Opinion
Open Access
CrossMark

Twin-to-twin transfusion syndrome: a complication of monochorionic pregnancy

Volume 16 Issue 2 - 2025

Emilija Jasovic-Siveska
Specialist of Gynecology and Obstetrics, Professor of Gynecology and Obstetrics, PHO Medihelp, Macedonia University St. Clement of Ohrid, Higher Medical School, North Macedonia

Correspondence: Emilija Jasovic-Siveska, MD, PhD, Specialist of Gynecology and Obstetrics, Professor of Gynecology and Obstetrics, PHO Medihelp, Bitola, University St. Clement of Ohrid, Higher Medical School, Bitola, North Macedonia

Received: April 13, 2025 | **Published:** April 8, 2025

Introduction

In the past three decades, the incidence of multiple pregnancies has significantly increased, presumably as a consequence of the increased application of assisted reproductive techniques. Multiple pregnancies can be a serious challenge, as they have been associated with a multiple increase of perinatal mortality and morbidity, especially in terms of long-term handicap in comparison with monofetal pregnancies. Multiple pregnancies are also linked to preterm births and intrauterine growth restriction, which contribute to perinatal mortality and morbidity by large.[1]

The real number of multiple pregnancies is difficult to estimate, because a large number ends in early miscarriages, while there is also the possibility of a case of a vanishing twin in the early embryonal phase, where one embryo may „vanish“ due to different factors. Consequentially, the pregnancy may continue with one or two fetuses, depending on the initial number of embryos. However, according to literature so far, it has been estimated that about one in eighty-nine conceptions may result in a twin birth, while the application of assisted reproductive techniques has drastically increased the incidence of multiple pregnancies worldwide.[2]

Monochorionic (MC) twin pregnancies are at increased risk of perinatal morbidity and mortality compared with dichorionic gestations, mostly owing to conditions arising from their placental vascular arrangement, such as twin–twin transfusion syndrome (TTTS), twin anemia–polycythemia sequence and twin reversed arterial perfusion sequence.[3]

TTTS is a common complication that typically presents in the second trimester of pregnancy in 10–15% of monochorionic twins due to net transfer of volume and hormonal substances from one twin to the other across vascular anastomoses on the placenta. When it is not detected on time, TTTS in more advanced stages may result in fetal dismissal in up to 90% of cases.[4]

Typical complications with MC twins are:

1) Twin-to-twin transfusion syndrome (TTTS)
2) Spontaneus twin anaemia polycythemia sequence (TAPS)
3) Twin reversed arterial perfusion sequence (TRAP)
4) Monoamniotic pregnancy
5) Conjoined twinning

TTTS is one of the complications of MC and a serious condition that complicates about 10-15% of MC diamniotic pregnancies.[3] It is a result of the imbalance of the volume of vascular anastomoses between twins and a leading factor in loss of pregnancies in MC twins. The diagnosis of MC in the first trimester and adhering to international guidelines for following these pregnancies give the best possibility for early diagnosis and appropriate treatment.

Characteristics of the MC placenta

In MC placenta, fetal vessels from each twin meet along the border between the placental territories. They may connect directly to form superficial vascular anastomoses or perfuse the common placental cotyledon by deep anastomoses of arterioles and venules. The imaginary line along the surface of the placenta connecting these anastomoses is called the vascular equator. This portion of the common placenta may represent 5-10% of the common vascular volume for each twin and is called the third circulation.[2,4,5]

Vascular anastomoses can be found in any number, size and arrangement between the arteries and veins. Arteriovenous (AV) anastomoses occur when the common placental cotyledon is perfused by an artery from one twin and drained by a vein from the other. This results in a unidirectional transfer of volume, hemoglobin and substances from one fetus to the other. Arterio-arterial (AA) and veno-venous (VV) anastomoses connect directly to each other across the chorionic surface and allow bidirectional flow between twins based on pressure gradients. In most MC twins, the net exchange between twins remains balanced in their shared circulation.

Pathophysiology of TTTS

The pathophysiology of TTTS is not entirely understood. There are several theories: abnormal placentation, unbalanced vasular communication and villous insertion of the umbilical cord. Vascular communication is present in 98% of MC placentas. Unidirectional or unbalanced blood flow is what explains the pathological changes in TTTS. Vascular anastomoses are essential for the development of TTTS, but there is no single pattern of anastomoses that causes TTTS.[4,5]

In 10-15% of MC twins, the balance is disturbed due to volume shunting through the AV anastomoses. AA or VV anastomoses are considered protective against TTTS because bidirectional flow allows for more efficient volume redistribution.[4,5]

The impaired net transfer of volume and vasoactive substances in TTTS leads to an abnormal intravascular volume status and compensatory response in both twins that can be diagnosed by ultrasound. The hemodynamic effects of TTTS contribute to functional and structural heart disease in each fetus. Changes in

the recipient's cardiac function may be observed even before the development of TTTS (cardiac dilatation, biventricular hypertrophy, valvular regurgitation, impaired contractility, etc.).[2,4]

Diagnosis of TTTS

Ultrasound (US) is crucial in the diagnosis of twin pregnancy. The ideal period is between 11+0-13+6 weeks of gestation (w.g.). US details that are important to note in the first trimester are: determining crown-rump length- CRL, location of placenta/placentas and characteristics of the amniotic membranes. If the pregnancy is >14 w.g., gestational age is determined by measuring head circumference.[5] Determining chorionicity and amnionicity in twin pregnancy is a necessity. With US <13+6 w.g. chorionicity is identified with approximately 95% certainty. The presence of two placentas is the detection of the characteristic "lambda" or "delta" sign (thickening at the site of membrane insertion). An additional US sign is the presence of 2 placental masses. Detection of different sexes of the fetuses indicates dizygotic pregnancy.[2,6,7] Amnionicity is determined by the so-called T-sign (presence of an intraamniotic septum).[2,3,6–8]

The diagnosis of TTTS is exclusively through US. Therefore, serial US examinations are recommended in MC from the beginning of the second trimester. Early identification of MC defines the risk and scope of complications that may occur. US should show a single placenta: one twin with polyhydramnios and the other with oligoamnios. Since the volume of AT varies depending on gestation, in most European centers the cut-off value for determining polyhydramnios in the recipient is the deepest vertical pocket >8 cm throughout the pregnancy. The cut-off value for oligoamnios in the donor is the same in Europe and the USA and is <2 cm in the donor sac. Fetal echocardiography is recommended in MCP, as it can detect structural and functional abnormalities of the heart.[2,9]

The severity of TTTS is usually assessed according to the Quintero Staging system, based on the presence (Stage I) or absence (Stage II) of the ballder fullness, abnormal Doppler of the umbilical artery, umbilical vein and ductus venosus (Stage III), hydrops (Stage IV) and intrauterine death (Stage V). However, this staging system is questionable, as pregnancies can progress directly from Stage I to Stage V.[2,7,10]

Cardiovascular manifestations of TTTS may be evident early in the disease, which may contribute to the assessment. Fetal hydrops resulting from fetal heart failure is a late manifestation of the disease. Donors are more likely to show signs of increased placental resistance and much less likely to show cardiac dysfunction. Cardiovascular evaluation cannot predict the final outcome of the pregnancy, but it allows the detection of significant dysfunction of the heart.[2,4,5]

Screening for TTTS

According to some guidelines for TTTS, screening should start in 16 w.g., although others may suggest the period of 18-22 w.g., when screening for fetal anomalies is conducted. For US, it is recommended that examinations take place about 2-4 weeks apart.[7,8,11] This confirms the need for unified guidelines for the management of multiple pregnancies, especially the diagnosis and screening of TTTS, which will increase the confidence in the management of this problem.

Treatment of TTTS

Historical knowledge of TTTS dates back to the early 17th century. Placental anastomoses were first described in 1687. In 1875 Schatz, a German obstetrician, first identified their significance. All subsequent researchers have contributed to the understanding of TTTS and the development of treatment options.[12]

Untreated TTTS has a poor prognosis. Advanced TTTS results in 90-100% mortality of one or both twins or loss of pregnancy due to premature birth (overdistension of the uterus from polyhydramnios, especially if it occurs <28 w.g.). When TTTS occurs in the third trimester, outcomes are more favorable because delivery can be planned adequately. In the early stage, TTTS should be carefully observed, and referral to a fetal therapy center where laser coagulation is performed is recommended.[2,4,5] According to the updated ISUOG practice guidelines from 2025, laser ablation is the method of choice for TTTS in Quintero stages II, III and IV. When this method is not possible, an alternative is serial amnioreduction in the period after 26 w.g. Conservative treatment and observation are recommended in Stage I cases (Quintero Staging system) and pregnancies where the cervix is longer than 15 mm.[7]

Laser ablation is the optimal treatment for advanced TTTS that manifests by 26 w.g. This minimally invasive procedure is usually performed between 16-26 w.g. using local anesthesia. MCPs complicated by TTTS undergoing laser treatment using the Solomon technique had a significantly higher survival rate and lower recurrence rate of TTTS but were associated with an increased risk of placental abruption. Selective coagulation of AV, AA and VV anastomoses is recommended. Performing the intervention before 16 w.g. increases the risk of preterm rupture of membranes (PROM) and after 26 w.g. coagulation disorders due to increased diamete of blood vessels.[13,14]

The history of the treatment of TTTS also includes other methods that will be listed in the text that follows.

Expectative treatment: The course of TTTS ia almost certain to be fetal death with other severe complications. The Quintero staging system provides a predictive ability. Untreated stage I TTTS has an 86% survival rate, with a possibility of deterioration in 10-30% of cases. This means that ¾ of patients with stage I TTTS remain stable or regress spontaneously.[12]

Amnioreduction can be utilized from 15 w.g., when the deepest vertical pocket in the recipient sac is >8 cm, with the aim of achieving a pocket <5 cm, thereby reducing the risk of preterm delivery. The reduced amount of AT reduces the intraamniotic and placental vascular pressure, resulting in improved placental flow. Relieving pressure of the VV anastomoses may restore their compensatory function. Despite the evident beneficial effect on TTTS, numerous studies do not support amnioreduction as a first-line treatment for TTTS, unless other more sophisticated methods are available or while awaiting transfer to another center.[12,15–17]

Medical treatment is most often used in conjunction with amnioreduction or laser ablation. DeLia et al.[18] first suggested administering digoxin to the mother in the presence of signs of heart failure in the recipient. This demonstrated withdrawal of the cardiac decompensation in the fetus, with both twins surviving.[18] However, the evidence is limited and digoxin is no longer prescribed for the treatment of TTTS. In the medical treatment of TTTS, there are also studies with indomethacin (prolongs pregnancy and reduces polyhydramnios but worsens oligoamnios) and nifedipine (given to the mother 24-48h before laser ablation in cases of TTTS with fetal cardiomyopathy). Nonetheless, medical treatment of TTTS is not currently recommended as a first-line or routine adjunctive therapy.[12]

Septostomy, or iatrogenic puncture of the amniotic septum between twins at the time of amnioreduction, was an attempt to correct polyhydramnios and improve the hemodynamic status of the donor. Studies have shown that septostomy does not improve perinatal survival and carries a risk of intraamniotic membrane damage. Therefore, septostomy has been abandoned as a treatment for TTTS.[12]

Citation: Jasovic-Siveska E. Twin-to-twin transfusion syndrome: a complication of monochorionic pregnancy. *Obstet Gynecol Int J.* 2025;16(2):61–63.
DOI: 10.15406/ogij.2025.16.00790

Selective feticide involves termination of the transfusion by intentional feticide of one twin, preventing exsanguination from one twin to the other. It was first performed unsuccessfully in 1967 by cord ligation. Since then, many other techniques have been used: interstitial laser coagulation, radiofrequency ablation, and bipolar cord coagulation. Experience has shown an average survival rate 79% for the remaining twin. Data regarding neurological outcomes in the survival twin are limited. Therefore, this option is reserved only for severe cases of TTTS where the death of one twin is inevitable or highly probable.[7,12]

Prognosis, complication and management of TTTS

Overall survival of fetuses with TTTS has improved significantly with experience and modification of the laser technique since its initial description.

Prognosis varies depending on the stage and gestational age. The occurrence of TTTS at a younger gestational age is associated with a worse prognosis. Survival of one twin ranges from 15-70%, with about 50% survival of both twins, even with treatment. The prognosis is best for stage I, with an overall survival of 86%. About 75% of TTTS in stage I remain stable or regress. Less information is available for stages II-IV. The perinatal mortality rate for ≥stage III is 70-100%. In stage V, after the death of one twin, there is a 10% risk of death of the other twin and a 10-30% risk of neurological complications in the surviving twin. Studies have shown that if laser coagulation is performed at an earlier gestational age, the neurological outcome of the surviving twins is improved.[14]

In addition to the above, possible complications include: cardiac complications in both twins, increased risk of premature birth, increased risk of cerebral palsy and long-term neurodevelopmental impairment. Some complications are also a consequence of the methods used to treat TTTS (PROM, premature birth, extravasation of AF (amniotic fluid) outside the uterus, placental abruption, vaginal bleeding, infection, fetal death, recurrent TTTS and TAPS).[2,14]

Conclusion

Although curative treatment for TTTS with laser surgery is more widely available with improved fetal and maternal outcomes, this condition continues to increase morbidity and mortality in MC pregnancies. Accurate diagnosis and timely referral of TTTS cases to a laser center combined with effective treatments are important to improve perinatal outcomes.

Educating patients about the symptoms that may be signs of TTTS (contractions, sudden uterine enlargement) and advising them to report them promptly can significantly aid in early diagnosis of TTTS. Once diagnosed, the patient should be informed of the prognosis based on the stage, the treatment options available, along with their risks and benefits, the expected progression of the condition and the potential for long-term complications after delivery.

Standardization of procedures is an important step that treatment centers should adopt in order to improve the outcome of TTTS pregnancies.

Acknowledgments

None.

Funding

None.

Conflicts of interest

The author declares that they have no competing interests.

References

1. Oliver E, Navaratnam K, Gent J, et al. Comparison of international guidelines on the management of twin pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2023;285:97–104.
2. Coady AM, Bower S. Twining's textbook of fetal abnormalities E-book. 3rd edn. Elsevier Health Sciences. 2014.
3. Leombroni M, Liberati M, Fanfani F, et al. Diagnostic accuracy of ultrasound in detecting birth-weight discordance in twin pregnancy: systematic review and meta-analysis. *Ultrasound Obstet Gynecol.* 2017;50(4):442–450.
4. Miller JL. Twin to twin transfusion syndrome. *Transl Pediatr*. 2021;10(5):1518–1529.
5. Lynn LS, Russell SM. Twin-twin transfusion syndrome. In: Joshua A Copel, Mary E D'Alton, Helen Feltovich, editors. Obstetric Imaging: Fetal Diagnosis and Care (Second Edition), Elsevier, 2018.
6. Salomon LJ, Alfirevic Z, Da Silva Costa F, et al. ISUOG Practice Guidelines: ultrasound assessment of fetal biometry and growth. *Ultrasound Obstet Gynecol*. 2019;53(6):715–723.
7. Khalil A, Sotiriadis A, Baschat A, et al. ISUOG Practice Guidelines (updated): role of ultrasound in twin pregnancy. *Ultrasound Obstet Gynecol*. 2025;65(2):253–276.
8. Oliver E, Navaratnam K, Gent J, et al. Comparison of international guidelines on the management of twin pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2023;285:97–104.
9. Khalil A, Liu B. Controversies in the management of twin pregnancy. *Ultrasound Obstet Gynecol*. 2021;57(6):888–902.
10. Quintero RA, Morales WJ, Allen MH, et al. Staging of twin-twin transfusion syndrome. *J Perinatol*. 1999;19(8 Pt 1):550–555.
11. Couck I, Ponnet S, Thewissen L, et al. The detection, outcome, and presentation of twin-twin transfusion syndrome in monochorionic diamniotic twin pregnancies followed with a protocol of fortnightly ultrasound examination. *Fetal Diagn Ther*. 2021;48(5):353–360.
12. Glennon CL, Shemer SA, Palma-Dias R, et al. The history of treatment of twin-to-twin transfusion syndrome. *Twin Res Hum Genet*. 2016;19(3):168–174.
13. Ville Y, Hyett J, Hecher K, et al. Preliminary experience with endoscopic laser surgery for severe twin-twin transfusion syndrome. *N Engl J Med*. 1995;332(4):224–227.
14. Borse V, Shanks AL. Twin-to-twin transfusion syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
15. Sileo FG, D'antonio F, Benlioglu C, et al. Perinatal outcomes of twin pregnancies complicated by late twin-twin transfusion syndrome: A systematic review and meta-analysis. *Acta Obstet Gynecol Scand*. 2021;100(5):832–842.
16. Allameh F, Javadi A, Dadkhahfar S, et al. A systematic review of elective laser therapy during pregnancy. *J Lasers Med Sci*. 2021;12:e50.
17. D'Antonio F, Herrera M, Oronzii L, et al. Solomon technique vs selective fetoscopic laser photocoagulation for twin-twin transfusion syndrome: systematic review and meta-analysis of maternal and perinatal outcomes. *Ultrasound Obstet Gynecol*. 2022;60(6):731–738.
18. De Lia J, Emery MG, Sheafor SA, et al. Twin transfusion syndrome: successful in utero treatment with digoxin. *Int J Gynaecol Obstet*. 1985;23(3):197–201.

Citation: Jasovic-Siveska E. Twin-to-twin transfusion syndrome: a complication of monochorionic pregnancy. *Obstet Gynecol Int J*. 2025;16(2):61–63. DOI: 10.15406/ogij.2025.16.00790