one twin, as these choices affect both fetuses. It may be beneficial to evaluate the various options, including expectant management, in utero therapy, pregnancy termination, and selective feticide, if this is deemed appropriate for the specific type of abnormality and gestational age.. It would be beneficial for patients who choose to continue the pregnancy to have an understanding of how the anomalous fetus

might affect the co-twin's outcome, including the potential for preterm birth and organ damage. This understanding could extend to the role of chorionicity..(Khalil et al., 2016; Morin & Lim, 2017)

4.4. Prematurity

Most problems in twin pregnancies happen before the babies are born. Most cases of high preterm labour are caused by medical intervention. Multiple pregnancies have a higher chance of premature delivery. This is linked to more frequent and larger contractions of the myometrium, which is the muscle of the womb. ("Multifetal Gestations: Twin, Triplet, and Higher-Order Multifetal Pregnancies," 2021)

There is no evidence that using tocolysis, a pessary, cerclage or extra progesterone in the second trimester to prevent preterm delivery works. A history-based cerclage is a reasonable option for patients with a history of cervical insufficiency in a previous singleton pregnancy.(Hack et al., 2008)

A study of 13 trials of progestins to prevent preterm birth in multiple pregnancies found that progesterone did not reduce preterm birth or severe neonatal morbidity in those with no recorded risk factors. (Leduc, Takser, & Rinfret, 2005)

Tocolytic therapy may be recommended for patients with preterm labour. Patients with asymptomatic cervical dilatation may be treated with cerclage. Patients with a short cervix may be treated with vaginal progesterone or cerclage or a pessary. (Adegbite, Castille, Ward, & Bajoria, 2004)

Systematic reviews of studies on hospitalisation or bed rest in twin pregnancies have not shown that either of these increases the length of pregnancy. Bed rest may increase the risk of blood clots. (Dubé, Dodds, & Armson, 2002)

A high fetal fibronectin level may predict preterm birth, but we do not test for it in symptom-free patients.

Postterm and macrosomia rates are lower than in singleton pregnancies.

If one twin dies in a set of twins, it is not a good reason to deliver the other twin early. If a condition affects both twins, follow them closely and deliver the surviving twin as soon as possible to prevent further loss or harm to the mother. Timely delivery depends on the situation.(Mackie, Hall, Morris, & Kilby, 2018; Sebire, D'Ercole, Soares, Nayar, & Nicolaides, 1998)

4.5. Fetal Demise

About 5% of twin pregnancies end in one fetus dying after 20 weeks. The placenta of monochorionic twins can cause problems if one twin dies. This can lead to problems for the other twin. This could kill the other twin. If one twin is dying, we suggest you deliver the other twin. If one twin has already died, it is not helpful to deliver the other twin. This could make the surviving twin more likely to have a premature birth.(Chauhan, Scardo, Hayes, Abuhamad, & Berghella, 2010)

5. Maternal Risks

Mothers carrying twins are more likely to have problems than mothers carrying one baby. However, studies show that whether the babies are joined together or not does not affect this risk. Some studies have reported that twins conceived by IVF are more likely to have complications. However, the data are inconsistent and this may be due to factors related to infertility. (Francisco, Wright, Benkő, Syngelaki, & Nicolaides, 2017)

Twin pregnancy affects the mother's body more than singleton pregnancy. The heart pumps more blood in twin pregnancies, increasing the risk of lung problems when other factors are present. Twin pregnancies often cause anaemia, but the body makes more red blood cells than in singleton pregnancies. (Kametas, McAuliffe, Krampl, Chambers, & Nicolaides, 2003)

Pregnant women with more than one baby are more likely to have high blood pressure.

Some conditions are more common in multiple pregnancies. These include itchy skin, liver problems, anaemia, hyperemesis gravidarum and placental abruption.(Ghi et al., 2015)

6. Delivery and Management

The timing and mode of delivery for uncomplicated twin pregnancies depends on the position of the twins. In complicated twin pregnancies, the decision is based on the specific complication.

Twin pregnancies are usually managed in the same way as singleton pregnancies, but it is wise to deliver in a room where a caesarean section can be performed if needed. There should be paediatric staff to help with the transition of each newborn, including resuscitation if necessary. The health centre should be able to provide a level of neonatal care appropriate to the risk.Time Interval between Twins ChallengedRayburn W, Lavin J, Miodovnik M, Varner M:

The time of labour for uncomplicated twin pregnancies depends on the number of chorions and amnion.

For uncomplicated twin pregnancies, planned delivery is recommended between 38+0 and 38+6 weeks.

For twin pregnancies where one baby is growing slowly, delivery is recommended between 36+0 and 37+6 weeks.

For complicated twin pregnancies with other problems, the time of delivery should be decided on a case-by-case basis.

The optimal route of delivery is largely dependent on presentation.

Vaginal delivery is the recommended mode of delivery for cephalic/cephalic diamniotic twins unless there are standard indications for a caesarean sectionIt might be a good idea to think about trying to have the second twin delivered by trial of labour and breech extraction, if the obstetrician has the necessary experience and the patient is happy for this to happen.In the case of a non-cephalic presenting twin, we suggest a caesarean delivery. We advise that these patients have another caesarean section, but some doctors

may decide differently, allowing labour to begin with close monitoring.

The utilisation of cervical ripening techniques and oxytocin dosing for the induction and augmentation of labour is consistent with that employed in singleton pregnanciesThe following section will address the aforementioned issue. In the event that two distinct monitors are employed, it is of paramount importance to synchronise their respective internal clocks, guarantee identical paper speeds and ensure the display of contractions on both fetal heart rate tracings. It is also a good anaesthetic for when the womb needs to be manipulated or an operation is needed.

All twin pregnancies are delivered in an operating room, where a caesarean birth can be performed if necessary.

It is not safe to delay clamping the cord on monochorionic twins. This can cause serious blood loss between the twins during labour.

Subsequent to the birth of the initial twin, an assessment of the heart rate and position of the subsequent twin should be conducted through the utilisation of ultrasound and electronic fetal monitoring.. If the fetal heart rate is normal, there is no minimum time between the birth of the first twin and the second twin can be delivered. About 6-25% of second twins are delivered by caesarean section after the first twin is born.

In the event that the second twin is in a cephalic presentation, it may be advisable to consider oxytocin augmentation of labour, given that there is a possibility of a temporary reduction in contraction frequency following the first birthIf the second twin is head-down but not engaged, there are two main options. One is to do a controlled needle puncture of the amniotic sac between contractions. The other is to perform internal podalic version and breech extraction. (Hayata, Nakata, & Morita, 2022)

If the second twin isn't in a cephalic presentation (e.g. breech or transverse), our advice is to go ahead with a breech extraction, as

long as there are no reasons why this shouldn't be done.(M., C., M., & M., 2019)

7. Conclusion

Multiple pregnancies are high-risk. Chorionicity and zygosity should be determined early and pregnancy follow-up planned.(“Multifetal Gestations: Twin, Triplet, and Higher-Order Multifetal Pregnancies,” 2021)

An ultrasound scan during the first or early second trimester is the best way to diagnose a twin pregnancy, find out the due date and see if the babies are identical or not.

The best way to tell if you're having two separate babies is to look for two placentas and different sexes. If there is one placenta, you can tell if the twins are dichorionic or monochorionic by looking for an intertwin membrane. In dichorionic twins, you will see a twin peak or lambda sign. In monochorionic twins, you will see a T sign. You can also look at how thick the placenta is and how many layers it has.

Monochorionic twins of the same sex are always "identical". In the case of same-sex twins, this is the case in 18% of cases. If you don't know if your twins are identical, you can tell them that 37% of all same-sex twins are.

It is reasonable to conclude that there are more cases of dizygotic twins than of identical twins. It would appear that there is a greater prevalence of dizygotic twins in some populations than in others. It is estimated that there are approximately three to five cases of monozygotic twins per 1,000 births worldwide. It is believed that monochorionic twins may be more susceptible to complications during pregnancy and childbirth than dichorionic twins. They are also considered to be at a higher risk of developing complications during pregnancy, such as twin-twin transfusion syndrome, twin anemia polycythemia sequence, twin reversed arterial perfusion sequence, and selective fetal growth restriction. Monoamniotic twins may be at risk of cord entanglement and conjoined twins. Routine prenatal care for twin pregnancies is different from singleton

pregnancies. These include higher weight gain, minor changes to supplements, routine preeclampsia prophylaxis, choice of Down syndrome screening, and ultrasound monitoring. For more on prenatal care for twins, see the separate section.

The timing and route of birth in uncomplicated twin pregnancies is based on the position of the twins. If there are complications, the decision-making process is similar to that for singleton pregnancies.

Outcome: 16 to 37 percent of pregnancies conceived by in vitro fertilisation end in early spontaneous reduction of one sac. The following table shows the rates of late fetal and infant death.

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CHAPTER III

Monochorionic Twins

Ruken DAYANAN[3]

Introduction

Monochorionic twins represent a classification of twin pregnancies observed in monozygotic gestations. In these pregnancies, a single fertilized oocyte splits into two separate embryos after the third day of normal embryonic development. Approximately 20% of twin pregnancies are monochorionic, and they exhibit significantly higher rates of complications compared to dichorionic twins. These complications arise due to vascular anastomoses that develop between the fetuses, which disrupt fetal blood flow and lead to increased fetal morbidity and mortality for both twins. Such complications are potentially life-threatening and will be discussed in detail in subsequent sections. As a result, monochorionic pregnancies require more intensive monitoring and management compared to singleton and dichorionic pregnancies.(ISUOG, t.y.)

This chapter will address the determination of gestational age in monochorionic pregnancies, the identification of chorionicity, associated complications, and recommended monitoring protocols.

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Sonographic Determination of Chorionicity and Amnionicity

The early and precise determination of chorionicity and amnionicity in twin pregnancies is of critical importance for antenatal management. Ideally, chorionicity should be identified during the first trimester, as it is essential for managing the following clinical situations:

- Structural anomaly management,
- Screening and diagnosis of aneuploidy,
- Determination of the etiology of fetal growth or fluid imbalance,
- Early diagnosis of twin-to-twin transfusion syndrome,
- Management of the surviving twin following intrauterine loss.

It has been well-established that monoamniotic twins are associated with high rates of morbidity and mortality. Intensive monitoring and early intervention initiated in the early stages of pregnancy can significantly improve outcomes for these pregnancies.(Allen, Windrim, Barrett, & Ohlsson, 2001; DeFalco vd., 2006; Heyborne, Porreco, Garite, Phair, & Abril, 2005)

Sonographic Findings Before 10 Weeks of Gestation

The following ultrasonographic findings are used to determine chorionicity before 10 weeks of gestation:

1. **Number of Gestational Sacs**
   The number of gestational sacs and the presence of embryonic cardiac activity provide strong evidence for chorionicity. Each gestational sac forms its own placenta and chorion. The presence of two gestational sacs indicates dichorionic pregnancies, whereas two cardiac activities within a single gestational sac suggest monochorionic pregnancies.(Monteagudo & Roman, 2005)
2. **Number of Amniotic Sacs Within the Chorionic Cavity**
   In diamniotic twins, separate and distinct amniotic sacs can be visualized on ultrasound before 10 weeks. However, these delicate

structures may not always be seen with transabdominal ultrasound; transvaginal ultrasound is often more successful in their detection.

3. **Number of Yolk Sacs**
   The presence of two yolk sacs in the extraembryonic coelom indicates diamniotic pregnancies, while a single yolk sac typically suggests monoamniotic pregnancies.(Bromley & Benacerraf, 1995) If a single yolk sac is observed alongside two embryos, follow-up during the first trimester is recommended to confirm amnionicity.

Sonographic Findings After 10 Weeks of Gestation

After 10 weeks, the gestational sacs are no longer distinct, and the intertwin membrane forms. At this stage, additional sonographic markers are employed to determine chorionicity and amnionicity:

1. **Discordant Fetal Sex**
   Phenotypic discordance almost always indicates dichorionicity. However, phenotypic concordance does not exclude dichorionicity.

2. **Number of Placentas**
   A single placenta suggests monochorionicity, while two separate placentas indicate dichorionicity. However, differentiating between closely apposed placentas requires careful ultrasonographic examination.

3. **Chorionic Peak (Lambda Sign or Twin Peak Sign)**
   A triangular projection of tissue, echoing the texture of the placenta and extending into the intertwin membrane, is known as the lambda sign. The presence of the lambda sign confirms dichorionicity, whereas its absence indicates monochorionicity.(Wood, Onge, Connors, & Elliot, 1996)

4. **Membrane Characteristics**
   In dichorionic pregnancies, the membrane consists of two amniotic and two chorionic layers, making it thicker (>2 mm) and more echogenic. Monochorionicity is suspected when the membrane thickness is ≤2 mm. The absence of a membrane necessitates an evaluation for

monoamniotic pregnancy or conditions such as oligohydramnios. In monoamniotic pregnancies, cord entanglement is the most distinctive sonographic feature, and color Doppler imaging is useful for its detection.(D'Alton & Dudley, 1989; Winn vd., 1989)

Ultrasound evaluations conducted before 14 weeks are more accurate in determining chorionicity. After 14 weeks, the accuracy of determination declines, necessitating the combination of multiple sonographic markers. For instance, the lambda sign may disappear in approximately 7% of dichorionic pregnancies during the second trimester; thus, its absence does not rule out dichorionicity. Early and detailed ultrasound examination is essential for the accurate determination of chorionicity and amnionicity, ensuring optimal management and improved outcomes in twin pregnancies.

Dating Pregnancy

Although guidelines recommend determining gestational age between 11 weeks and 13 weeks 6 days, chorionicity can often be identified as early as the 8th week of pregnancy to accurately identify high-risk pregnancies and ensure appropriate care. Ideally, nuchal translucency measurement should be performed when the crown-rump length (CRL) is between 45 and 84 mm .

In twin pregnancies, it is generally recommended to estimate gestational age based on the CRL of the larger fetus. However, some studies suggest using the CRL of the smaller fetus or the average CRL of both fetuses, as these methods have been shown to yield more accurate results in both prospective and retrospective analyses. Nevertheless, concerns remain that these two methods may lead to misclassification of the larger twin as large for gestational age (LGA). Such misclassification could mislead healthcare providers into believing that the smaller twin is appropriately grown, potentially resulting in monitoring deficiencies and management errors, which may lead to adverse outcomes.

When a woman presents for evaluation after 14 weeks of gestation, the gestational age should be determined based on the head circumference of the larger fetus. In pregnancies conceived through in vitro fertilization (IVF), gestational age is calculated based on the age of the embryo.(ISUOG, t.y.)

Monochorionic Damniotic Twin Pregnancies

Approximately 20% of twin pregnancies are classified as monochorionic diamniotic (MCDA). In such pregnancies, vascular anastomoses, which are invariably present, can lead to transfusion imbalances. The most severe imbalance is twin-to-twin transfusion syndrome (TTTS), which is typically diagnosed via ultrasound before 26 weeks of gestation as a significant disparity in amniotic fluid volumes. Another transfusion imbalance, twin anemia-polycythemia sequence (TAPS), is characterized by significant hemoglobin differences and usually manifests after 26 weeks in pregnancies previously free of complications. These transfusion imbalances are primarily caused by vascular anastomoses, which can be treated via fetoscopic laser coagulation.

Beyond transfusion imbalances, the monochorionic placenta may be unevenly divided or partially non-functional, resulting in a growth disparity of more than 20% between the twins. While laser ablation does not completely resolve this condition, it aims to protect the appropriately growing twin if the growth-restricted twin succumbs.

Structural anomalies are twice as common in monochorionic twins compared to singleton pregnancies, likely due to teratogenic effects during embryonic splitting or complications from transfusion imbalances. However, chromosomal anomalies are less frequent, presumably because they are more likely to result in early fetal loss.

Selective reduction is an option in monochorionic pregnancies but carries increased risks of loss, miscarriage, and preterm birth compared to selective reduction in dichorionic pregnancies. Lastly, when one monochorionic twin spontaneously demises, the surviving twin may

experience acute blood loss to the deceased twin. This phenomenon can result in the loss of both twins or brain damage in the surviving twin.

The subsequent sections will explore the pathophysiology, diagnosis, and management of these common complications in monochorionic diamniotic twin pregnancies.(Lewi, 2022)

Monochorionic Monoamniotic Pregnancies

Definition and Epidemiology

Monoamniotic twin pregnancies are rare, occurring in approximately 8 out of every 100,000 pregnancies.(Glinianaia vd., 2019) These pregnancies result from the division of a single fertilized ovum between the 9th and 13th days of embryonic development. The hallmark of monoamniotic twin pregnancies is the sharing of a single placenta and a single amniotic sac. Even rarer are conjoined twin pregnancies, reported at a frequency of only 1.5 cases per 100,000 pregnancies, which occur when the embryo divides later, after the 13th day.(Mutchinick vd., 2011) In conjoined twins, not only are the placenta and amniotic sac shared, but parts of the body are also physically connected.

The incidence of monochorionic and monoamniotic twin pregnancies increases significantly following procedures involving embryo manipulation and assisted reproductive technologies, such as "assisted hatching".(Knopman vd., 2014) Approximately 1.9% of pregnancies achieved through assisted reproductive technologies are monochorionic, and about one-third of these are monoamniotic. Additionally, monoamniosity can develop in diamniotic twin pregnancies as a result of spontaneous rupture of the interamniotic membrane(Fleming & Miller, 2012) or accidental rupture during invasive procedures such as amniocentesis(Feldman, 1998) or fetoscopic surgery.(Gordon vd., 2017)

Interestingly, approximately two-thirds of monoamniotic twins are female, and one-third are male.(K. E. Hack vd., 2009) This phenomenon may be explained by the hypothesis that X-chromosome inactivation in female

embryos delays embryonic division, thereby predisposing them to monoamniosity.(Monteiro vd., 1998)

Diagnosis of Monoamniotic Twins

The determination of chorionicity and amnionicity is a critical component of first-trimester ultrasonography in multiple pregnancies. This is particularly important as monochorionic and monoamniotic twins exhibit significantly higher rates of complications compared to dichorionic or diamniotic twins and require distinct pregnancy management protocols. While chorionicity can typically be identified early in pregnancy with relative ease, the diagnosis of amnionicity is more challenging before the 10th week of gestation due to the difficulty in identifying the thin amniotic membrane.(Bora, Papageorghiou, Bottomley, Kirk, & Bourne, 2008)

Certain conditions complicate the early diagnosis of amnionicity, including maternal obesity, a retroverted uterus, the presence of fibroids, or adenomyosis. In cases where amnionicity determination is uncertain, a transvaginal approach may sometimes be helpful. Alternatively, patients can be rescanned after the 10th week of gestation or referred to a more experienced center for evaluation.

The definitive ultrasonographic marker of monoamniosity during the first trimester is the absence of a separating amniotic membrane between the two fetuses. Indirect (and therefore less definitive) ultrasonographic findings that support a diagnosis of monoamniosity include the presence of cord entanglement, which is almost universally observed in monoamniotic twins, and the number of yolk sacs. Approximately two-thirds of monoamniotic twins have a single yolk sac, while one-third exhibit two yolk sacs, similar to diamniotic twins.(Sebire, Souka, Skentou, Geerts, & Nicolaides, 2000)

Pathogenesis

Monoamniotic pregnancies typically originate from a single fertilized ovum, in which the embryo splits between 8 and 13 days after fertilization. Conjoined twin pregnancies represent a subset of monoamniotic

pregnancies and occur when the embryo divides later, after the 13th day. This condition is exceedingly rare, with an incidence of approximately 1.5 cases per 100,000 pregnancies.

Additionally, monoamniotic pregnancies can result from the rupture of the interamniotic membrane in diamniotic pregnancies. Such ruptures may occur spontaneously or in association with invasive procedures such as amniocentesis or fetal surgery. This phenomenon is commonly referred to as spontaneous or iatrogenic "septostomy".(Van Mieghem vd., 2022)

Classification of Complications

The complications associated with monoamniotic twin pregnancies can be categorized into two groups:

1. Complications specific to monochorionicity and monoamniosity,
2. Complications common to all twin pregnancies.

Focusing on complications specific to monochorionic pregnancies, monoamniotic pregnancies, like diamniotic pregnancies, are at risk for:

- Twin-to-twin transfusion syndrome (TTTS),
- Twin reversed arterial perfusion (TRAP) sequence (acardiac twin),
- Selective fetal growth restriction (sFGR).

The incidence of TTTS in monoamniotic pregnancies is lower compared to monochorionic diamniotic pregnancies, ranging from 2% to 6%. This reduced incidence is thought to be associated with the presence of arterio-arterial anastomoses, which are almost universally observed in monoamniotic placentas and may play a protective role against TTTS.(K. E. A. Hack vd., 2009) Conversely, the incidence of TRAP sequence is reported to be higher in monoamniotic pregnancies for the same reason.

Complications Specific to Monoamniosity

Monoamniotic pregnancies are particularly associated with the following complications:

1. **Cord Entanglement**

Cord entanglement is observed in nearly all monoamniotic pregnancies. The primary concern is that intermittent obstruction of umbilical cord blood flow may lead to neurological morbidity or, in cases of prolonged obstruction, fetal death. However, the overall survival rate in cases of cord entanglement is reported to be approximately 89%, with no significant difference in mortality between pregnancies with or without entanglement. Moreover, visualization of cord entanglement on ultrasound has not been shown to improve perinatal outcomes.(Dias, Mahsud-Dornan, Bhide, Papageorghiou, & Thilaganathan, 2010; Rossi & Prefumo, 2013)

2. **Conjoined Twins**

Conjoined twins are a rare subset of monoamniotic pregnancies, characterized by the physical fusion of parts of one twin's body with the other. Based on the anatomical site of fusion, conjoined twins are classified as follows:

- Cephalopagus (head fusion),
- Thoracopagus (chest fusion),
- Omphalopagus (abdominal fusion),
- Ischiopagus (pelvic fusion),
- Parapagus (side fusion),
- Craniopagus (skull fusion),
- Rachipagus (spinal fusion),
- Pygopagus (sacral fusion).

More than half of conjoined twin pregnancies result in fetal loss.[21]

Complications Common to All Twin Pregnancies

Monoamniotic twins are also susceptible to complications common in other twin pregnancies, including:

- Spontaneous preterm birth,
- Gestational diabetes,

- Hypertensive disorders of pregnancy and preeclampsia,
- Severe cardiovascular disorders such as stroke and deep vein thrombosis,
- Cholestasis.(Van Mieghem vd., 2022)

Associated of Anomalies

Monoamniotic pregnancies carry a higher risk of congenital anomalies compared to singleton pregnancies and dichorionic or monochorionic diamniotic pregnancies. The estimated prevalence of these anomalies ranges between 10% and 25%. The most commonly observed anomalies are congenital heart defects, accounting for approximately 30% of all cases. Structural anomalies are often asymmetrically distributed between the two fetuses, with only one fetus typically being affected.

Chromosomal anomalies, on the other hand, are relatively rare in these cases, with a prevalence of approximately 4%. The underlying mechanism is thought to involve hemodynamic imbalances within the monochorionic placental anastomoses.(K. E. Hack vd., 2009; Khairudin & Khalil, 2022; Monteiro vd., 1998; Van Mieghem vd., 2022)

Surveilance and Management of Monochorionic Pregnancies

Due to the increased risk of complications in monochorionic twin pregnancies, regular surveillance is essential for the early detection of potential abnormalities and the provision of appropriate management. Early determination of chorionicity is also crucial for patient counseling and planning. Clinical practice guidelines recommend biweekly screening for uncomplicated monochorionic twins starting from the 16th week, following the first-trimester ultrasound.(Khalil vd., 2016)

11–14 Weeks

- Ultrasound should be performed to establish gestational age, label the twins, and determine chorionicity. This evaluation aids in surveillance, counseling, and pregnancy planning.

- Major anomalies should be screened for during the first-trimester ultrasound, and nuchal translucency measurements should be obtained [63].
- Screening for fetal chromosomal abnormalities, such as Trisomy 21, is recommended. (Khalil vd., 2016) Options include the combined test or non-invasive prenatal testing (NIPT).
- However, the reliability of chromosomal anomaly screening tests is lower in twin pregnancies compared to singleton pregnancies, with an increased risk of false results in cases of fetal loss, vanishing twin syndrome, or detection of an anomaly in one fetus.("Multifetal Gestations Twin Triplet and Higher-Order Multifetal Pregnancies", t.y.)

16–18 Weeks

- Assess fetal growth, measure the deepest vertical pockets (DVP), and record the umbilical artery Doppler pulsatility index (UA-PI). These assessments aid in the early detection of TTTS and fetal growth restriction.(Khalil vd., 2016)
- If parameters are normal, biweekly scans should continue.(Khalil vd., 2016)
- In cases of abnormal DVP, weekly UA and middle cerebral artery (MCA) Doppler studies are required.(Khalil vd., 2016)
- Documentation of fetal bladder status via ultrasound may be necessary for TTTS staging.

18–20 Weeks

- Perform detailed anatomic screening to identify potential anomalies such as neural tube defects, cardiac abnormalities, gastrointestinal malformations, craniofacial defects, and brain abnormalities.(Salomon vd., 2013)
- All monochorionic twins should undergo fetal echocardiography by an experienced sonographer between 18–22 weeks.(Patient Safety and

Quality Committee, Society for Maternal-Fetal Medicine. Electronic address: smfm@smfm.org, Hoskins, & Combs, 2020)

- Cervical length should be measured to screen for preterm birth, with a threshold of 25 mm.(Khalil vd., 2016)
- Serial growth ultrasounds should be performed every 2–4 weeks using biometry to screen for fetal growth restriction.(Salomon vd., 2011)
- Discrepancies in growth should be documented starting from the 20th week to monitor for growth discordance and selective fetal growth restriction (sFGR).(Khalil vd., 2016)

22–36 Weeks

- Continue monitoring fetal growth every 2–4 weeks.(Salomon vd., 2011)
- Measure DVP, UA-PI, and MCA-PSV every two weeks to monitor for FGR, TTTS, and TAPS development.(Khalil vd., 2016)
- In MCDA (monochorionic diamniotic) twins, antenatal testing (e.g., cardiotocography or biophysical profile) should begin at 32 weeks.("Antenatal Surveillance in Twin Pregnancies Using the Biophysical Profile - PubMed", t.y.; "Risk of late-preterm stillbirth and neonatal morbidity for monochorionic and dichorionic twins - PubMed", t.y.; Russo vd., 2013)
- For MCMA (monochorionic monoamniotic) twins, individualized antenatal testing is recommended. Many clinicians advocate for early inpatient management with daily fetal monitoring between 24–28 weeks.(Baxi & Walsh, 2010; DeFalco vd., 2006; Ezra vd., 2005)

Timing of Delivery

- For MCDA twins, delivery should be planned at 36 weeks in uncomplicated pregnancies, with the mode of delivery dependent on fetal presentation [3].

- For MCMA twins, delivery should be performed via cesarean section at 32–34 weeks to prevent cord-related complications. (Baxi & Walsh, 2010; DeFalco vd., 2006; Ezra vd., 2005)

Prognosis

In recent decades, the overall survival rate of monoamniotic twins has improved significantly.(D'Antonio, Khalil, Dias, Thilaganathan, & Southwest Thames Obstetric Research Collaborative (STORK), 2013) However, among all twin pregnancies, monoamniotic pregnancies carry the highest risk of mortality during both early and late gestation. Even after 24 weeks of gestation, the risk of fetal death in monoamniotic twins is nine times higher compared to dichorionic twin pregnancies.(Van Mieghem vd., 2022)

The most recent evidence evaluates the outcomes of monoamniotic twins without anomalies who reach 24 weeks of gestation. According to the findings:

- The overall fetal death rate is reported as 5.8%.
- The rate of single intrauterine death is 2.5%, while the rate of dual intrauterine death is 3.8%.
- Fetal death rates are as follows:
    - 4.3% between 24–30 weeks,
    - 1.0% between 31–32 weeks,
    - 2.2% between 33–34 weeks.(D'Antonio vd., 2019)

Risks of Neonatal Morbidity

In addition to concerns about mortality, monoamniotic pregnancies are reported to carry a higher risk of neonatal morbidity.

- The composite morbidity rate is approximately 46%, predominantly associated with respiratory morbidities and prematurity.

- Regardless of gestational age at birth, two-thirds of neonates are admitted to the neonatal intensive care unit (NICU).
- Neonatal morbidity rates decrease with advancing gestational age, with a significant reduction observed around 33–34 weeks.(Buca vd., 2022)

Careful monitoring of mortality and morbidity and the implementation of appropriate management plans are critical in monoamniotic twin pregnancies.

Conclusion

The risk of fetal and maternal morbidity is significantly higher in multiple pregnancies. Monochorionic twins are particularly prone to unique complications, including twin-to-twin transfusion syndrome (TTTS), twin anemia-polycythemia sequence (TAPS), twin reversed arterial perfusion (TRAP) sequence, selective fetal growth restriction (sFGR), and conjoined twins. For this reason, determining chorionicity at an early stage of pregnancy is essential to identify high-risk cases, provide accurate counseling, and ensure timely referral to a maternal-fetal medicine specialist. Early recognition and intervention enable the effective management of complications linked to specific chorionicity types, thereby improving pregnancy outcomes.

Surveillance protocols should encompass evaluations of fetal growth, deepest vertical pocket (DVP), umbilical artery pulsatility index (UA-PI), middle cerebral artery peak systolic velocity (MCA-PSV), comprehensive anatomical screening, cervical length measurements, and fetal echocardiography. While standardized monitoring intervals exist, modifications may be required depending on individual case characteristics and specific clinical concerns. Prompt detection and management of conditions like TTTS and TAPS have been shown to substantially reduce associated morbidity and mortality. Therefore, consistent and frequent monitoring throughout the course of pregnancy remains vital for optimal care.

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CHAPTER IV

Selective Fetal Growth Restriction

Merve ÖZKAN[4]

Introduction

Selective Fetal Growth Restriction (sFGR) is defined as a condition where the estimated fetal weight (EFW) of one of the fetuses is below the 10th percentile, or the discordance in EFW between twins exceeds 25%. The formula used to calculate discordance is: **(Large fetus EFW - Small fetus EFW) / Large fetus EFW** (Bennasar et al., 2017). sFGR complicates approximately **10-25%** of monochorionic pregnancies. It is a complication that increases morbidity and mortality in monochorionic twins (Lewi et al., 2008).

Pathophysiology

While Fetal Growth Restriction (FGR) in singleton pregnancies and dichorionic twin pregnancies is associated with

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placental insufficiency, the primary cause of **selective Fetal Growth Restriction (sFGR)** in monochorionic pregnancies is often unequal placental sharing (Burton and Jauniaux, 2018). **Anatomical factors** can also contribute to sFGR. **Velamentous cord insertion** is present in approximately **30% of monochorionic twins** and significantly increases the risk of sFGR (Kalafat et al., 2018).

The **number and size of vascular anastomoses** between fetuses is another important parameter that plays a role in sFGR. A **low number of vascular anastomoses** will result in Doppler findings similar to FGR in normal singleton pregnancies. In particular, **artery-to-artery anastomoses** and large-diameter anastomoses can positively affect unequal placental sharing and alleviate FGR findings. This occurs because blood flow from the normal-weight fetus can be directed to the FGR-affected fetus via anastomoses. However, if **unpredictable and sudden large amounts of blood flow** occur through these anastomoses, **sudden bradycardia** and **fetal demise** may be observed in the donor fetus (X. Wang et al., 2022).

Clinical Presentation

In monochorionic pregnancies, differences in **crown-rump length (CRL)** measurements between the two fetuses during the first-trimester ultrasound examination may be the first sign of **selective fetal growth restriction (sFGR)**. However, sFGR is frequently diagnosed during the early weeks of the second trimester. If sFGR presents as late as the **third trimester**, the prognosis is generally favorable (Y. Wang et al., 2022).

The frequency of follow-ups and the procedures to be performed to detect potential sFGR or other twin complications **early** in monochorionic pregnancies are listed in **Table 1**.

Table 1. Follow-Up in Monochorionic Pregnancies

Gestational Age	Recommended Examinations
11-14 weeks	- Calculate gestational age and estimated due date. - Determine chorionicity. - Perform trisomy 21 screening.
16-18 weeks	- Evaluate fetal growth. - Assess bladder size. - Assess amniotic fluid. - Evaluate fetal Doppler parameters (MCA-PSV Doppler, UA Doppler).
20-22 weeks	- Evaluate fetal growth and perform a detailed obstetric ultrasound. - Assess bladder size. - Assess amniotic fluid. - Evaluate fetal Doppler parameters (MCA-PSV Doppler, UA Doppler). - Determine cord insertion sites. - Assess cervical length. - Perform fetal echocardiography.
22-32 weeks	- Monitor fetal growth (every 4 weeks). - Assess amniotic fluid (every 2 weeks). - Evaluate fetal bladder size and presence (every 2 weeks). - Evaluate fetal Doppler parameters (MCA-PSV Doppler, UA Doppler) (every 2 weeks).
32-36 weeks	- Monitor fetal growth (every 4 weeks). - Perform weekly: - Biophysical profile assessment. - Evaluate fetal Doppler parameters (MCA-PSV Doppler, UA Doppler).

(Khalil et al., 2016)

Accurate determination of **chorionicity** and **gestational age** is crucial for diagnosing, monitoring, and detecting complications early in monochorionic twin pregnancies.

Diagnosis

Diagnostic criteria:

The diagnosis of **selective Fetal Growth Restriction (sFGR)** is made using fetal biometric measurements, UA Doppler, and the discordance of Estimated Fetal Weight (EFW) between fetuses.

According to the **ISUOG diagnostic criteria** (Khalil et al., 2016):

- EFW of one twin must be **below the 10th percentile**, and
- The discordance in EFW between twins must be **greater than 25%**.

According to the **Delphi diagnostic criteria** (Gordijn et al., 2016);

- EFW of one fetus must be **below the 3rd percentile**,
- Or at least **two** of the following criteria must be present:
    - EFW of one fetus is below the **10th percentile**,
    - Abdominal circumference (AC) of one fetus is below the **10th percentile**,
    - Umbilical Artery Pulsatility Index (UA PI) for the growth-restricted fetus is **above the 95th percentile**,
    - Discordance in EFW between twins is **greater than 25%**.

(The formula to calculate discordance is: (Larger fetus EFW - Smaller fetus EFW) / Larger fetus EFW) (Bennasar et al., 2017))

UA Doppler measurements are a parameter that shows **placental and hemodynamic sharing** between the fetuses. In monochorionic twin pregnancies diagnosed with sFGR, UA Doppler may show **increased PI resistance**, **absent** or **reversed end-diastolic flow** (either transient or permanent). These waveform abnormalities often result from **large arterio-arterial anastomoses** between the two fetuses. These flow changes can be observed from the **early weeks of pregnancy** and may vary as gestation progresses (Rustico et al., 2017)(Bennasar et al., 2017). UA Doppler measurements taken **closest to the point where the umbilical cord inserts into the placenta** provide a more accurate diagnosis of the described waveforms. This is because the effects of **placental vascular anastomoses** are most prominent in these regions (Eschbach et al., 2020).

Classification

In monochorionic twin pregnancies diagnosed with **sFGR**, classification is based on **changes in the Umbilical Artery (UA) Doppler waveform**.

Type 1 sFGR: Describes a situation where the UA Doppler waveform progresses normally or shows only an **increase in resistance** without any pathology. The prognosis is better compared to other types, with a survival rate of **over 90%** (Khalil et al., 2016).

Type 2 sFGR: Defined as the presence of **persistent absent end-diastolic flow (AEDF)** or **reversed end-diastolic flow (REDF)** in the UA Doppler waveform of the smaller fetus. There is a **high risk of fetal loss** for the smaller fetus and a high risk of the pregnancy ending in **preterm delivery**. If the smaller fetus is lost,

there is an **increased risk of neurological damage** in the surviving fetus (Gratacós et al., 2004; Khalil et al., 2016).

Type 3 sFGR: Characterized by **variable changes** in the UA Doppler waveform of the smaller fetus. Normal flow, absent end-diastolic flow, and reversed flow may occur **intermittently**. There is an **increased risk of sudden and unpredictable fetal death** in the growth-restricted fetus. In the event of death, the surviving fetus has an **increased risk of neurological sequelae** (Gratacós et al., 2004; Khalil et al., 2016).

Management

In **dichorionic pregnancies**, since the circulations of the two fetuses are separate, management is carried out similarly to singleton pregnancies diagnosed with FGR. Monitoring of UA Doppler, MCA Doppler, and DV Doppler parameters is continued, and delivery timing is decided as in singleton pregnancies(Khalil et al., 2016).

In managing **monochorionic pregnancies** diagnosed with sFGR, the critical point is identifying cases that require **expectant management** or **fetal intervention**. Currently, there is insufficient evidence and studies regarding the follow-up and management of monochorionic sFGR pregnancies(Khalil et al., 2016).

Type 1 sFGR

After diagnosis, **weekly ultrasound assessments** and **biophysical profile evaluations** (starting from the 28th week) should be performed. Fetal growth monitoring should be added **at least every two weeks**. Ultrasound assessments must include **UA Doppler, MCA Doppler, and DV Doppler** parameters. If **UA PI > 95th percentile** or **MCA PI < 5th percentile**, the monitoring

frequency should be increased to **twice weekly**. As long as **absent end-diastolic flow (AEDF)** or **reversed end-diastolic flow (REDF)** does not develop in the UA Doppler, severe fetal deterioration and death are not expected (Khalil et al., 2016)(Ishii et al., 2009).

Delivery Timing: Delivery is recommended between **34+0 and 35+6 weeks**, as long as fetal well-being is maintained. ("Multifetal Gestations," 2021). In the presence of obstetric indications, earlier delivery may be required regardless of gestational age.

Type 2 and Type 3 sFGR

After diagnosis, **weekly ultrasound assessments** (UA Doppler, MCA Doppler, DV Doppler) and **biophysical profile evaluations** (starting at 28 weeks) should be performed. In cases of **fetal deterioration**, fetal intervention may be preferred. If fetal death occurs, this may cause **acute transfusion** and **volume shifts** that can lead to neurological damage or death in the surviving fetus (Gratacós et al., 2004)(van Klink et al., 2015). Based on gestational age and fetal deterioration, **delivery** or **fetoscopic interventions** can be considered. After **cord occlusion**, fetal death of the sFGR fetus is certain. Although fetal death may occur after **fetoscopic laser ablation**, the risk of neurological damage in the healthy fetus is reduced with both procedures. In **pre-viable pregnancies**, fetal intervention can be considered in Type 2 or Type 3 sFGR cases with venous Doppler abnormalities or oligohydramnios. Selective fetal reduction (cord occlusion) or **fetoscopic laser technique** can be performed (Parra-Cordero et al., 2016)(Bebbington et al., 2012)(Monaghan et al., 2019). After **cord occlusion**, follow-up is continued as in singleton pregnancies. If the sFGR fetus dies after

fetoscopic laser treatment, follow-up continues as a singleton pregnancy. If both fetuses survive, follow-up is conducted as in **dichorionic-diamniotic pregnancies**.

In **viable pregnancies**, if **progressive reversed flow in UA Doppler**, DV Doppler > 95th percentile, or **oligohydramnios** occurs, ultrasound and biophysical profile assessments should be performed **2-3 times per week**. Hospitalization and daily monitoring should be considered (Weisz et al., 2011).

Delivery Timing:

In the case of **absent end-diastolic flow** in UA Doppler, delivery should be considered between **32+0 and 34+0 weeks**. In the presence of **reversed end-diastolic flow**, delivery should be considered between **30+0 and 32+0 weeks**. In the presence of obstetric indications, earlier delivery may be planned. Some sources recommend delivery at **32+0 weeks** for pregnancies with **Type 2 or Type 3 sFGR** but reassuring fetal well-being (Bennasar et al., 2017)(Shinar et al., 2021). **Corticosteroids** should be administered before planned delivery. If a delivery indication arises earlier than planned, corticosteroid administration should not be overlooked.

Management of the Surviving Fetus After the Death of a Co-Twin

In **monochorionic twins**, complications observed after the death of one twin include: Death of the surviving twin (**15%**), Preterm delivery (**68%**), Postnatal detection of cranial damage in the surviving twin (**34%**), Neurodevelopmental disorders in the surviving twin (**26%**). These complications are significantly less

common in **dichorionic twins** following the death of one twin, with rates of **3%**, **54%**, **16%**, and **2%**, respectively (Shek et al., 2014).

In monochorionic twins, when one fetus dies, **blood loss** from the surviving fetus to the dead fetus occurs. This leads to **hypotension** in the surviving fetus, which can subsequently cause **hypoperfusion, brain damage,** and **death** in the surviving twin (Khalil et al., 2016).

Key Considerations for Management in Monochorionic Pregnancies After the Death of One Twin

Anemia Assessment: Anemia in the surviving fetus should be evaluated using **MCA-PSV measurements**.

Conservative Management: Emergency delivery is **generally not indicated**. This is because neurological damage has often already occurred by the time fetal death is detected. Emergency delivery is unlikely to prevent neurological damage. Parents should be informed in detail about the situation, and long-term **neurodevelopmental problems** should be discussed.

Delivery Timing: If the pregnancy is already at term **from an obstetric perspective**, delivery should be planned. In early gestational weeks, **conservative management** should be considered (Khalil et al., 2016).

Prognosis

Type 1 sFGR has a better prognosis compared to other types. The risks of **fetal death, neonatal death**, and **cerebral damage** are lower. Twin pregnancies with Type 1 sFGR often deliver at a later gestational age and more safely compared to Type 2 and Type 3 sFGR (el Emrani et al., 2022).

In terms of overall survival rates, the reported rates for **Type 1, Type 2, and Type 3 sFGR** are **96%, 55%, and 83%, respectively** (Couck et al., 2020).

Meta-analyses indicate that the **long-term neurodevelopmental impact** of sFGR carries a **higher risk** compared to uncomplicated monochorionic and dichorionic twins. Additionally, the smaller fetus in pregnancies diagnosed with sFGR has an even higher risk (Couck et al., 2020; Groene et al., 2019).

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CHAPTER V

Twin-To-Twin Transfusion Syndrome

Gizem AKTEMUR[5]

INTRODUCTION:

Placental anastomoses occur in monochorionic twin (MC) pregnancies as a result of shared placental tissue. This results in disparities in blood circulation among the fetuses. Monochorionic twins have risks of issues associated with elevated maternal and fetal morbidity and mortality, including twin-to-twin transfusion syndrome (TTTS), twin anemia polycythemia sequence (TAPS), twin reversed arterial perfusion (TRAP), and selective intrauterine growth retardation (sFGR). Consequently, serial sonographic evaluations should be conducted biweekly commencing at the 16th week in all twin pregnancies with a monochorionic placenta. This section will assess the diagnosis and therapy of TTTS, TAPS, and TRAP. Methods for monitoring these complications comprise

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expectant management, fetoscopic laser coagulation, amnioreduction, and selective feticide. Treatment choices are contingent upon the patient's symptoms of polyhydramnios (such as respiratory distress and preterm uterine contractions), cervical length (less than 25 mm), and gestational age at the time of diagnosis. In all complex monochorionic twin pregnancies, parents should receive thorough education about the disease's natural history, therapeutic choices, and associated dangers.

DEFINITION:

In monochorionic twin pregnancies, two distinct fetuses share a single placenta. All monochorionic pregnancies exhibit vascular anastomoses in the placenta that link the circulatory systems of the two fetuses. These anastomoses induce imbalances in fetal blood flow. Consequently, hypovolemia manifests in one fetus (the donor fetus) and hypervolemia in the other (the receiver fetus). The initial manifestation of this disease, known as TTTS, is oligohydramnios in the donor fetus and polyhydramnios in the recipient fetüs (Zhao et al., 2013).

TTTS is categorized based on the Quintero staging system. Stage 1 involves the occurrence of oligohydramnios in one fetus (donor twin) and polyhydramnios in the other. If the bladder of the donor twin cannot be checked, this condition is classed as Stage 2. If one of the twins exhibits a decline in Doppler characteristics (loss of flow/reversal in end diastolic flow, reversed) A wave in the ductus venosus and pulsatile flow in the umbilical vein classify it as Stage 3. Hydrops in one twin is categorized as Stage 4, whereas cessation of the heartbeat is defined as Stage 5 (Quintero et al., 1999).

PREVALENCE:

Twin-to-twin transfusion syndrome (TTTS) manifests in up to 15% of monochorionic diamniotic twin gestations (Sebire, Snijders, Hughes, Sepulveda, & Nicolaides, 1997). TTTS occurs in approximately 2-4% of monochorionic monoamniotic twins, as 98% of these pregnancies exhibit bidirectional arterioarterial anastomoses, which are recognized as protective against TTTS ('Monochorionic Monoamniotic Twin Pregnancies - ScienceDirect', n.d.). Timely identification of TTTS is crucial, as perinatal survival rates are 30% when untreated at stage 2 or above (Berghella & Kaufmann, 2001). Consequently, the assessment of amniotic fluid and the monitoring of fetal biometry are crucial beginning at the 16th week in monochorionic twin gestations (Oepkes & Sueters, 2017).

PATHOPHYSIOLOGY:

The pathophysiology of TTTS involves multiple intricate pathways, including vascular endothelial growth factor (VEGF), the renin-angiotensin-aldosterone system (RAAS), and hypoxia-inducible factor (HIF), rendering the physiological alterations of this disease challenging to elucidate (Kajiwara, Ozawa, Wada, & Samura, 2022). There are four classifications of placental anastomoses: arteriovenous (AV), venoarterial (VA), arterioarterial (AA), and venovenous (VV), with the first type designating the donor fetus and the second type designating the recipient fetus. The precise pathophysiology of TTTS remains unexplained; nonetheless, the type, quantity, and width of these anastomoses are significant in the progression of the disease (Zhao et al., 2013). A greater quantity of AA anastomoses seems to confer protection against TTTS (Umur, van Gemert, Nikkels, & Ross, 2002).

DIAGNOSIS:

TTTS is identified through ultrasound examination. In TTTS, one fetus experiences hypovolemia (donor), while the other exhibits hypervolemia (receiver). The initial indication of this disease is oligohydramnios (deepest vertical pocket <2 cm) resulting from donor RAAS activation (Mahieu-Caputo et al. 2000), in the recipient twin, polyhydramnios (deepest vertical pocket > 8 cm) arises from RAAS suppression caused by elevated secretion of atrial natriuretic peptide and brain natriuretic peptide due to hypervolemia (Bajoria, Ward, & Chatterjee, 2002). In advanced phases, there exists a danger of intrauterine growth restriction in the donor twin and cardiac failure or hydrops secondary to hypervolemia in the recipient twin (Oepkes & Sueters, 2017).

TREATMENT:

Advising parents regarding TTTS treatment presents a challenging scenario for obstetricians due to limited treatment alternatives, ambiguous success rates, and complex post-treatment follow-ups. T TTS monitoring encompasses the expectant approach, fetoscopic laser coagulation, amnioreduction, and selective feticide alternatives. The gestational age at diagnosis and symptoms associated with polyhydramnios (including respiratory distress or preterm contractions) or cervical length are critical factors in determining treatment options.

1.Fetoscopic Laser Ablation:

Despite the deep location of placental anastomoses within the placenta, their afferent and efferent branches are situated superficially. The Solomon approach, a preferred method for laser

ablation, involves identifying the placental equator and coagulating all visible anastomoses on the placental surface. Following the removal of the laser, amnioreduction is conducted until the amniotic fluid levels normalize. Excessive fluid consumption should be avoided due to the potential danger of placental abruption (Leung, Jouannic, Hyett, Rodeck, & Jauniaux, 2004). The most prevalent problems following laser treatment include preterm premature rupture of membranes (PPROM), twin anemia-polycythemia sequence (TAPS), and intertwin membrane rupture. Intraamniotic bleeding and fetal demise may also transpire. Uncommon problems encompass amniotic fluid leakage into the maternal peritoneal cavity; however, this is typically mitigated by analgesic management. In laser-treated TTTS cases, the perinatal mortality rate ranges from 30% to 50%, with long-term neurological problems occurring in 5% to 50% of cases.

2.Amnioreduction:

The procedure involves the extraction of amniotic fluid to alleviate uterine pressure resulting from polyhydramnios. Amnioreduction is advised until the amniotic fluid normalizes; nevertheless, draining more than 5 liters poses a risk of placental abruption (Leung et al., 2004).

3.Selective Fetal Reduction:

Coagulation of the umbilical cord to terminate one twin is a viable technique that may enhance the prognosis for the surviving twin. Despite the availability of techniques like laser cord coagulation and bipolar cord coagulation, radiofrequency ablation may be favored owing to its minimal maternal risks (Rahimi-Sharbaf, Ghaemi, Nassr, Shamshirsaz, & Shirazi, 2021). For

reduction, a fetus with a diminished likelihood of life, such as a donor fetus exhibiting developmental delay or a recipient fetus presenting with heart anomalies or hydrops, should often be chosen.

In Stage 1 TTTS; occurring from 16 to 26 weeks, if asymptomatic, expectant management is advised. During follow-up, the patient should be assessed weekly for amniotic fluid volume and biweekly for fetal biometry (Nassr et al., 2023). In instances of selective intrauterine growth restriction, Doppler parameters must be assessed. Beginning in the 16th week, the peak systolic velocity of the middle cerebral artery (MCV PSA) should be assessed for potential twin anemia polycythemia syndrome (TAPS). In the absence of difficulties necessitating early birth, it is advised that delivery occur between 34 and 37+6 weeks of gestation.

In cases of Stage 1 Twin-to-Twin Transfusion Syndrome (TTTS) occurring from 16 to 26 weeks of gestation, accompanied by symptoms or a cervical length of less than 25 mm, fetoscopic laser ablation is advised (Wagner et al., 2009). Weekly ultrasound examinations are advised for two weeks post-laser surgery, followed by biweekly assessments until the 30th week (Khalil et al., 2016). The donor's amniotic fluid is anticipated to regenerate in the fifth week post-treatment, while the recipient twin's amniotic fluid is projected to recover in the eighth week (Assaf, Korst, & Chmait, 2010). Given that TAPS may manifest within the initial six weeks post-laser surgery, it is imperative to do MCA-PSV measurements alongside assessments of amniotic fluid and biometry in fetuses.

In stage 1 TTTS, post 26 weeks; amnioreduction may be advised if symptoms are present or if cervical length is diminished (<25 mm). Corticosteroids must be provided before lung maturation.

Amnioreduction may be performed again if polyhydramnios is symptomatic.

For patients with Stage 2-4 TTTS; fetoscopic laser ablation is advised between 16 and 26 weeks of gestation. Laser intervention is preferable due to a diminished likelihood of surviving without neurological problems in infants who endure post-amnioreduction (‘Interventions for the Treatment of Twin-Twin Transfusion Syndrome - PubMed’, n.d.).

In stages 2-4 of TTTS, amnioreduction may be favored post 26 weeks. The FDA restricts fetoscopic laser ablation after the 26th week of gestation due to technical challenges, including compromised image quality from vernix and complications in coagulating thicker fetal arteries; yet, some publications advocate for laser use after this gestational period (Valsky et al., 2012; Zhao et al., 2013). The prenatal monitoring and birth schedule are identical to those for stage 1 TTTS patients.

In Stage 5 TTTS, the potential impact on the brain of one fetus due to the demise of the other necessitates that the danger of consequences from preterm be disregarded at this juncture. Amnioreduction or laser therapy is not advised at this juncture. Fetal anemia must be assessed with MCA PSV in the viable fetus; the prognosis is comparatively more favorable in fetuses devoid of anemia (Shek, Hillman, & Kilby, 2014). Intrauterine transfusion may be scheduled for anemic fetuses within the initial 24 hours (Quarello et al., 2008).

CONCLUSION:

TTTS is a pathological disease resulting from vascular anastomoses in monochorionic placentas that lead to imbalanced blood flow among fetuses. This condition, characterized by oligohydramnios in the recipient fetus and polyhydramnios in the donor twin, is detected via ultrasonography. This syndrome may result in heart failure in the receiver fetus and developmental delays in the donor fetus during later stages, potentially leading to the demise of one or both twins. Furthermore, the loss of one twin may lead to the other twin developing a neural developmental abnormality. Follow-up for TTTS encompasses expectant care, fetoscopic laser coagulation, amnioreduction, and selective feticide; nonetheless, death and morbidity rates remain elevated after intervention. In pregnancies monitored for TTTS, parents must be thoroughly educated about treatment options, outcomes, and potential consequences.

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CHAPTER VI

Twin Anemia-Polycythemia Sequence and Twin Reversed Arterial Perfusion Clinical Characteristics and Management

Nurten ÇİLEK[6]

TWİN ANEMİA-POLYCYTHEMIA SEQUENCE

DEFINITION:

TAPS is a complication of monochorionic twin pregnancies marked by hemoglobin incompatibility between the twins. This phenomenon arises from the uneven and sluggish circulation of red blood cells through arteriovenous (AV) anastomoses measuring less than 1 mm (E. Lopriore et al., 2007; Moaddab et al., 2016). This asymmetrical flow results in a hemoglobin disparity between the twins over time, leading to anemia in one twin and polycythemia in the other. Complications in monochorionic twins are challenging to

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diagnose due to their potential occurrence simultaneously or in various combinations.

TYPES OF TAPS:

1.Spontaneous:

It pertains to a variant of chronic TTTS characterized by small-diameter AV anastomoses. It has been identified in 3-6% of simple third trimester monochorionic diamniotic twin pregnancies (Kanagaretnam, Nayyar, & Zen, 2021; Lisanne S. A. Tollenaar et al., 2021).

2.Post-laser ablation:

It is a complication that occurs after laser ablation used in the treatment of TTTS. It occurs in 3-12% of pregnancies that undergo laser ablation, usually 1 month after the procedure (Robyr et al., 2006; Lisanne S. A. Tollenaar et al., 2020). The vast variations in incidence are believed to result from the diverse laser methods employed. Risk factors include a limited number of anastomoses and the absence of arterio-arterial (AA) anastomosis prior to laser ablation (Donepudi et al., 2016).

PATHOPHYSIOLOGY:

All monochorionic twin pregnancies exhibit arteriovenous (AV), arterioarterial (AA), and venovenous (VV) anastomoses inside the placenta. AV anastomoses are unidirectional, whereas AA and VV anastomoses are bidirectional (Zhao et al., 2013). In spontaneous TAPS, the placenta has 3-4 <1 mm AV anastomoses, which facilitate a bidirectional imbalanced flow of roughly 5-15 ml per hour from the donor fetus to the recipient fetus. This results in a hemoglobin imbalance between the two fetuses (Robyr et al., 2006).

The donor twin develops anemia, resulting in hydrops, while the recipient twin becomes polycythemic, leading to fetal and placental thrombosis (Assaf, Benirschke, & Chmait, 2011; Enrico Lopriore et al., 2009). The gradual flow resulting in the existing disease facilitates compensation on the placental fetal side. This does not induce oligohydramnios or polyhydramnios as shown in TTTS (E. Lopriore et al., 2008). Moreover, the limited quantity of AA anastomoses and their diminutive size (<1 mm) significantly contribute to the pathogenesis of TAPS. A crucial observation is that in monochorionic twins without TAPS, whereas the smaller twin had a comparably smaller placental segment, the donor fetus in TAPS has a greater placental burden (Lisanne S. A. Tollenaar et al., 2021).

The pathophysiology of TAPS following laser ablation is attributed to partial ablation and several minor anastomoses of less than 1 mm. These are generally arteriovenous anastomoses. The persistent sluggish flow via the remaining anastomoses results in a progressive hemoglobin gradient, akin to the pathophysiology of spontaneous TAPS (Robyr et al., 2006). In these pregnancies, the receiver twin develops anemia prior to ablation for TTTS, but the donor twin exhibits polycythemia. This indicates that the blood flow in the remaining anastomoses is inverted (Assaf et al., 2011; Enrico Lopriore et al., 2009).

CLINICAL PRESENTATION:

In clinical practice, all monochorionic twins must be followed for the onset of TTTS, TAPS, and Sfgr. The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) and the Society for Maternal-Fetal Medicine recommendations advocate for biweekly monitoring of TAPS, akin to TTTS, utilizing MCA-

PSV commencing at the 16th week of gestation (Khalil et al., 2016; Society for Maternal-Fetal Medicine (SMFM) et al., 2024). TAPS is a complication that should be suspected in case of discordance in MCA-PSV measurements. In a fetus, discordance in placental echogenicity and cardiomegaly may be observed.

DIAGNOSTIC CRITERIA:

Diagnosing this issue with ultrasonography is challenging because to its similarity to TAPS, TTTS, and sFGR, which often coexist and do not rule out any of these conditions. Furthermore, to validate the diagnosis, cordocentesis must be conducted on both infants, and hemoglobin levels should be presented. TAPS is anticipated antenatally when one twin exhibits an MCA-PSV value beyond 1.5 multiples of the median (MoM) whereas the other twin presents with a value below 0.8 MoM (Slaghekke et al., 2015). The primary supporting finding is the variation in placental echogenicity. It is the most prevalent corroborative evidence. The placenta of the anemic donor is thicker and hyperechoic, whereas the placenta of the recipient twin is normal, exhibiting a clear differentiation between the two (Bamberg, Diemert, Glosemeyer, & Hecher, 2018). Cardiomegaly, tricuspid regurgitation, and/or hydrops may be observed in the donor twin as secondary manifestations of anemia. The recipient twin may exhibit an ultrasound finding known as 'Starry sky liver,' characterized by diminished echogenicity of the liver parenchyma and the presence of bright echogenic patches posteriorly (Lisanne S. A. Tollenaar et al., 2020). MCA Doppler discordance between twins is considered a more reliable indicator for diagnosing TAPS than the distinct lines of MCA-PS (Fishel-Bartal et al., 2016; L. S. A. Tollenaar et al., 2019).

STAGING:

Conventional staging system (mostly reliant on MCA-PSV thresholds):

Stage 1: Donor twin MCA-PSV exceeds 1.5 MoM, recipient twin is below 1.0 MoM, with no additional indicators of fetal distress.

Stage 2: Donor MCA-PSV >1.7 MoM, recipient twin <0.8 MoM, without additional indicators of fetal distress

Stage 3: Stage 1 or 2 plus donor cardiac compromise by any of the following:

Umbilical artery (UA): Absent or reversed end-diastolic velocity

Ductus Venosus (DV): Increased pulsatility index or reversed flow

Stage 4: Stage 1 or 2 plus donor hydrops

Stage 5: Demise of one or both fetuses preceded by TAPS

Novel staging mechanism (predominantly founded on intertwin MCA-PSV discordance):

Stage 1: Delta MCA-PSV >0.5 MoM; absent indications of fetal distress

Stage 2: Delta MCA-PSV >0.7 MoM; absent indications of fetal distress

Stage 3: Stage 1 or 2 delta MCA-PSV results combined with cardiac impairment in either the donor or recipient fetus, indicated by aberrant Doppler flow tests in the umbilical artery or ductus

venosus, or the presence of hydrops fetalis, primarily in the donor fetus.

Stage 4: Demise of one or both fetuses preceded by TAPS

(DV: ductus venosus; MCA-PSV: middle cerebral artery peak systolic velocity; MoM: multiples of the median; TAPS: twin anemia-polycythemia sequence; UA: umbilical artery).

DIFFERENTIAL DIAGNOSIS:

MCA-PSV discordance indicates TAPS and is absent in pure TTTS. Amniotic fluid discordance (oligohydramnios and polyhydramnios sequence) is critical in pure Twin-to-Twin Transfusion Syndrome (TTTS) but absent in pure Twin Anemia-Polycythemia Sequence (TAPS). Spontaneous TAPS is discovered between 14 and 35 weeks of gestation, whereas TTTS is usually identified in the early to mid-second trimester (Lisanne S. A. Tollenaar et al., 2021; Weingertner et al., 2010).

Postnatally, a reticulocyte ratio between twins over 1.7 is necessary for the diagnosis of TAPS, as a significant hemoglobin disparity at birth may indicate acute peripartum TTTS instead of TAPS. Accurate diagnosis is crucial as anemia resulting from TAPS is generally euvolemic, while anemia in peripartum TTTS need prompt rectification of hypovolemia (Lisanne S. A. Tollenaar et al., 2017).

PROGNOSIS:

TAPS resolves spontaneously in 16% of instances. In certain instances, it is feasible to achieve the birth of two healthy neonates by techniques like blood transfusion. Additional significant parameters are difficulties that may arise as a consequence of brain

injury and the demise of one of the twins (Lisanne S. A. Tollenaar et al., 2020). These pregnancies exhibit an elevated risk of fetal demise, neonatal demise, significant neonatal and neurodevelopmental morbidity, and preterm labor (Giorgione, D'antonio, Manji, Reed, & Khalil, 2021).

PREGNANCY MANAGEMENT:

TAPS does not entail an elevated risk for chromosomal, genetic, or structural anomalies. Consequently, it does not warrant the provision of genetic diagnostic alternatives to patients.

Stage 1 TAPS; <32 weeks : Weekly Doppler evaluation to determine stage progression. If there is no progression or resolution, deliver between 34 weeks and 37 weeks of gestation. Complex situations are addressed within the initial 10 days of this period, while simpler instances are managed in the final 10 days. In the event of progression, manage in accordance with the stage and gestational age, as delineated below.

Stage 2 TAPS; <32 weeks: Administer prenatal corticosteroids between 24+0 and 32+0 weeks of gestation to mitigate neonatal hazards associated with premature birth. Doppler assessments conducted biweekly to evaluate for persistence or progression, indicated by the emergence of fetal heart failure and secondary symptoms of TAPS, such as discordant placental echogenicity and starry liver. If stage 2 TAPS resolves, provide delivery between 34+0 weeks and 37+0 weeks of gestation. Complex situations are addressed in the initial 10 days of this period, while simpler instances are managed in the final 10 days. If stage 2 TAPS endures for over one to two weeks or advances while the pregnancy is under 32 weeks, handle it as stage 3 or 4 TAPS. If stage

2 TAPS continues for over one to two weeks or worsens while the pregnancy is between 32 to 34 weeks, proceed with delivery.

Stage 3 or 4 TAPS <32 weeks: No consensus exists on the appropriate treatment; expectant management, laser surgery, in utero transfusion, selective feticide, and early birth have all been employed (Lisanne S. A. Tollenaar et al., 2020, 2021).

In cases of post-laser ablation TAPS occurring within two weeks of the treatment, pregnancy termination should be contemplated due to the unfavorable prognosis; alternatively, a second laser procedure may be performed up to 28+0 weeks of gestation (Baud et al., 2013; Valsky et al., 2012).

A subsequent laser surgery may frequently be challenging due to hemorrhagic amniotic fluid resulting from the first intervention. Amnioinfusion and/or amnioreduction may enhance the visibility of delicate anastomoses across the intertwin membrane.

For spontaneous TAPS prior to 28+0 weeks, fetoscopic laser ablation is likely the optimal choice. The anemic fetus may receive a transfusion of red blood cells. Both intravenous (IV) and intraperitoneal (IP) transfusions are viable techniques for rectifying fetal anemia. We favor IP transfusion as the gradual absorption of red blood cells associated with this method may better replicate fetal physiology. A dual technique is occasionally employed: intravenous transfusion to rectify severe anemia, alongside intraperitoneal transfusion of a portion of the blood for gradual absorption, hence reducing the necessity for frequent multiple transfusions. Following treatment, we do weekly ultrasounds until the resolution of TAPS and deliver these pregnancies between 34+0 and 37+0 weeks of

gestation. In cases of suspected cerebral lesions, we conduct fetal MRI.

For spontaneous or post-laser ablation TAPS occurring between 28+0 and 32+0 weeks of gestation, either of two alternatives is acceptable. Certain clinics administer red blood cell transfusions to anemic fetuses, while others conduct fetal transfusions for the anemic fetus in conjunction with partial exchange transfusions for the polycythemic twin to potentially mitigate issues related to hyperviscosity. In these instances, 5 mL aliquots of blood are extracted and substituted with equivalent quantities of sterile saline. Subsequent MCA-PSVs determine the necessity for repeat transfusions or partial exchanges.

Following treatment, we conduct weekly ultrasounds until TAPS resolution and deliver these pregnancies between 34+0 and 37+0 weeks of gestation. In cases of suspected cerebral lesions, we conduct fetal MRI.

TWİN REVERSED ARTERİAL PERFUSİON (TRAP) SEQUENCE:

INTRODUCTION:

Twin reversed arterial perfusion (TRAP) sequence is an uncommon complication of monochorionic twin pregnancies, characterized by one twin possessing a non-functional heart (acardiac twin). The pump is completely perfused retrogradely by the twin due to aberrant aortic anastomoses. Acardiac twins generally exhibit many malformations, including the absence of a head. None of the acardiac twins possess viability.

If the acardiac twin exceeds the size of the pump twin, the pump twin faces the risk of cardiac failure. If untreated, cardiac failure and other issues may arise, potentially resulting in preterm labor and the demise of a healthy fetus.

INCIDENCE:

The incidence is estimated at 2.6% in monochorionic twin pregnancies and 1 in 9,500 to 11,000 in general pregnancies (van Gemert, van den Wijngaard, & Vandenbussche, 2015). Triplets are exceedingly uncommon in monochorionic or multiple gestations. 11 cases have been reported in the literatüre (Pan et al., 2017).

PATHOPHYSIOLOGY:

Normal fetal circulation: In typical fetal circulation, substantially oxygenated blood is sent to the fetal liver through the umbilical vein. The ductus venosus channels 80% of this blood flow to the inferior vena cava, facilitating its circumvention of the liver and its amalgamation with venous blood from the lower extremities and kidneys before to entering the right atrium. The umbilical artery, derived from the internal iliac arteries, transports relatively deoxygenated blood to the placenta, while the more robust umbilical vein returns it to the fetus.

Fetal circulation in TRAP: In the TRAP sequence, the pump twin sustains the aforementioned normal circulation. Furthermore, a segment of the cardiac output traverses one or more AA anastomoses with the twin, generating a retrograde flow that directs deoxygenated blood into one or both umbilical arteries and reintroduces it into the twin's systemic circulation (‘Placental Pathology in Trap Sequence:

Clinical and Pathogenetic Implications - PubMed', n.d.; van Gemert, Ross, Nikkels, & Wijngaard, 2016).

PATHOGENESIS:

The etiology of the TRAP sequence remains unidentified. One hypothesis posits that early atypical development of the AA anastomoses causes retrograde flow of deoxygenated blood from one twin to the other, resulting in aberrant cardiac development in the recipient twin. Another idea posits that poor cardiac development in one twin results in diminished systemic arterial pressure, subsequently causing retrograde blood flow from the other twin via AA anastomoses. Regardless of the etiology, one of the twins is unequivocally acardiac and relies on the retrograde blood flow from the pump twin for circulatory support from the early stages of the first trimester. The reverse circulation of deoxygenated blood from the pump twin can induce many abnormalities in the acardiac twin (Van Allen, Smith, and Shepard 1983). For instance, the acardiac twin's lower half predominantly relies on the circulatory support from the pump twin, resulting in necrotic or underdeveloped upper extremities and head, while the bottom extremities and abdomen are generally well developed.

DIAGNOSIS:

In a pregnancy with monochorionic multiples, the presence of the TRAP sequence should be considered in the absence of cardiac activity in a fetus, accompanied by extensive skin edema and multiple abnormalities, particularly affecting the cranium and/or upper extremities. This can be classified as a monochorionic twin pregnancy in which one twin succumbed during the first trimester.

Nevertheless, the surviving twin will have developed during the follow-up period.

The diagnosis is validated by the presence of blood in the umbilical artery of the acardiac twin, directed towards the acardiac twin, as evidenced by color Doppler imaging (Benson, Bieber, Genest, & Doubilet, 1989). The manifestation of this reverse current is characteristic of the TRAP sequence and must be exhibited (Bornstein, Monteagudo, Dong, Schwartz, & Timor-Tritsch, 2008).

The spectrum of ultrasound findings in TRAP sequence include:

An acardiac fetus invariably exhibits aberrant morphology, which varies significantly: May present as an amorphous tissue mass, without identifiable fetal components or heart - either absent or present as a basic pumping component.

Head: Absent or present with major defects (eg, anencephaly, holoprosencephaly, other major neuroanatomic malformations) and/or severe edema.

Extremities: The lower extremities are more prone to development than the upper extremities. When extremities are observed, they are usually swollen. Lower extremities partially or totally missing limbs, widely spaced bones or joints. Upper extremities: more likely to be totally missing than lower extremities; when present, often poorly developed.

Pelvis and abdomen: Often underdeveloped.

Viscera: Lungs, kidney, spleen, and/or liver may be present, underdeveloped, or absent.

Umbilical cord: Contains only two vessels in 70 percent of cases. The cord is typically very short, limiting fetal movement (Benson et al., 1989).

Pump fetus: Generally has normal morphology, but heightened risk for congenital abnormalities, especially cardiovascular defects.

May exhibit indications of high-output cardiac failure, directly correlated with the relative size of the acardiac twin (‘Placental Pathology in Trap Sequence: Clinical and Pathogenetic Implications - PubMed’, n.d.). Indicators of manifest or progressing heart failure may encompass:

Polyhydramnios, cardiomegaly, pericardial effusions, pleural effusions, ascites, subcutaneous edema/anasarca, hydrops fetalis, tricuspid regurgitation.

POSTDIAGNOSTIC EVALUATION:

The initial actions to undertake include assessing the anatomical development of the two fetuses, identifying amniocentesis, evaluating the volume of amniotic fluid, conducting a fetal echocardiogram of the pump twin, performing diagnostic genetic testing, executing Doppler measurements to demonstrate reverse flow, and calculating the estimated fetal weights of the acardiac and pump twins, along with determining the acardiac: pump twin weight ratio.

Fetal genetic testing should be provided to these pregnant mothers because of the heightened risk of aneuploidy. Numerous autosomal trisomies and sex chromosomal aneuploidies have been documented (Blaicher, Repa, & Schaller, 2000; Rehder et al., 2012).

Acardiac: the pump twin weight ratio is a critical component. The pump twin is assessed based on standard criteria. Multiple formulas exist for acardiac twins. These formulas are predicated on the measurement of their lengths in three dimensions (such as; Weight (grams) = [(-1.66) x (longest length [cm])] + [(1.21) x (longest length [cm])2]).

PROGNOSIS WITHOUT INTERVENTION:

The acardiac twin is incapable of surviving outside the uterus. The pump twin faces a significant risk of perinatal mortality due to heart failure, potentially resulting in pregnancy loss at any trimester, and/or the consequences of preterm birth, which may be medically indicated or occur naturally due to preterm premature rupture of membranes (PPROM) or preterm labor associated with uterine overdistention and/or other less clearly defined factors.

For the pump twin, one or more of the following characteristics elevate the mortality risk to over 50 percent (Brassard, Fouron, Leduc, Grignon, & Proulx, 1999; Moore, Gale, & Benirschke, 1990). The interpretation of these data is constrained, as one series documented instances from almost thirty years ago, while another series included just a restricted number of well managed cases (Moore et al., 1990; Quintero et al., 2006).

High-output cardiac failure; indicators of progressing or manifest heart failure may encompass cardiomegaly, tricuspid regurgitation, reduced contractility, and/or inverted a-wave in the ductus venosus or umbilical vein pulsations observed through Doppler investigations and echocardiography.

Hydrops fetalis; pump twin anomaly Doppler investigations indicate consistently absent or reversed end-diastolic velocity in the umbilical artery (AEDV, REDV), pulsatile blood flow in the umbilical vein, and/or a reversed a-wave in the ductus venosus Doppler waveform, potentially signifying developing or manifest heart failure.

The weight ratio of the acardiac twin to the pump twin exceeds 0.70. In one study, when this ratio exceeded 0.70, the odds of heart failure, preterm birth, and polyhydramnios were 30%, 90%, and 40%, respectively. In contrast, when this ratio fell below 0.70, the odds of heart failure, preterm birth, and polyhydramnios were reduced to 10, 75, and 30 percent, respectively.

Polyhydramnios.

Monoamniotic pregnancy.

PREGNANCY MANAGEMENT:

Counseling and referral: Upon diagnosis of TRAP sequence, patients should be directed to a specialized fetal diagnosis and therapy center experienced in managing such pregnancies for further evaluation and discussion of prognosis and therapeutic measures. For ongoing pregnancies, these techniques encompass expectant care and/or ligation of the umbilical chord of the acardiac twin. Cord occlusion provides a superior prognosis compared to expectant care in pregnancies exhibiting one or more adverse prognostic indicators.

If referral to a facility offering acardiac twin cord occlusion is unfeasible, amnioreduction can address polyhydramnios (if present) and mitigate its repercussions (e.g., preterm birth, preterm prelabor rupture of membranes [PPROM]). Nevertheless, it is a

provisional solution that fails to tackle the fundamental TRAP pathophysiology. A referral to a fetal therapy clinic proficient in cord occlusion treatment is strongly advised. Patients may also be presented with the option of pregnancy termination during counseling.

Fetal monitoring: There are no substantial data to support a specific evidence-based surveillance method for monitoring pregnancies affected by TRAP sequence. Consultation or co-management with a centre with expertise in TRAP assessment and management is recommended wherever possible, as this can assist in formulating monitoring measures.

According to our clinical experience; monitor twin weights and acardiac pump twin weight ratios every three weeks, commencing in the midtrimester.

The pump twin should be monitored weekly for signs of evolving or overt failure starting at 16 weeks; however, for a small, stable acardiac twin, biweekly monitoring may be deemed appropriate.

Conduct a weekly biophysical profile assessment during the third trimester.

In the presence of adverse prognostic characteristics, we may enhance second-trimester surveillance to biweekly to optimize the timing of cord occlusion therapy, if preferred. In instances when cord occlusion is recommended but refused or deemed unnecessary, biweekly monitoring can assist in determining the optimal date for delivery after a gestational age conducive to ex utero survival is attained.

Cord occlusion therapy involves the interruption of vascular connections between twins, alleviating the hemodynamic strain on the pump twin that supports its acardiac counterpart. The pump twin is not at heightened risk of ill effects from the demise of the acardiac twin, as all blood is provided by the pump twin and the cord is blocked, unlike the consequences shown in monochorionic twins following one natural mortality.

The objective is to enhance the prognosis of the pump twin, as the acardiac twin lacks the capacity for autonomous survival.

Selection of patients: Cord occlusion therapy is advised for pregnancies affected by TRAP sequence when at least one unfavorable prognostic factor is present. In the absence of any adverse prognostic indicators, expectant management is warranted.

While a ratio of the estimated weight of the acardiac twin to that of the pump twin exceeding 0.70 is recognized as a bad prognosis indicator, numerous facilities currently provide cord occlusion therapy for ratios greater than 0.50 or in cases where there is evidence of a fast enlarging acardiac twin. The decision to intervene must be tailored to the specific clinical findings of the pregnancy, weighing maternal and obstetric risks against the potential benefits for the twin. Local legal rules concerning termination may be a supplementary consideration; however, it is important to emphasize that acardiac twins typically lack both hearts and heads and are universally recognized as having no possibility of surviving outside the uterus. The minimum gestational age for providing cord occlusion is specific to the modality. For instance, laser photocoagulation may be conducted in the late first trimester,

while radiofrequency ablation (RFA) or bipolar coagulation is generally administered during 16 to 18 weeks of gestation.

No consensus exists on a maximum gestational age for cord occlusion; however, around 26 to 28 weeks, it may be prudent to consider birth instead of cord occlusion in cases with pump twin compromise. State and institutional constraints may also limit the gestational age at which cord occlusion therapy is available. It is highly advisable to consult a clinic proficient in TRAP sequence that provides cord occlusion therapy for the evaluation and management of afflicted pregnancies.

The selection of cord occlusion strategy for a particular pregnancy must be tailored according to the operator's expertise, available resources and procedures at the facility, clinical presentation, gestational age, and patient preferences. Modern cord occlusion methods encompass (King et al., 2017; Lee et al., 2007; Ville, Hyett, Vandenbussche, & Nicolaides, 1994).

Contemporary cord occlusion techniques include:

Radiofrequency ablation (RFA)

Bipolar cord coagulation

Laser photocoagulation

In the United States, RFA is the predominant method for cord occlusion. In numerous treatment facilities, RFA and/or bipolar coagulation are designated for pregnancies of at least 16 weeks gestation, ideally 18 weeks or more, owing to apprehensions regarding an increased incidence of procedure-related problems, such as PPROM, with earlier interventions. Proponents of RFA argue that its smaller caliber uterine entry, compared to bipolar

occlusion, may result in a reduced complication rate and thus enhanced efficacy for midtrimester cord occlusion. Nevertheless, insufficient data have not definitively shown enhanced results with RF (Bebbington, Danzer, Moldenhauer, Khalek, & Johnson, 2012; Gaerty, Greer, & Kumar, 2015).

The ideal management of TRAP sequence occurring before 16 to 18 weeks remains ambiguous. Laser photocoagulation of the umbilical arteries in the acardiac fetus may be performed as early as 12 to 14 weeks gestation. At this early gestational stage, ultrasound results may not reliably detect TRAP pregnancies that are at elevated risk of fetal demise, which has been documented to occur suddenly and unpredictably in 33 to 83 percent of these cases (Lewi, Valencia, Gonzalez, Deprest, & Nicolaides, 2010). Although laser photocoagulation may offer a potentially decisive treatment as early as the late first trimester, it has not demonstrated superiority over expectant care until 16 to 18 weeks. An worldwide trial is currently comparing early intervention (13 to 14 weeks) utilizing intrafetal laser under ultrasound guidance with an 18- to 20-gauge needle against later intervention (16 to 19 weeks) employing the same intrafetal ablation technique or fetoscopic laser coagulation. This trial aims to enhance our comprehension of intrafetal laser therapy for TRAP sequence and the timing of intervention (Berg et al., 2014).

COMPLİCATİONS:

Significant maternal complications arising from cord occlusion are infrequent and encompass severe uterine hemorrhage, additional maternal vascular trauma, maternal thermal injury (extremely rare with contemporary RFA grounding pads),

chorioamnionitis (which may result in maternal sepsis), placental abruption, and disseminated intravascular coagulation. Laparotomy may be necessary to address bleeding issues that do not respond to conservative treatment. In the North American Fetal Therapy Network Registry of RFA cord occlusion therapy for TRAP, 98 individuals were found, with no maternal fatalities, no patients need blood transfusions, and the majority of patients being hospitalized for one day or less post-procedure. The predominant obstetric consequence was preterm premature rupture of membranes (PPROM), occurring in 17 pregnancies often within 10 weeks post-procedure (Lee, Bebbington, Crombleholme, & North American Fetal Therapy Network, 2013).

Injury from a pump twin, whether direct or indirect, including perioperative mortality, is a potential risk.

The occurrence of aplasia cutis congenita has been documented as a problem linked to laser photocoagulation; additional research is necessary to assess the frequency of this condition (‘Interstitial Laser Therapy for Fetal Reduction in Monochorionic Multiple Pregnancy: Loss Rate and Association with Aplasia Cutis Congenita - PubMed’, n.d.).

Acardiac twin: A temporary interruption of blood flow to the acardiac twin due to vasospasm, which may subsequently be restored, is feasible, particularly with radiofrequency ablation (RFA). This problem is inadequately described and is hence either exceedingly rare or hypothetical. Nonetheless, it is essential to verify the cessation of umbilical cord blood flow in acardiac twins using color Doppler imaging after cord occlusion and during subsequent sonographic assessment.

Confirmation of the absence of blood flow in the umbilical vessels of the acardiac twin should be conducted via Doppler investigations at the conclusion of the procedure and during subsequent ultrasonography evaluations. Subsequent sonograms of the pump twin should assess: restoration of cardiac function, normalization of Doppler tests (if abnormalities were present prior to treatment), resolution of hydrops (if previously shown), and normalization of amniotic fluid volume (if polyhydramnios was noted).

No consensus or evidence exists to endorse any particular monitoring technique following cord occlusion therapy. Weekly sonograms are advised for several weeks post-RFA until consistent normalization of results is evident. Furthermore, serial examinations of twin growth via ultrasound are necessary approximately every three weeks during pregnancy.

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CHAPTER VII

Triplets and Beyond, Conjoined Twins, Fetus in Fetu

Ahmet Arif FİLİZ[7]

1. Triplets and Beyond

1.1 Introduction

Compared to twin and singleton gestations, triplets and other multiple gestations are associated with a higher risk of neonatal and maternal morbidity. Iatrogenic or spontaneous preterm births are the main cause of the increased neonatal risk: two-thirds of triplet pregnancies end before 34 weeks, compared with one-fifth of twin pregnancies and 2% of singleton pregnancies (Osterman et al. 2023).

1.2 Prevalence

The number of triplets and other multiple births exceeds the normal rate in places where access to medically assisted conception is common. About 80 percent of triplets and higher-order

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multiple births are caused by assisted reproductive technology (ART), particularly in vitro fertilization (IVF). In 2022, there were 78.9 higher-order triplet and multiple births per 100,000 live births in the United States. Due to the transfer of fewer embryos and an increase in fetal reduction procedures, the triplet birth rate in 2022 was the lowest in three decades and about 60% below the 1998 peak (193.5 per 100,000 births) (Anon 2024).

1.3 Clinical Presentation and Diagnosis

The ultrasound examination, which is usually performed to identify the gestational age or cardiac activity of the fetus, forms the basis for the diagnosis of a triplet pregnancy. The use of assisted reproductive technology for conception and/or a uterus that is too large for the gestational age may raise suspicion of a triplet pregnancy (Geipel et al. 2005).

1.4 Counseling

1.4.1 Risks – The fetal, maternal and neonatal risks are increased in these pregnancies. It is important to discuss possible risks (such as fetal growth restriction or discordance, pre-eclampsia and preterm labor,) and how to deal with them. Carrying a triplet pregnancy to term has a greater impact on the mother's underlying medical problems, which are exacerbated by the physiological changes of pregnancy, if present. For example, for pregnant women with certain heart conditions (such as cardiomyopathy or mitral stenosis), a triplet pregnancy can be extremely difficult or even fatal. In singleton pregnancies, the median maternal peak cardiac output is 6.1 L/min at the same gestational age, while the median maternal peak cardiac output in five triplet pregnancies ranged from 32 to 36

weeks were a median of 8.44 L/min (Ladhani et al. 2013; Sanghavi and Rutherford 2014).

1.4.2 Options – The risk of spontaneous preterm birth and various obstetric and neonatal problems is decreased with multifetal reduction. A meta-analysis found that reducing pregnancy from triplets to twins was associated with lower rates of pregnancy loss, preterm birth, cesarean delivery, low birth weight babies and neonatal deaths than expectant management. These rates were comparable to those of twin pregnancies conceived spontaneously (Dodd and Crowther 2003).

1.4.3 Prenatal care – Due to the increased risk of maternal problems, pregnancy requires thorough monitoring of both the mother and the fetus. This includes regular ultrasound examinations to monitor the growth and health of the fetus, as well as frequent visits to the doctor's office, especially after 20 weeks of gestation. Pregnancy problems commonly result in hospitalization during antenatal follow-up (Anon 2021).

1.4.4 Delivery – For triplets and other multipeple gestations, a cesarean delivery is recommended; a vaginal birth should generally be avoided. Given the risk of preterm birth, it is advisable to consider whether it makes sense to plan the birth in a hospital that has a neonatal intensive care unit on the premises (Vintzileos et al. 2005).

1.5 Basic Antepartum Care

1.5.1 Ultrasound examination — The monitoring of triplet pregnancies requires routine ultrasound examinations. Measurement of fundal height and fetal heart rate, which are commonly used to monitor the growth and viability of singleton pregnancies, are not

sufficient to detect problems in triplets. In addition, triplets can only be monitored for complications such as twin-to-twin transfusion and congenital anomalies using ultrasound. In all triplet pregnancies, a thorough ultrasound examination is performed around the 20th week of gestation to assess the fetal anatomy. Because three babies need to be examined, it can be difficult to get a clear anatomical survey of each fetus and may need to be repeated. Also, any abnormalities found need to be matched to the correct fetus, so the examination is more complicated than for singletons.

- ✓ Evaluation of gestational age
- ✓ Assesing chorioamnionicity
- ✓ Screening for congenital anomalies
- ✓ Labeling the triplets

1.5.2 Second- and third-trimester ultrasound monitoring – Chorionicity and amnionicity serve as a basis for the planning and frequency of ultrasound examinations in the second and third trimester.

1.5.2.1 Monochorionic triamniotic and dichorionic triamniotic triplets – The fetuses in a multiple gestation with a common chorionic sac are at risk for TAPS, selective fetal growth restriction and TTTS. The ultrasound procedure is similar to that commonly used to follow pregnancies with monochorionic twins (Simpson 2013).

1.5.2.2 Monochorionic monoamniotic or dichorionic diamniotic triplets – In every multiple gestation with a shared amniotic sac (monoamniotic component), there is a high risk for the umbilical cord entanglement and die due to cord compression for the

fetuses involved. In order to monitor the fetal heart rate for one hour every eight hours, experts advise that patients with this kind of placentation should be hospitalized at 26 weeks of gestation (Dias et al. 2010).

1.5.2.3 Trichorionic triamniotic triplets – Trichorionic triamniotic placentation is associated with better perinatal outcomes than a triplet pregnancy in which the fetuses share a placenta/chorion or amniotic sac. To monitor fetal growth, ultrasound examinations are usually performed every three to four weeks from the 20th week onwards, as growth restriction is still a serious issue. As the placenta is not shared, there is no need to monitor for TTTS and TAPS (Kawaguchi et al. 2013).

1.6 Office visits — In the first half of pregnancy, office visits can be scheduled per usual obstetric follow-up for a singleton. From the 24th week of pregnancy, patients should be examined once a week to monitor them intensively for preterm birth and pre-eclampsia symptoms. However, there is little evidence that weekly visits lead to better outcomes. For trichorionic triamniotic triplets, visits at 20, 24, 28, 32 and 34 weeks have been suggested, and for monochorionic and dichorionic triamniotic triplets at two weeks interval from 20 to 34 weeks. From 34 weeks until delivery, which is usually planned by 35+6 weeks, weekly follow-ups are recommended (Bricker 2014).

1.7 Physical and sexual activity — Due to the lack of conclusive research, there is no agreement regarding physical activity for pregnant women with triplets. In general, recommendations for physical activity are similar to those for pregnant women with singleton gestations, especially before 20

weeks of pregnancy. The uterus reaches a similar size to a singleton pregnancy in the middle to end of the second trimester. Sexual activity does not appear to increase the risk of premature birth, so abstinence is not required (Yost et al. 2006).

1.8 Weight gain — There are no evidence-based guidelines for weight gain and nutrition in triplet pregnancies. The following target values can be use for weight gain during pregnancy, which reflect the upper end of the National Academy of Medicine guidelines for weight gain in twin pregnancies coming to term (Rasmussen and Yaktine 2009):

- Body mass index (BMI) 18.5 to 24.9 kg/m^2 (normal weight) – 25 kg
- BMI 25.0 to 29.9 kg/m^2 (overweight) – 23 kg
- BMI ≥30.0 kg/m^2 (obese) – 19 kg

However, almost no triplet pregnancies reach to term. A more clinically practical recommendation is a maternal weight gain of approximately 0.7 kg per week and >16.2 kg by 24 weeks of gestation, as weight gain below this threshold has been associated with lower birth weight in triplets (Flidel-Rimon et al. 2005).

1.9 Preeclampsia prophylaxis — Low-dose aspirin should be prescribed at 12 to 16 weeks of gestation and continued daily until delivery (Davidson et al. 2021).

1.10 Aneuploidy screening and diagnosis — All patients with a triplet pregnancy must be offered genetic counseling to discuss the risk of aneuploidy in one or more fetuses. The risk of aneuploidy in a trizygotic triplet pregnancy is higher than in a

singleton or dizygotic twin pregnancy, since there are three independent fetal risks for aneuploidy. The trisomy 21 risk of a 28-year-old woman carrying a trizygotic triplet pregnancy is similar to the trisomy 21 risk of a 35-year-old woman carrying a singleton pregnancy. Therefore, the conventional application of advanced maternal age in relation to aneuploidy risk can be considered a maternal age ≥28 years at the estimated time of delivery (Malone and D 2014).

1.10.1 Screening – NT can be used to screen for trisomy 21 and other anomalies, as the distribution of NT measurements in triplets is the same as in singletons. One study (Maslovitz et al. 2004; Sepulveda, Wong, and Casasbuenas 2009) validated increased NT (defined as greater than the 95th percentile for gestational age) as a screening test for trisomy 21 and trisomy 18 in triplets. For triplet pregnancies, certain laboratories now offer commercial cell-free DNA (cfDNA) tests to screen for common fetal trisomies. The sensitivity for trisomy 21 was 100 percent (95% CI 15.8-100) and the specificity was 99.4 percent (95% CI 96.6-100) in a retrospective analysis of 255 triplet pregnancies, 165 of which had a neonatal outcome. Trisomy 18 showed similar results: 100 percent sensitivity (95% CI 2.5-100) and 100 percent specificity (95% CI 97.8-100) (Zakaria et al. 2024).

1.10.2 Fetal diagnosis – Aneuploidy can be diagnosed in utero by means of a chorionic villus sampling (CVS). This procedure is particularly helpful for women with multiple pregnancy who are planning a fetal reduction and have a high age-related risk for fetal aneuploidy. Aneuploid fetuses can be identified and selectively reduced, because the karyotype results are usually

available before reduction through CVS. However, triplet pregnancies are a greater challenge for CVS than singleton pregnancies. Another method for prenatal diagnosis is genetic amniocentesis. The rate of pregnancy loss after process is most likely comparable to the rate after genetic amniocentesis in a singleton pregnancy (Antsaklis et al. 2002; Wapner et al. 1993).

1.11 Screening for neural tube defects — A specific anatomical examination of the neural tube should be carried out on all triplets in the second trimester.

1.12 Screening for gestational diabetes — Pregnancy screening for diabetes can be recommended early (before the 20th week of pregnancy), as there is a higher risk of gestational diabetes in triplet pregnancies than in singleton pregnancies (12.8 and 2.9 percent respectively) and a significant percentage of these patients have insulin resistance associated with polycystic ovary syndrome. In the 24th to 28th week of pregnancy, when screening for gestational diabetes is normally carried out, screening is repeated if the results of the early screening are negative (Weissman and Drugan 2016).

1.13 Antepartum fetal monitoring — The timing and frequency of antepartum fetal monitoring in triplets is not supported by any study. Chorioamnionicity is the basis for fetal testing:

1.13.1 Monochorionic triamniotic and dichorionic triamniotic triplets – Because the shared placenta in all of these pregnancies carries a high risk of fetal problems, needs to be obtained a weekly biophysical profile at 28 weeks' gestation. By being able to identify each fetus, ultrasound circumvents the technical challenges of performing non-stress testing in higher order

multiple pregnancies. Nevertheless, the non-stress test is a suitable substitute (Elliott and Finberg 1995).

1.13.2 Monoamniotic or diamniotic triplets – When the mother is admitted to hospital at around 26 weeks of pregnancy, we recommend that these triplets are monitored three times a day for one hour with continuous fetal heart rate monitoring. Prolonged fetal heart rate monitoring with the biophysical profile facilitates the detection of decelerations that indicate umbilical cord entanglement with cord compression in the shared amniotic sac (Dias et al. 2010).

1.13.3 Trichorionic triamniotic triplets – The biophysical profile score should be assessed weekly from the 32nd week according to indirect findings on dichorionic twins in which the probability of stillbirth increases with increasing gestational age (Cheong-See et al. 2016).

1.14 Monitoring for preterm labor — The most common cause of death and morbidity in triplet pregnancies is preterm birth. In a study including 125 triplet pregnancies, the rates of early preterm birth (<32 weeks: 56 versus 34 percent) and very early preterm birth (<28 weeks: 33 versus 8 percent) were higher in dichorionic triplet pregnancies than in trichorionic pregnancies. In the multivariate analysis, however, chorionicity did not prove to be an independent risk factor for early preterm birth (Levy-Coles et al. 2024).

1.15 Role of sonographic cervical length measurement — Measurements of cervical length is not recommended in triplet pregnancies. In the three retrospective studies that examined this issue, short cervical length was not a

sensitive screening test for predicting preterm birth in triplets, although it is a common screening test for predicting preterm birth in singleton and twin pregnancies (Pils et al. 2017). In none of these studies was a threshold helpful in predicting preterm birth, although the median cervical length was above 30 mm until around 24 weeks and then decreased. Furthermore, the paucity of evidence regarding the effectiveness of any intervention (such as cerclage or progesterone supplementation) to prevent preterm birth in patients with triplets and short cervical length suggests that there is no benefit, unlike in singleton and twin pregnancies (Caritis et al. 2009; Rafael, Berghella, and Alfirevic 2014).

1.16 Potential Complications

1.16.1 Spontaneous fetal reduction — In a significant proportion of triplet pregnancies, one amniotic sac disappears spontaneously during the first trimester; this is known as a "vanishing twin" The initial number of gestational sacs correlates with the rate of loss. In one study of 132 triplet pregnancies detected before 12 weeks gestation, 53% were found to have spontaneous reduction of one or more amniotic sacs and/or embryos, and 6% had loss of all three amniotic sacs. The majority of losses occurred before the ninth week of pregnancy (Dickey et al. 2002).

1.16.2 Risk for preterm birth — The most common cause of death and morbidity in triplet pregnancies is preterm birth. In certain series, iatrogenic preterm births are as common as spontaneous preterm births (Razavi et al. 2017).

1.16.2.1 Potentially useful interventions — Numerous strategies have been investigated to reduce the risk of premature birth. Although none has been shown to be effective, the

administration of magnesium sulfate and prenatal corticosteroid treatment may reduce neonatal morbidity similar to that seen in singleton pregnancies.

- ✓ **Antenatal corticosteroids for fetal maturation** – Since steroids are most effective within the next seven days, we administiration of a course of betamethasone to non-monoamniotic triplets can be considered if the clinical findings indicate a higher risk of birth during this period. For example, to patients with ruptured membranes who are at risk of preterm birth or who develop a maternal or fetal condition that could necessitate a preterm birth within a few days. Since the overall incidence of births within seven days before 32 weeks was less than 10% in one study, routine universal administration of steroids in triplet pregnancies is not justified. As a result, many triplet pregnancies that received early steroid treatment would require repeated treatments to ensure exposure just before birth (Van De Mheen et al. 2016). There is no strong evidence that the dosage of betamethasone should be increased as the number of fetuses increases; standard amounts are administered. If the previous treatment with prenatal corticosteroids was more than one week ago, the patient has an increased risk of premature birth within the next seven days and the pregnancy is less than 34 weeks, second treatment is recommended. Since there is no information on the efficacy of steroids in multiple pregnancies at this late stage of pregnancy,

steroid administiration to this group of patients is not recommended after 34 weeks (Socha et al. 2022).

- ✓ **Magnesium sulfate for neuroprotection** – In triplet pregnancies where there is a risk of imminent delivery (i.e. within 24 hours) between 23+0 and 31+6 weeks, magnesium sulfate treatment for neuroprotection is reccommended. The use of the Marret regime may be considered as a first choice. Omitting the continuous infusion may reduce the pulmonary edema, because the risk of such a condition is greater in triplet pregnancies while receiving this medication. Marret regimen: 4 g of magnesium sulfate as a bolus over 30 minutes without continuous infusion. It is also possible to use the other regimens (e.g. 4 g bolus with 1 g/hour continuous infusion) (Marret et al. 2007; Poggi et al. 2003).

1.16.2.2 Unproven Interventions

- o **Tocolytics for treatment of preterm labor** – Tocolytics are not used by the author for the treatment of triplets, which could be preterm birth. Compared to a placebo, no tocolytic has been shown to improve neonatal outcomes, and the use of tocolytics during multiple pregnancies increases the risk of side effects such as pulmonary edema (Pisani and Rosenow 1989). Others may give a tocolytic for 48 hours so that betamethasone can be administered. The tocolytic chosen is either

indomethacin or nifedipine, depending on the gestational age (Anotayanonth et al. 2004; Crowther et al. 2014; King et al. 2003, 2005).

- **Prophylactic tocolytics** – The prophylactic use of tocolytics is not relevant in a multiple pregnancy, including triplets. Preterm birth, low birth weight and neonatal mortality have not been shown to be reduced (Yamasmit et al. 2015).
- **Prophylactic cerclage** – In women without a history of cervical insufficiency, prophylactic cerclage — defined as cerclage performed solely because of a triplet pregnancy — does not appear to prolong pregnancy or improve neonatal outcomes (Rebarber et al. 2005). In small observational studies of triplet pregnancies with asymptomatic cervical shortening during serial sonographic monitoring of cervical length, placement of an ultrasound-indicated cerclage when the cervical length was <25 mm did not improve neonatal outcomes compared with expectant management (Young et al. 2014).
- **Bed rest** – Bed rest can be harmful because of the risk of thrombosis and deconditioning, and there is no solid evidence that it improves the outcome of triplet pregnancies (da Silva Lopes et al. 2017).

- **Progesterone supplementation** – Since there is little data to support its efficacy, the use of progesterone is not recommended to reduce the risk of preterm birth (Combs et al. 2016).

1.16.3 Preeclampsia — Compared to singleton pregnancies, pre-eclampsia occurred more frequently in triplet pregnancies (10 versus 3 to 5 percent). Multiple pregnancies increase the risk of HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count) and pre-eclampsia, which manifests earlier and is more severe (Wen et al. 2004). The United States Preventive Services Task Force recommends low-dose aspirin to reduce the incidence of preeclampsia and its related complications such as preterm birth and intrauterine growth restriction in multifetal pregnancies. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine support this recommendation. It is best to start taking low-dose aspirin between 12 and 28 weeks (ideally before 16 weeks) and take it daily until the birth (Davidson et al. 2021).

1.16.4 Late fetal demise — In one study, fetal demise occurred in 0.8 percent of trichorionic triplet pregnancies (12 of 1521) compared with 2.7 percent of monochorionic triamniotic triplet pregnancies (4 of 150). This rate is associated with chorioamnionicity (Kawaguchi et al. 2013).

1.16.5 Fetal growth restriction or discordant growth — Fetal growth restriction is diagnosed according to the same standards as in singleton pregnancies. According to Alexander et al. (1998), the use of these criteria can lead to an overdiagnosis of

poor fetal growth, as the growth of triplets begins to diverge from that of singleton pregnancies in the third trimester. For this reason, a number of authors have published growth charts (median, 10th and 90th percentiles) tailored to triplet pregnancies. It is not known whether these tables are more effective in identifying fetuses that are more likely to have a poor fetal or neonatal outcome (Vora et al. 2006).

1.16.6 Twin-twin transfusion — As already mentioned, triplets with a shared placenta need to be monitored for TTTS.

1.16.7 Twin-anemia polycythemia sequence — Triplets rarely have a twin anemia polycythemia sequence (TAPS); very few cases have been documented. The same treatment is given same as in twin pregnancies complicated by TAPS (Griersmith, Fung, and Walker 2014).

1.16.8 Cord entanglement in monoamniotic multiples — In any multiple pregnancy, monoamniotic placentation carries the risk of umbilical cord entanglement and compression-related mortality for the fetuses. As mentioned earlier, these patients need to take corticosteroids before delivery, deliver them by cesarean section at 32-33 weeks gestation and admit them to the hospital at 26 weeks for intensive fetal heart rate monitoring (one hour of continuous monitoring every eight hours) (Dias et al. 2010).

1.16.9 Other complications — In addition, the following pregnancy problems are more likely to occur with triplet pregnancies than with singleton pregnancies. The same problem is diagnosed and treated in a similar way to singleton pregnancies.

- Nausea and vomiting of pregnancy

- 1.6 percent of triplet pregnancies were found to have placental abruption, compared to less than 1 percent of singleton pregnancies (Wen et al. 2004).
- Thrombocytopenia develops in up to a third of triplet pregnancies, usually due to pre-eclampsia (Al-Kouatly et al. 2003).
- Compared to 1 in 10,000 singleton births, up to 7% of triplet pregnancies have been documented to have acute fatty liver of pregnancy (Malone et al. 1998).
- Pregnancy-related intrahepatic cholestasis is more frequently seen in multiple gestations (Gonzalez et al. 1989).
- Multiple pregnancies are a risk factor for uterine atony, which can lead to postpartum hemorrhage, transfusions and possibly a hysterectomy (di Marco et al. 2023).
- Following a multiple pregnancy, postpartum depression and other psychological illnesses are more prevalent (Garel, Salobir, and Blondel 1997).
- As multiples have a larger placental volume and are more likely to use assisted reproductive techniques, a multiple pregnancy has been associated with an increased risk of placenta previa (Ananth et al. 2003; Karami, Jenabi, and Fereidooni 2018).

1.17 Delivery

1.17.1 Timing — The timing of birth depends on amnionicity.

Monoamniotic or diamniotic triplets – Based on the extrapolation of the finding that the risk of fetal demise in a monoamniotic multiple pregnancy in utero exceeds the risk of postnatal non-respiratory complications at this gestational age, these triplets are delivered by cesarean section at approximately 32+4 weeks of gestation (i.e. between 32+0 and 32+6 weeks) (Mieghem et al. 2014).

Triamniotic triplets – Regardless of whether it is a monochorionic, dichorionic or trichorionic pregnancy, uncomplicated triplet pregnancies with three amniotic sacs are delivered between 35+0 and 35+6 weeks of gestation. Earlier birth is recommended for complicated pregnancies; the exact timing depends on the clinical situation. Based on their clinical experience and the lack of research evidence on the timing of birth of triplets, the Committee concluded in a review commissioned by the National Institute for Health and Clinical Excellence that carrying an uncomplicated trichorionic or dichorionic triamniotic triplet pregnancy beyond 35+6 weeks of gestation would increase the risk of fetal death (Van De Mheen et al. 2016).

1.17.2 Route of delivery — For all triplet births, delivery by cesarean section is the recommended method. Compared to delivery by cesarean section, vaginal birth of triplets was associated with a higher risk of stillbirth and neonatal and infant deaths, according to an analysis of data from a national database (Vintzileos et al. 2005). A multicenter, retrospective US cohort study confirmed this

conclusion, finding that the rate of successful vaginal birth attempts was only 16.7 percent (four triplet births) and that vaginal birth was associated with a higher risk of maternal transfusion and neonatal mechanical ventilation, along with a trend toward higher composite neonatal morbidity (Lappen, Hackney, and Bailit 2016).

1.17.3 Anesthesia — Neuroaxial anesthesia is recommended for cesarean delivery (Marino et al. 2001).

1.18 Perinatal Mortality and Morbidity

The most common causes of death and morbidity in triplet pregnancies are preterm birth and low birth weight. Monochorionic triplet pregnancies had a 2.6-fold higher risk of perinatal death than trichorionic triplet pregnancies (odds ratio 2.6, 95% CI 1.17-5.76), and overall perinatal mortality was about 2.5 percent in two population-based cohort studies (Kawaguchi et al. 2013). Given the early gestational age of these deliveries, neonatal morbidity was common, and the mean gestational age at birth was about 33 weeks in both studies. In a study comparing the pregnancies of dichorionic and trichorionic triplets, the mean gestational age at birth for the two groups was 31 and 33 weeks, respectively, and the neonatal mortality rate was 22 and 7 percent, respectively (Levy-Coles et al. 2024; Mol et al. 2019).

2. Conjoined Twins

2.1 Definition and classification — Conjoined twins are a subgroup of monoamniotic twins in which the body parts of one twin fuse with the body parts of the other twin; the degree of fusion can range from slight to significant. Depending on the location of the fusion, they are classified as cephalopagus, thoracopagus,

omphalopagus, ischiopagus, parapagus, craniopagus, rachipagus and pygopagus (Mian et al. 2017).

2.2 Epidemiology — Compared to 8 per 100,000 births for all monoamniotic twins, the estimated incidence for this condition worldwide is 1.5 per 100,000 births. Compared to male twins, female twins are more frequently affected (Mutchinick et al. 2011).

2.3 Prenatal diagnosis — If the embryonic and fetal poles are closely connected and do not shift against each other on imaging, this diagnosis should be suspected in monoamniotic twin pregnancies in the first trimester (Baken et al. 2013; Mahalingam and Dighe 2014). A single umbilical cord with more than three vessels, inseparable fetal parts, fewer limbs than expected, increased nuchal translucency (NT) or cystic hygroma, hyperextension of the fetuses' nuchal spines facing each other, or both heads or breeches consistently at the same level to each other are additional findings that support the diagnosis but are not unique to conjoined twins. Up to 50% of cases of polyhydramnios occur in late pregnancy (McHugh, Kiely, and Spitz 2006).

Prenatal and postnatal decisions depend on confirmation of the diagnosis and clarification of the anatomy by color Doppler, fetal echocardiography and 3D ultrasound examinations. In addition, fetal magnetic resonance imaging (MRI) can help with surgical pre-planning and defining the anatomy (Turner et al. 1986; Ünal et al. 2010).

2.4 Management

- ✓ Multidisciplinary team: Patients should be treated in an institution that has already dealt with conjoined

twins. The treatment team should include at least experts in pediatric surgery, neonatology, imaging and maternal-fetal medicine.

- ✓ Delivery timing: Given the higher risk of stillbirth or difficulties due to polyhydramnios and preterm birth, it is sensible to deliver the baby 35 weeks after starting antenatal corticosteroid treatment. There is not enough information to determine a specific gestational age for the time of delivery (O'Brien, Nugent, and Khalil 2015).
- ✓ Cesarean birth: In order to prevent dystocia, cesarean delivery is recommended in the majority of instances, particularly in third-trimester pregnancies.
- ✓ Although there have been cases in which unrecognized conjoined twins have been successfully delivered vaginally, there is a significant risk of dystocia and maternal and/or fetal damage, such as uterine rupture and fetal mortality (Harma et al. 2005).

2.5 Prognosis — Of the 379 cases of conjoined twins examined, 45.6 percent were born alive, 27.2 percent were stillborn and in 27.2 percent the pregnancy was terminated. Because congenital defects are always present and often prevent one or both twins from surviving, even in cases where surgical separation has been performed, the prognosis for newborns is poor (Mutchinick et al. 2011).

3. Fetus in Fetu

An unusual embryonic aberration, known as "fetus in fetu", occurs when a deformed parasitic twin is discovered in the body of the normally developing host (Arlikar et al. 2009). The incidence is reported to be 1 in 500,000 births, and most cases manifest in infancy (Hoeffel et al. 2000). The parasitic twin is often anencephalic, with developing limbs and a spinal column. The upper limbs are less developed than the lower limbs (Escobar, Rossman, and Caty 2008). Although the monozygotic diamniotic twin and a mature teratoma are similar in some ways, a mature teratoma differs from a fetus in that it can grow independently and has the potential to become malignant (Spencer 2001). Preoperative diagnosis is often made using magnetic resonance imaging (MRI), computed tomography (CT), conventional radiography or ultrasound. Complete excision is the recommended treatment, and histopathologic results confirm the diagnosis. The treatment for FIF is surgery (Prescher et al. 2015).

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