

# Twin to Twin Transfusion Syndrome in Discordance Twins: Diagnostic and Management Approach

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## ABSTRACT

Twin to twin transfusion syndrome (TTTS) is a rare condition that affects the identical twin pregnancy or other multiples. TTTS occurs when there is an imbalance in blood flow between fetuses who share one placenta. This condition can cause one fetus to be dominant among other fetuses or is called discordant twins. The cause of discordant twins is still unclear. But one of the causes is Twin-to-Twin Transfusion Syndrome. The incidence of discordant twin pregnancies is around 15-29% of total pregnancies. The chance of developing TTTS is estimated to be around 10-15% of monochorionic diamniotic. TTTS is diagnosed by ultrasonography with measuring the single deepest pocket (SDP). TTTS can be treated by fetoscopy laser ablation. The aim of this treatment is to close the connection of blood vessels. There are alternative treatments such as amnioreduction, selective fetal reduction, or termination of pregnancy.

**Keywords:** discordant, fetoscopy, twin to twin transfusion syndrome.

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## I. INTRODUCTION

Twin pregnancy is a pregnancy with 2 or more fetuses. Multiple pregnancies are considered high-risk pregnancies, because perinatal mortality is 3-5 times higher than singleton pregnancies, and neonatal mortality is 10 times higher than singleton pregnancies. Perinatal mortality of the first fetus is 9 times that of singleton pregnancies and perinatal death of the second fetus is 11 times that of singleton pregnancies. Twin fetuses are more common as a result of fertilization of two separate ova (double-ova, dizygotic twins or fraternal twins). About a third of twin pregnancies originate from a single fertilized ovum, and then divide into two similar structures, each with the ability to develop into a single ovum on its own (monozygotic or identical twin pregnancies). One or both processes may be involved in the formation of a larger number of fetuses [1], [2].

In dizygotic and monozygotic twin pregnancies, various complications can occur for both the mother and the fetus. The dominance of one twin fetus over its twin fetuses or called discordant twins is one form of complication that occurs in twin pregnancies. This situation can cause one fetus to grow larger than its twin fetuses, in addition to causing

growth abnormalities and even death of the twin fetuses. The incidence of discordant twins is 15-29% of the number of twin pregnancies. The causes of discordant twin pregnancies are often unclear, differences in placental mass, genetic and hemodynamic imbalances in the inter-fetal transfusion syndrome or also called twin-to-twin transfusion syndrome (TTTS) are the causes of discordant twins [3].

TTTS is a condition that can occur as a complication of multiple monochorionic pregnancies. The chance of TTTS is estimated at 10-15% of monochorionic diamniotic pregnancies. TTTS is defined ultrasonically by the combination of polyhydramnios in one amniotic sac and oligohydramnios in the other, and is one of the deadliest perinatal complications, with a mortality rate of between 80-100% if untreated. The diagnosis of monochorionicity in the first trimester, at least by examination every 2 weeks after 16 weeks, provides the best results in early diagnosis and definitive treatment. Current techniques allow >70% survival of at least one twin but preterm delivery is a common consequence of intervention. In this literature review will describe the approach to diagnosis and management of TTTS in discordance twins' cases [4], [5].

## II. DISCUSSION

TTTS most often occurs between 16-26 weeks of gestation. The combination of serial ultrasound assessments starting in the first trimester and every two weeks after 16 weeks combined with counseling the mother about symptoms of polyhydramnios allows early risk stratification and timely identification of the condition. The diagnosis of TTTS in a confirmed monochorionic pregnancy is based on ultrasonographic measurements of the single deepest pocket (SDP). It is used for the diagnosis of oligohydramnios (SDP  $\leq 2$  cm) in one amniotic sac and polyhydramnios (SDP  $\geq 8$  cm) in the second amniotic sac. TTTS staging is also based on hemodynamic measurements using pulsed Doppler on the tricuspid valve, ductus venosus, umbilical vein and umbilical artery [3], [6].

The Quintero scale includes 5 stages of clinical severity, ranging from mild disease to severe form resulting in the death of one or both twins. The first stage is characterized by the presence of oligohydramnios or polyhydramnios sequences. The lack of bladder visualization in the donor fetus represents the second stage. The third stage is the detection of at least one pathology on ultrasound with pulsed Doppler such as umbilical vein pulsation, tricuspid valve or ductus venosus backflow, lack of or diastolic return in the umbilical artery. The atypical third stage (3a) was defined as the coexistence of circulatory disturbances with the bladder visualized on ultrasound examination of the donor. Stage 4, which is a pregnancy with generalized swelling of at least one fetus. The final stage (stage 5) on the Quintero scale is characterized by intrauterine death of one or both fetuses [7].

In the second trimester, discrepancies in amniotic fluid, umbilical cord insertion, and abdominal circumference can help to identify >70% of monochorionic pregnancies at risk for an adverse pregnancy outcome but have a positive predictive value for TTTS of only 22%. This may be due to the fact that these factors contribute to the entire range of complications specific to monochorionic pregnancy. For this reason, there is international agreement that ultrasound surveillance of monochorionic twins should include determination of chorionicity followed by assessment at least every two weeks after 16 weeks to evaluate complications including TTTS. Couck *et al*'s study found that a biweekly ultrasound scan from 16 weeks onwards could detect 9 out of ten TTTS pregnancies on time. Most stage 5 cases are outside the typical window period (beyond 16 and 26 weeks). Most stage 3-4 cases have abnormal Doppler findings prior to the diagnosis of TTTS [5], [8].

Untreated TTTS has a very poor prognosis. Advanced TTTS results in 90-100% of deaths from either single or multiple twin deaths or miscarriage from preterm labor due to uterine overdistention due to polyhydramnios. Since the later stages of TTTS have a poorer prognosis than the early stages, when severe TTTS occurs at a very early gestational age (before 16 weeks), the option of termination of pregnancy may be considered. Various therapies involve balancing fluid volume between the two sacs and interfering with vascular communication between the fetuses [7].

Fetoscopy laser ablation of the placental vessels is the only intervention that aims to cure TTTS by closing the interconnected vascular communications between the fetuses that give each fetus a chance to survive. This procedure is

usually performed between 16-26 weeks of gestation using local anesthesia with intravenous sedation as needed, an epidural or occasionally under general anesthesia. Preoperative ultrasound mapping of umbilical cord insertion, intertwin membranes and consideration of fetal size discrepancies were used to estimate the location and orientation of the vascular equator. Using ultrasound guidance, the receiving fetal sac is inserted with a fetoscope which has an outer trocar diameter of up to 65%. It also minimizes the risk of residual anastomosis and post-laser recurrence or development of TAPS (Twin anemia polycythemia sequence) [5], [9].

Alternative management options for TTTS are amnioreduction, selective fetal reduction, or termination of pregnancy. Amnioreduction is a consideration for situations where referral to a laser center is not feasible or as a temporary measure especially in late pregnancy. Selective fetal reduction is usually performed for cases with fetal anomalies or where survival is not possible after treatment for TTTS. Selective fetal reduction (sFGR) is considered if there is severe impairment of amniotic fluid volume and impaired growth before 20 weeks of gestation. In such cases, due to the mutual circulation between the fetuses, both fetuses will usually die without any intervention. Various techniques, which can be used for fetal killing, include injection of an occlusive agent into the umbilical vein of selected twins or radiofrequency ablation, fetoscopic ligation, and laser coagulation of one umbilical cord. Despite this procedure, other fetuses remain at considerable risk [7].

The study of Groene *et al*. showed that with significantly lower perinatal survival for donors in the TTTS + sFGR group (72% (224/311) compared to TTTS alone 81% (173/215;  $p=0.027$ ). At long-term follow-up with severe NDI (neurodevelopmental impairment), it was found that the TTTS group alone experienced 7% (13/198), while the TTTS + sFGR group was 9% (27/299) ( $p=0.385$ ). Good sFGR (OR 1.5; 95% CI 1.1–2.0,  $p=0.013$ ) and lower gestational age with laser (OR 1.1; 95% CI 1.0–1.1,  $p=0.001$ ) were independently associated with decreased perinatal survival. Thus, sFGR before laser surgery is associated with more severe initial presentation and decreased donor perinatal survival [10].

Another treatment can be selective cord coagulation. In this procedure, under ultrasound guidance, one of the fetuses is intentionally sacrificed to save the life of the other fetus. This procedure is used when laser ablation of the connecting vessels is not possible or if one of the fetuses is so close to death that laser ablation is unlikely to be successful. By stopping the flow of the dying fetus, the other fetus can be protected from the consequences of his sibling's death. In this procedure, the umbilical cord is grasped, and an electric current is applied to thicken the blood vessels in the cord to stop blood flowing through it. Complications of this procedure include premature birth and premature rupture of membranes [7].

## III. CONCLUSION

TTTS most often occurs between 16-26 weeks of gestation. Serial ultrasound assessments starting in the first trimester and every two weeks after 16 weeks allow for early risk stratification and timely identification of the condition. In

terms of management, fetoscopy laser ablation of the placental vessels is the only intervention that aims to cure TTTS by closing the interconnected vascular communication between the fetuses.

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