

Twin-Twin Transfusion Syndrome

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ABSTRACT

An imbalance in circulation is developed as the consequence of vascular communication at the placenta level between monozygotic monochorionic twins, a condition known as Twin-Twin Transfusion Syndrome (TTTS). Multiple pregnancies have become more common as per recent studies because more people are using fertility drugs and procedures, such as IVF, to help conceive a baby. The surge in multiple births makes them prone to TTTS which has a 10-15% possibility of occurrence in the case of monochorionic twins and if left untreated leads to death. This research paper analyses in detail the causation of this complication in pregnancy and surveys the maternal and foetal risks along with appropriate and necessary treatment procedures. The goal of this research is to build an overview idea and illustrate the diagnosis, the diagnosis-based Quintero staging system and the recoverable prognosis. The study also documents how the TTTS diagnosis helps develop methods suitable for various foetal surgeries and covers future pregnancy complications as well.

NEED TO KNOW

What are multiple pregnancies?

Multiple babies are conceived at a time when more than one egg is fertilized with exceptions elaborated below. A pregnancy carrying two babies at the same time is called twins. Similarly, three babies conceived at a time are called triplets. There are high-order pregnancies too for more than three babies carried during one pregnancy. Multiple pregnancies are prone to higher risks compared to single pregnancy.

Multiple Pregnancy

There are two ways in which multiple pregnancies can occur-

- A single egg is fertilised by a sperm and then splits before implantation in the lining of the uterine wall.
- Two different eggs are fertilized simultaneously by different sperm.

In the first type of pregnancy identical twins develop since the same egg is split and the newly formed embryos are thus identical and do not vary genetically. It could be either all boys or all girls. Fraternal twins (non-identical) are developed in the case of the second type of pregnancy, due to it being two separate fertilizations caused by separate egg and sperm. When the ovary releases two eggs it causes the birth of fraternal twins. The sex of the babies can be different in fraternal pregnancy and they differ genetically a lot too!

Increase in the rate of multiple pregnancies.

There are certain factors that can cause a higher risk of getting pregnant with multiple babies. A woman who is older (in her 30s) is at a higher risk since at an older age multiple eggs are released at a time. An increased possibility of multiple pregnancies is seen in the ones who have had multiple themselves or have them in the family, this is due to genetics. Fertility drugs and treatment increase the chance of multiple births too. For example, during In vitro fertilization, a procedure under ART (assisted reproductive technology), the transfer of more than one embryo would lead to multiple births.

INTRODUCTION

What is Twin-Twin Transfusion Syndrome (TTTS)?

Where twins are concerned, fraternal twins always have separate placentas since they are formed from different eggs being fused by different sperms but in the case of identical twins, 70% of them share a placenta as they are formed by splitting of the same egg. Identical twins (monozygotic) sharing a placenta are called monochorionic. Monochorionic twins have risks unique to them. Twin-Twin transfusion syndrome is a condition that is a consequence of vascular communication at the placenta level between twins. One twin (DONOR TWIN) pumps the blood to the other twin (RECIPIENT TWIN) leading to too much blood received by the recipient twin and a lack of blood experienced by the donor twin. It is a serious complication in monozygotic monochorionic twins. Blood vessels are always connected because of the lack of any barriers in monochorionic twins, these connections result in a blood imbalance. About 10-15% of monochorionic twins have Twin Twin Transfusion syndrome (TTTS) where the unequal flow of blood between the foetuses is noticed. If no measures are taken for treatment after the discovery of TTTS there is a 90% risk that the twins will die in-utero. There are in-utero procedures performed to prevent foetal death.

BLOOD IMBALANCE

Looking into the detail of blood imbalance we would get a broader idea of how the blood flow affects each of the twins. As said earlier TTTS occurs when there is an unequal blood count in twins in the womb. The umbilical cord of the donor twin splits into an artery, obtaining oxygen and nutrients for the blood from the mother's circulation and entering the placenta. Unfortunately, this anomalous "arterio-venous" link causes the corresponding vein that would ordinarily return the now nutrient-rich blood to the identical foetus to instead be sent into the other twin.

Pumping deoxygenated blood into the recipient's shared cotyledon from a donor placental artery. The oxygenated blood exits the cotyledon through a placental vein of the recipient twin after oxygen exchange in the chorionic villus is complete. If not compensated for, this unidirectional flow causes volume depletion in the donor and volume excess in the recipient. Typically, this is done through superficial arterio-arterial anastomoses.

The donor twin - Blood is transfused such that the donor twin becomes anaemic (deficiency of red blood cells and haemoglobin) and therefore its growth is restricted so the donor twin is small and pale. This progressive loss of blood volume is hypovolemia. With the decrease in the blood flow of the donor twin, urination also decreases as the kidney does not have to filter as much fluid from the blood. This in turn affects other developments such as that of the bladder and also leads to low level amniotic fluid. Abnormal reduction in amniotic fluid (low-level) is termed *oligohydramnios*. Amniotic fluid is the clear liquid surrounding the fetus, providing a cushion in the womb. The amniotic fluid plays a vital role in the development of the urinary, respiratory and gastrointestinal systems of the fetus. If there is a complete loss of amniotic fluid, it is termed *anhydramnios*. A baby cannot survive without amniotic fluid. Apart from these, cardiovascular system dysfunction is quite common when enough blood does not reach the body. The ultimate risk of such dysfunctions and restrictions leads to fetal death.

The recipient twin - The blood from the donor twin is taken up by the recipient twin leading to successive high volumes of blood in this twin (hypervolemia). Hypervolemia affects the cardiovascular system by exceeding its capacity leading to heart failure or death. In contrast to the donor twin, the recipient becomes polycythemic due to a greater blood count obtained from the donor twin. The recipient twin is larger and has higher volume and is prone to suffer hyperviscosity and occlusive complications. Large amounts of

fluid filled in tissues and organs cause swelling (edema) called hydrops fetalis. Polycythemia in the recipient twin may also lead to severe hyperbilirubinemia (too much bilirubin) and kernicterus (brain damage due to a high level of bilirubin).

RISK FACTORS

Foetal brain damage- There are chances of neurological damage as well. It might be due to ischemic necrosis leading to cavitory brain lesions. The blood pressure instability and episodes of hypotension is the reason for ischemia in recipient twin. For, donor twin it results from ischemia due to anaemia, hypotension, or both. Preterm delivery could cause cerebral lesions as well. If one twin dies and the other survives there is a good 40% risk of being diagnosed with foetal brain damage. The blood is transfused with high pressure after the demise of one twin which rapidly leads to hypertension and there is a risk of possible ischemic antenatal (stroke in the womb before birth). Even with delivery right away following the recognition of a co-twin death, the hypotension that occurs at the time of death is likely to have already resulted in irreparable brain damage.

Untreated TTTS - Untreated twin-twin transfusion syndrome has serious consequences. According to reports, there is a 70-80% chance of both twins dying if left untreated. Without treatment, TTTS is dangerous to both the foetus and the mother.

Maternal risks - Hydrops cause a syndrome called maternal mirror syndrome, a pregnant woman is at risk of this syndrome when diagnosed with TTTS. The mirror reflects, in the same way as the name of this syndrome, it reflects the symptoms experienced by the twins. The mother's condition mimics the foetus's condition. The high flow high volume cardiovascular state in the mother causes the symptoms of preeclampsia that includes vomiting, hypertension, body swelling, proteinuria (excess protein in urine) and pulmonary oedema (fluid in lungs). The pregnancy needs to be carefully monitored. There are furthermore physical risks to the mother due to overdistended ovaries. Loss of pregnancy is quite difficult to process and needs delicate handling of the situation as it may be very serious for the family. Every risk should be taken into account for the management of treatment of TTTS.

DIAGNOSIS

- Undergoing a routine prenatal ultrasound, a doctor would be able to suspect a twin twin transfusion. Detailed testing (by a maternal-fetal medicine specialist) in amniotic fluid volume, bladder filling and blood flow in donor and recipient twins can provide a confirmed diagnosis.
- When there is a sudden surge in amniotic fluid, the uterine cavity grows at an accelerated rate, putting the woman at risk for preterm labour or shortening of the cervix. To avoid ruptures of the membrane cervical length and uterine cavity maternal assessment
- One of the important factors in prognosis and diagnosis is monitoring foetal heartbeat in both recipient and donor twins, which is called a foetal echocardiogram.

Foetal echocardiogram - The ultrasound examination used to assess the foetal heart during pregnancy is called foetal echocardiography. Twin-twin transfusion syndrome affects both sets of twins' circulatory systems. heart structural, diastolic, and systolic changes could occur; these have been the focus of intensive research over the past 20 years, and the use of echocardiography in the evaluation of these pregnancies has spread throughout facilities that provide care for the condition. A tiny device known as a transducer, which transmits sound waves at a frequency that is unheard, is positioned on the mother's abdomen. The baby's

heart is the ultimate location where the ultrasonic sound waves go after passing through the mother's and the baby's skin, various bodily tissues, and the transducer. The generated image of the heart is produced after the transducer picks up the reflected waves and delivers them to a machine for analysis.

First changes in the foetal heart are noticed in the recipient's twin, its heart must work extra for the huge volume of blood and thus the signs of heart failure occur. The echocardiogram exams reveal increased heart chamber size, and irregularity in blood flow in the valves (tricuspid regurgitation). If the stress on the recipient twin's heart is continued to not treated there will be progressive changes such as decreased heart functions and possible development of narrowing of one of the valves (pulmonary stenosis).

High-resolution foetal ultrasonography - The non-invasive ultrasound test performed by specialists is called High-resolution foetal ultrasonography. The sound waves are used to create images of twins in the womb on the monitor to check their development of internal organs and overall growth. It is also used to check the level and volume of amniotic fluid that surrounds them as well. Since the donor and recipient twins have large differences in their amniotic fluid and such inconsistency between the twins would indicate suspected TTTS.

Umbilical artery blood flow - After receiving the information from the foetal echocardiogram and foetal ultrasonography exams the doctor conducts an analysis of the blood flow pattern in the umbilical artery and vein and other major foetal blood vessels. In the umbilical artery the blood flows towards the placenta and away from the foetus in an attempt to gain fresh nutrients and oxygen from mother's circulation. If the condition of the placenta worsens it becomes tougher for the blood flow within and towards the placenta. The foetus pushes blood towards the placenta through the umbilical artery with each heartbeat (the systole phase), and typically, that beat is powerful enough to maintain blood moving forward, towards the placenta, even while the heart re fills for its next beat (the diastole phase).

- Sometimes, when TTTS worsens, the donor's umbilical artery's forward flow may decrease in the intervals between heartbeats. When the foetal heart is filling back up (diastole phase), there may be no flow or even a change in flow direction if the problem worsens.
- The severity of TTTS for each specific pregnancy is determined by taking into account all of the findings from the echocardiography and ultrasound examination.

QUINTERO STAGING SYSTEM

Once TTTS is identified, a staging system is used for the classification of the severity of the condition. This system is known as Quintero staging system (1999). It helps in deciding the appropriate treatment required at a particular stage and whether an intervention is needed or not. The different stages of the Quintero system is described below:

- Stage I: The ultrasound shows unequal blood flow between the twins where the donor twin on the left side has oligohydramnios and recipient twin on the right side has polyhydramnios. There is an imbalance of amniotic fluid around the twins. The bladder is still visible indicating that the donor twin is receiving enough nutrients and oxygen for blood flow.
- Stage II: Ultrasound shows heave imbalance in amniotic fluid but the bladder is not visible of the donor twin in this stage this means that urine is not being formed and the bladder is empty. Blood is being diverted from the kidney to the brain, heart and adrenal glands rather to the bladder. It is not that the bladder and kidney is not functioning, they are functioning in a slower manner.

- Stage III: Addition to stage I and stage II, abnormal blood flow patterns are seen within the umbilical cords of the twins that also include reversed flow in ductus Venosus. The heart function of one or both twins is affected as derived from the abnormal dopplers.
- Stage IV: The mother and the twins are at risk due to hydrops observed. The recipient twins show signs of heart failure due to the hydrops. Its heart is struggling to pump all excess blood that is being sent from the donor twin.
- Stage V: Demise of one or both the twin occurs.

TREATMENT

Early diagnosis and intervention are the key to twin-twin transfusion. The Quintero staging system helps in deciding the treatment plan according to the stage of TTTS since different criticality requires different methods.

Expected management - This method of treatment includes continuous close monitoring through ultrasound, this close surveillance treatment is applicable for stage I TTTS. Since the syndrome has not progressed much and if it continues to be in stage I then close look out is necessary. If more signs start to show up. The treatment plan moves forward.

Amnioreduction - As the name suggests, it is a procedure to remove excess fluid that is amniotic fluid present in the amniotic sac, thus reducing the content of amniotic fluid. It is a less invasive therapy. The doctor uses ultrasound imaging to help guide a fine, extremely long needle into the uterus of the mother to draw out amniotic fluid which is there in excess. The ultrasound images are of “real-time” for better viewing. Following amnioreduction therapy, both twins had an overall 80% survival rate. The outcomes are pleasing and positive. Doctors recommend such intervention either for TTTS stage one or when the diagnosis of TTTS was much later in cases where fetoscopy laser surgery was not possible anymore.

Fetoscopy laser photocoagulation - A laser is used to ablate that are responsible for the abnormal blood flow in both the twins, this is a minimally invasive surgery. All patients with TTTS stage II, III and IV are recommended to undergo this procedure. This foetal intervention could be suggested in some cases of TTTS stage I as well. According to reports and professionals in most cases the ideal intervention. A thin fibre-optic scope through the mother’s abdominal wall then through the uterine wall and finally into the amniotic cavity of the recipient twin, this is how a foetal is performed. The aberrant vascular connections between the twins can be identified and removed by focusing a laser beam on the blood vessels on the placental surface. The laser beam only coagulates vessels that connect one twin to the other. Each twin's regular blood vessels are still present and function normally. An amnioreduction is carried out following the laser surgery to reduce the likelihood of an early labour and to help the pregnancy feel more comfortable. At least one twin has a survival rate of more than 85%, while both twins have a survival rate of about 60%. Numerous studies have shown that the most successful therapy for infants with advanced TTTS is this surgery for the treatment of twin-to-twin transfusion syndrome.

Delivery- Delivery is the best choice if the TTTS is diagnosed later, when no treatment is possible. Premature birth is the norm for newborns with TTTS, and typically, clinicians aim to deliver their patients as near to their due date as possible. Laser ablation babies commonly give birth in the third or second trimester of pregnancy. The babies should be born in one of the specialised mother baby facilities.

RECOVERY

Mothers are often kept in the hospital for two to three days following laser ablation or any other prenatal treatment. Their obstetrician then releases them with instructions for follow-up care. To avoid an early delivery, bed rest will probably be advised along with medication. Additional ultrasounds may be necessary for the patient's ongoing pregnancy monitoring. Many women are successful in feeding their twins breast milk. Lactation consultants can assist mothers of multiples in learning how to breastfeed their children both individually and simultaneously as well as how to produce more milk. Mothers can pump their breast milk and save it for future feedings if their infants are unable to nurse due to illness or preterm birth.

PROGNOSIS

The long-term prognosis for infants with TTTS is influenced by both the age of the infants at delivery and how quickly the illness is addressed after it has developed. The less likely it is that difficulties would arise, the sooner the kids receive care and the longer they remain in the womb before birth. 90% of infants with advanced TTTS do not make it to term if untreated. Babies who receive fetoscopic laser photocoagulation have a significantly higher success rate. When TTTS twins receive the proper care during pregnancy, the majority of them survive and go on to have normal, healthy lives.

What about future pregnancies?

Following a TTTS pregnancy, the likelihood of TTTS happening in subsequent pregnancies remains unchanged from the first (about 1 in 1,000 pregnancies) and does not rise.

CONCLUSION

Approximately 6,000 babies may be affected each year with TTTS, so it is recommended that the mother goes to regular check-ups with their doctor in order to prevent the increase in the severity of this syndrome. The relationship of trust is very important when it comes to doctor and patient, same as a positive mindset as both play a vital role in recovery. Due to the advancement of science, we now live in an era where many minimally invasive techniques are a common treatment plan and thus we should be grateful to these doctors and scientists for making it better and easier for us.

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