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Review Article

A Comprehensive Review on Twin-twin Transfusion Syndrome Diagnosis and Treatment

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Abstract

Twin-twin Transfusion Syndrome (TTTS) in monochorionic pregnancies, characterized by inter-twin vascular anastomoses, poses significant risks to fetal and maternal health. This comprehensive review focuses on the diagnosis, risk factors, and palliative care strategies associated with TTTS, particularly emphasizing arterio-venous (AV) anastomoses.

In conclusion, the review underscores the critical need for an in-depth understanding of TTTS symptoms at different stages of cardiac malfunction for effective treatment selection. Future research endeavours should focus on advancing treatment strategies to mitigate the complexities associated with monochorionic TTTS, offering improved outcomes for both infants and mothers.

Keywords: TTTS; Monochorionic twins; Cardiac malfunctions; Hydramnios; Anastomoses.

Introduction

Twin-twin Transfusion Syndrome (TTTS) is a prenatal complication associated with monochorionic pregnancies. Monochorionic pregnancies are those where the twins rely on the same placenta. TTTS is primarily a result of inter-twin vascular anastomoses. Inter-twin vascular anastomoses are the mechanisms by which blood flow and circulation between two monochorionic twins are interconnected with each other. These inter-twin vascular anastomoses lead to complications in both twins and can lead to the death of the infant in the gestation stage itself.

This review currently focuses on the underlying diagnosis and the major steps in palliative care to prevent or reduce the proportion of TTTS in the population of twins [1,2]. Monochorionic pregnancies are usually associated with three types of vascular anastomoses, which are:

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- **Arterio-arterial anastomoses (AA):** These are arterial connections that aid in the transfer of an adequate amount of blood during incidents like heart blockage. There are two kinds of arterial anastomoses: functional and anatomical. Functional anastomoses are where the arteries suddenly open up to transfer blood, whereas anatomical arterial anastomoses are consistent. Example: Circle of Willis-brain.
- **Veno-venous anastomoses (VV):** VV anastomoses are mainly involved in changing the route of blood drainage. These anastomoses have more additional significance compared to those of AA anastomoses due to their clinical significance of aiding in being an alternative vascular system during ventricular obstruction. Example: Collateral veins in the hepatic system.
- **Arterio-venous anastomoses (AV):** AV anastomoses are major connections between arteries and veins. These AV anastomoses have different functions in the human body, such as AV shunts in the liver to transfer oxygenated blood and the AV shunts in the eyes for the transfer of blood to the retina. AV anastomoses are the major subtype of anastomoses that result in and thus increase the risk of TTTS in monochorionic twins [3-6].

Risk of AV anastomoses in causing TTTS

AV anastomoses increase the risk of TTTS in monochorionic twins by creating complications in blood flow and blood transfer. In monochorionic co-twins, generally one twin is considered to be the donor, from whose placenta there is a transfer of blood or metabolic fluids to the other co-twin, or the recipient.

AV anastomoses at the placenta can create connections where the arteries of the donor and the veins of the recipient are connected. This can cause an imbalance in blood transfer. While the recipient is receiving more blood volume, the donor gets less volume of blood retained in their system, which can cause several heart-related complications as well as other prenatal metabolic complications in both twins, which are listed in Table 1 [7,8].

These cardiac events can also be classified based on the negative effects observed in the pathophysiology of the cardiac dysfunction into four different stages, such as the early, middle, advanced and late stages. In the first or early stage, there is an increase in the vasoactive rate in the donor and the relative amount transferred to the recipient. The middle stage is where the twins are observed with conditions such as oligohydramnios and polyhydramnios in the donor as the recipient. The third and fourth stages are mostly evident with umbilical pulsations, cardiac (systolic dysfunctions) and cardiac failures in the recipient.

The application of placental injection is the most highly preferred diagnostic method for the detection of AV anastomoses and their risk in monochorionic twins. Let us explore the use of placental injection in the diagnosis of detecting AV anastomoses to evaluate the risk of TTTS [13-17].

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Category	Condition	Complication
Donor	**Hypovolemia**	Reduced blood volume in donor twin's heart.
	Reduced oxygenation	The amount of oxygen transfer is reduced in the donor kid which causes additional lung complications and can lead to premature death.
	Oligohydramnios	Reduced amount of amniotic fluid in the donor can cause fetal heart failure.
Recipient	**Dilated cardiomyopathy**	Increase in the volume of blood transferred can make the hearts enlarge beyond its capacity and thus cause the heart muscles to weaken.
	Hypertrophy	The increase in the volume of blood will make the heart muscles work harder and get weak and thus causes heart failure.
	Polyhydramnios	The excessive amount of amniotic fluid transfer can severely affect the heart performance and lead to pulmonary atresia in the recipient twin [9-12].

Table 1: Different complications arising in monochorionic twins due to TTTS.

Diagnosis of AV anastomoses

Placental dye injection, or colour dye injection, is the method that is most commonly used in the diagnosis of TTTS. At first, the basic diagnosis of TTTS is based on selective fetal growth restriction, or SFGR. SFGR is the condition that is caused by AV anastomoses in monochorionic twins. This is the destruction of the balance of relative metabolic fluids in the body, such as the amniotic fluid, leading to polyhydramnios and oligohydramnios in twins, thus altering the growth rate. The Quintero staging system criteria are used to diagnose AV anastomoses and TTTS based on the following criteria mentioned in Table 2.

Quintero stages	Associated symptoms
Stage 1-Mild stage	Increase in polyhydramnios in the recipient, oligohydramnios in the donor. Bladder in the donor twin (BDT) is visible.
Stage 2-moderate stage	BDT with increase in thickness or No BDT was observed.
Stage 3-Severe stage	Blood flow changes observed in both the twins. (also known as doppler studies).
Stage 4-Very severe	Hydrops or the accumulation of fluid in the body cavities of one or both the twins. Observed more at recipient twins [18].

Table 2: Quintero stage classification of TTTS.

Baseline characteristics come after the determination of maternal parameters such as gestational age, mother's age, the prevalence of any reproductive or uterine conditions like PCOS, and the incidence of ART use in pregnancy.

Parameters such as fetal weight abdominal circumference, estimated fetal weight and umbilical arterial pulsatility are determined mainly to diagnose TTTS. The oligohydramnios in the donor is accompanied by maximum vertical pocket (MVP) ≤ 2cm and polyhydramnios with MVP ≥ 10 cm in 20 weeks of pregnancy.

There are two forms of TTTS, the acute form and the chronic form. Acute TTTS occurs suddenly during the second week of pregnancy, combined with the sudden onset of symptoms, and is very rare, with an incidence of 2%. The acute form of TTTS is more commonly visible in women who had earlier monochorionic complications [19-21].

The chronic form of TTTS is more evident in the monochorionic twins' population, with a gradual increase in signs and symptoms. A colour dye-based injection system is widely used to test the chronic form of the disease. The full placenta is injected with colour dye, which is used to detect placental anastomoses such as AA, VV and AV.

AV is evidently found by the presence of a single pair of arterials and a single pair of veins connected, which are less than 1mm in distance from each of the twins. This colour dye method is more beneficial as we are also evaluating the diameter of these anastomoses along with the presence of superficial anastomoses.

The main advantage of the colour dye method is its rapid detection based on the different colours used to view the anastomoses. The placental share percentage was found for both twins, along with the diameter of the anastomoses. Later, at last, the spearman rank coefficient test is usually performed to relate birth weight and placental share to predict the risk of TTTS. Other statistical testing procedures that are usually preferred in TTTS diagnosis are t-tests to predict the risk in a group.

The colour dye method is more successful in diagnosing only monochorionic placental anastomoses compared to dichorionic placental anastomoses, which is more evident by looking at the findings from the research of Zhao, et al., where monochorionic placental anastomoses were found using colour dye injection, with a placental share percentage of 67% in the first twin and 33% in the second twin. No vascular anastomoses were visible in the dichorionic placenta, along with more unequal placental sharing in the monochorionic cases [22].

Treatment methodologies available for TTTS

There are currently three major treatment strategies available for TTTS: laser photocoagulation, Amnioreduction and selective fetoscopic laser coagulation (SFLP).

- Laser photocoagulation is the use of lasers to seal or block unwanted placental arteries, veins or blood vessels. A laser is inserted through the maternal abdomen, which makes this procedure invasive. This can cause hormonal changes and thus result in

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premature birth and neonatal complications.

- SFLP, on the other hand, is a specialised procedure for the diagnosis of TTTS. A fetoscope is used here, which targets amniotic fluid and aids in detecting regions with irrelevant placental anastomoses.

Amniotic reduction, on the other hand, is the use of a needle-like structure that is inserted via the abdomen into the amniotic cavity, and the excess amniotic fluid is withdrawn. This can release the pressure in the recipient twin by avoiding or reducing the chances of polyhydramnios and can give a temporary benefit based on gestational age and the stage of cardiac malfunctions observed in the twins [23-25].

Conclusion

The complexities associated with monochorionic TTTS is huge and is riskier in causing prenatal death and maternal complications. Appropriate understanding of the symptoms associated with monochorionic TTTS based on the cardiac malfunction stage is needed for the proper treatment strategy selection and execution. More research in the upcoming future should aim in providing a promising strategy as a treatment option for the syndrome.

Supplementary materials

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Data availability statement

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Conflicts of interest

The authors declare no conflict of interest.

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