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A CASE STUDY OF TWIN TO TWIN TRANSFUSION SYNDROME

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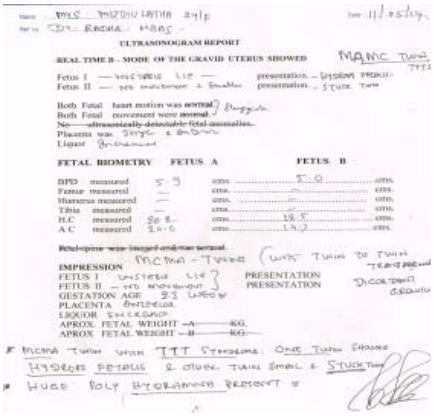
Abstract : Background Monochorionic twins have a risk of developing twin to twin transfusion syndrome, between 10-15 percent.. The mortality rate reaches up to 80-90 percent, if not treated. Twin to twin transfusion syndrome is characterised by the presence of multiple vascular placental anastomosis. The diagnosis of is primarily by USG through ,identification of peculiar sign, no intertwine dividing membrane, same sex, polyhydramnios of recipient twin, oligohydramnios anhydramnios of donor twin, IUGR of donor twin, permanently filled bladder of recipient twin, and slightly filled or empty bladder of donor twin .The severity of Twin to twin transfusion syndrome is established using the Quinteros staging. RESULTST win to twin transfusion syndrome is treated by several options like fetoscopic laser coagulation of placental vascular anastomosis and serial amniodrainage, selective feticide by cord coagulation, septostomy with or without amniodrainage. Timely diagnosis of TTTS is crucial because delay in diagnosis and treatment increases the perinatal mortality and morbidity. At the moment the best treatment seems to be the fetoscopic lasercoagulation of placental vessel anastomosis which showed survival rate between 76-88 percent.

Keyword : Twin to twin transfusion syndrome, Ultrasonogram, Estimated fetal weight, Gestational age, Intra uterine growth restriction.

CASE PRESENTATION

We present a case of Mrs X 24yrs ,gravid 3 para1,live1,abortion 1,previous full term normal delivery, regular menstrual cycles ,conceived spontaneously, Last menstrual period on 30-11 2013 ,Expected date of delivery on 7-9- 2014- with 23 weeks of gestation who is booked and immunized at local health post, referred by a private practitioner with the complaints of decreased fetal movements, draining per vaginum following which she developed lower abdominal pain for the past 2 hours, with Ultrasound taken on the same day with features of Monochorionic twin gestation with Twin to twin transfusion syndrome, with twin A showing features of hydrops fetalis and huge polyhydramnios, twin B showing features of stuck twin ,both fetal heart movements sluggish, both fetal movements sluggish, placenta single, with twin A corresponding to 25 weeks of gestation and twin B corresponding to 20 weeks of gestation .(picture 3).



Obstetric history:

Gravida three ,para one ,live one , abortion one ,.

1st pregnancy :

Full term normal delivery, male baby, birth weight 3.5 kilograms, alive and healthy .No history of any contraceptive usage .She regained her cycles after three months, which was regular.

2nd pregnancy:

She conceived after four months of her delivery which was confirmed by urine pregnancy test. She had spontaneous abortion at 50 days of amenorrhoea which was done in a private hospital.

3rd prenancy:

picture - 3

Present pregnancy was a spontaneous conception, confirmed at 50 days of amenorrhoea by urine pregnancy test in the local heaith post. First trimester scan was done on 12-2-2014 picture (1) picture

Patient Name	Mrs. MUTHULATHA	Age/Sex	24 Years / Female
Patient ID	A7052	Visit No	3
Referred by	Dr. (GOV.HEALTH POST)	Visit Date	12/02/2014
LMPDate	30/11/2013	LMP EDD	05/09/2014

Fetal heart rate - 162 bpm.

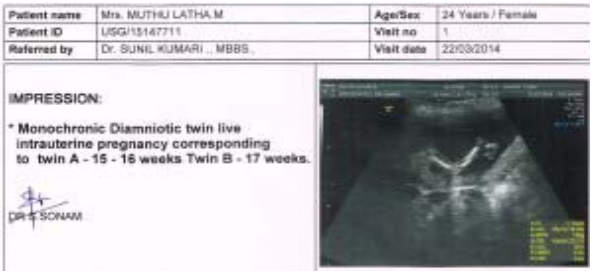
Fetal Biometry
CRL - 43 mm (11 weeks)

Impression

Twin gestation corresponding to a gestational age of 10 Weeks 4 Days
Gestational age assigned as per LMP
Fetus (A)
Placenta - Single fused Anterior placenta, not low lying.
Liquor - Normal
Fetus (B)
Placenta - Anterior
Liquor - Normal
VIABLE FETUSES
(Review after four weeks to assess interval growth)

picture - 1

which showed impression of twin gestation corresponding to gestational age of 10 weeks and 4 days. Chorionicity was not done. She was informed that her pregnany is a twin gestation. Advised to have routine follow up .Prescribed iron and folic acid tablets .First trimester was uneventful. She had her second antenatal visit on 22-3-2014 picture (2)



Patient name	Mrs. MUTHU LATHA.M	Age/Sex	24 Years / Female
Patient ID	USG/15147711	Visit no	1
Referred by	Dr. SUNIL KUMARI ., MBBS.,	Visit date	22/03/2014

IMPRESSION:

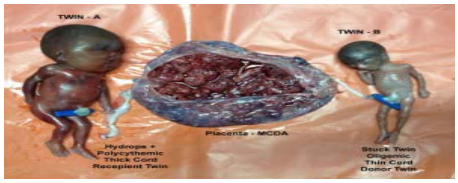
* Monochronic Diamniotic twin live intrauterine pregnancy corresponding to twin A - 15 - 16 weeks Twin B - 17 weeks.

DR S SONAM

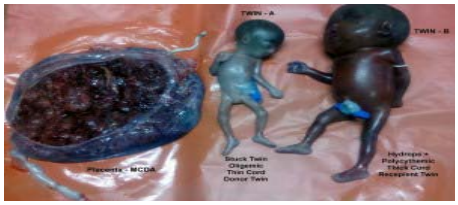
picture - 2

where she was advised to do repeat scan .Her second antenatal scan showed the features of monochorionic diamniotic twin gestation corresponding to Twin A 15 to 16 weeks of gestation, Twin B -17 weeks of gestation with adequate liquor. Her second trimester was uneventfull. Advised to have regular follow up. On 11-5- 2014 she had lower abdominal pain, decreased perception of fetal movements and draining per vaginum, for which she went to a private consultant and they have done antenatal scan ,picture (3) informed that her present twin pregnancy has developed complication due to sharing of placenta and advised hers to get admitted in a tertiary hospital and she got admitted in our hospital. Past history: Not a known case of hypertension, diabetic ,bronchial asthma heart disease ,thyroid disorder, seizure disorder. No history of previous surgery. Family history : no family history of twin gestation . General examination: Patient moderately built moderately and nourished : afebrile ,not anemic, no pallor, mild bilateral pedal edema present .Thyroid, breast, spine , gait appears normal Temperature –normal, Pulse rate -86 per minute , regular in rhythm .Blood pressure 110/80 mmhg , Respiratory rate 18 per minute. Cardiovascular system: S1 ,S2 heard. Respiratory system: Normal vesicular breath sounds heard. Abdominal examination; Over distended abdomen, skin stretched and shiny ,striae gravidarum seen, linea nigra seen. Umbilicus in mid position flushed with surface ,no scars, no dilated veins. Palpation: Uterus Acting ; not tense ; not tender; Symphysiofundal height 34 cms . Abdominal girth 98 cms. Multiple fetal parts felt. Head unengaged . Auscultation: TWIN A -96 beats per minute ,heard in the left spinoumibilical line. TWIN B -80 beats per minute, heared in the right spinoumbilical line. Pervaginal examination: Cervix well effaced ,cervical os dilated 4 centimeters, absent membranes, head felt at 0 station, pelvis gynecoid ,clear liquor draining pervaginum. Ultrasound done in labour ward showed twin gestation with both fetus in bradycardia , twin A cephalic with excess liquor and twin B breech with small for gestational age. Risk explained to the mother and her relations .Informed consent obtained. As the patient was in active phase of labour she was allowed for spontaneous progression . She delivered vaginally with Baby details of :

Twin A Fresh dead born female baby B.WT 1060 gms, hydrops+ Plethoric, Twin B Fresh dead born ,female fetus. small for gestational age, oligemic, B.WT 570 gms. Placenta monochorionic. (Pictures 4 and picture 5).



picture - 4



picture - 5

Postnatal period uneventfull.

CONCLUSION:

As this case got admitted to our hospital in stage 5 of twin to twin transfusion according to Quintero's staging we were not able to prevent the perinatal mortality of both the fetus. So we insist that twin pregnancies are high risk for the fetuses and associated with high perinatal mortality and morbidity. Timely diagnosis of TTTS is crucial because delay in diagnosis and treatment increases the perinatal mortality and morbidity. The natural history of advanced TTTS that is more than stage III is associated with 70 to 100 percent mortality when it is present less than 26 weeks of gestation. Up to 30 percent of survivors may have abnormal neurodevelopment as a result of the combination of profound antenatal insult and the complications of severe prematurity. At the moment the best treatment seems to be the fetoscopic laser coagulation of placental vessel anastomosis which showed survival rate between 76-88 percent. . All women with twin pregnancy should be offered with ultrasonogram at 10 to 12 weeks of gestation. Serial ultrasound examination has to be done for all twin with monochorionic diamniotic placenta beginning at around 16 weeks and continuing for about 2 weeks until delivery. Screening for congenital heart disease is warrented in all monochorionic placentas especially in TTTS. Extensive counseling has to be given to the patients with TTTS including complications and management options of the disease .

DISCUSSION:

Human twins are generally either monozygotic or dizygotic Twin pregnancies are characterized by an incidence of both fetal and maternal complications especially in monozygotic twins. In monozygotic twins, the majority of monochorionic twins have vascular anastomoses, and this shared blood supply can result in twin-to-twin transfusion syndrome (TTTS), a condition characterized by unequal sharing of the maternal blood supply, which results in asymmetrical fetal growth and fetal mortality in 80% or more of untreated cases, particularly if problems develop before 28 weeks' gestation. TTTS is a serious complication in about 10 to 20 percent of monochorionic twin gestations.. TTTS is a progressive disease in which sudden deteriorations in clinical status can occur, leading to death of a co-twin. The natural history of advanced TTTS that is more than stage III is associated with 70 to

100 percent mortality when it is present less than 26 weeks of gestation Up to 30 percent of survivors may have abnormal neurodevelopment as a result of the combination of profound antenatal insult and the complications of severe prematurity.

LITERATURE REVIEW

TTTS was first described by German Obstetrician Friedman Schantz in 1875. TTT Sis a condition that is believed to develop due to unequal sharing of blood flow that then leads to sharing of nutirients ,oxygen and fluid. According to Jackson and Mele (2009) there are three types of vascular anastomosis believed to cause TTTS, they are artery to artery anastomosis vein to vein anastomosis and artery to vein anastomosis. According to Cruz Martinez et al (2011) for severe TTTS laser photo coagulation is the first line of managament. According to Yamamoto and Ville (2005), there are two steps critical to outlining TTTS. First, the gold standard for diagnosing TTTS is visualization of the polyhydramnios /oligohydramnios on ultrasound regardless of other differences including: estimated hemoglobin levels or fetal weight. Second, randomized studies and literature research has shown laser therapy is more successful than amnioreduction in treating TTTS. It is very important to diagnose TTTS before 26 weeks of gestation . This helps improve efforts to increase survival rates and develop new strategies for complications that arise in treated patients. According to Jackson and Mele (2009), there are four common procedures to treat TTTS. These four procedures include amniotic septostomy, umbilical cord occlusion, amnioreduction, and laser therapy.

Amnioreduction (AR) was first introduced to help improve comfort of the mother by controlling polyhydramnios, but is also the most common treatment for TTTS (Jackson & Mele, 2009, AR utilizes amniocentesis to aspirate two to three liters of amniotic fluid from the other twinsacs as well as prolong pregnancy by decreasing premature membrane rupture and preterm contractions. AR does not repair the condition that causes the transfusion syndrome, so eventually amniotic fluid will re-accumulate and require sequential amnioreductions. The greatest disadvantage of AR is the probable need for multiple amnioreductions which increases risk of injury or infection for either mother and/or fetuses.

In a recent trial, 69 percent of patients that underwent AR required more than one procedure throughout gestation. Jackson and Mele (2009) also mention the deliberate perforation of the intertwin membrane in an effort to allow amniotic fluid volumes to equalize between recipient and donor twins. This is a treatment option for TTTS known as amniotic septostomy. Similar to AR, septostomy does not eliminate the underlying cause of TTTS, but may offer relief of symptoms for some patients.

A study performed to test results of septostomy was terminated before completion when results yielded similar rate of survival of at least one twin as AR. A common risk associated with septostomy is the potential for creating a hole in the intertwin membrane which will increase the risk for entanglement of umbilical cords, which could possibly lead to death of one or both twins . According to Jackson and Mele (2009), in 1990 a researcher by the name of De Lia led a group that initiated the use of laser photocoagulation (LPC) as a treatment opportunity for TTTS.

LPC is an invasive procedure that inserts a tiny camera using ultrasound guidance into the uterus through a laser beam that will then coagulate the vascular anastomoses intersecting vascular communication between twins. Advances made in this field led to the development of selective photocoagulation. The concept behind selective photocoagulation is to only coagulate the vessels participating in the syndrome instead of all vessels crossing the intertwin membrane. Laser surgery compared with AR dropped the perinatal death rate nearly 20 percent. Matched with serial amnioreduction, this study shows improvement in neonatal outcomes . Furthermore, fetoscopic cord coagulation uses ultrasound guidance along with an instrument used to occlude the umbilical cord of one twin are used during this procedure. The Goal is to coagulate the vessels in that twin's cord.It is noted that when this procedure is performed, vessels between the donor and placenta remain intact. Selective reduction is set aside for cases in which severe cardiomyopathy is evident in the recipient twin and there is no chance for survival of that twin. In these cases, if laser therapy is attempted, it likely will result in death of the donor twin due to unequal placental sharing between donor and recipient. Validation of cord coagulation states by sacrificing one twin, TTTS progression will stop and gestation will be sustained maximizing outcome of the donor twin.

In such cases, cord coagulation is performed as a last resort (Jackson & Mele, 2009,) O; Donoghue et al (2007) determined there is now reasonable evidence based on observational studies and randomized trial that laser therapy proves superior to conservative management and amnioreduction in cases of severe TTTS (Quintero stages III-IV). Recently, Eurofetus randomized trial published before 26 weeks gestation, laser photocoagulation (LPC) allows neonatal survival of at least one twin and intact survival of six months in 76 percent of cases, compared to 56 percent of cases treated by amnioreduction. Furthermore, re-analysis of allies in a stage-adjusted series suggested laser therapy resulted in a higher perinatal death rate than amnioreduction during Quintero stages I-II. Current evidence is not provided to determine optimal treatment for early stage I of TTTS due to the small number of cases treated at this stage to date. In this article, we present an overview of what is known about the pathophysiology and the diagnosis of TTTS, the treatment options available for TTTS.

PATHOPHYSIOLOGY

TTTS is a complex and dynamic pathologic condition that involves placental intertwin vascular anastomoses; fetal humoral, biochemical, and functional changes; and fetal hemodynamic changes. These changes appear to be responsible for the progression and outcome of TTTS.

PLACENTAL ARCHITECTURAL CHANGES

Placental vascular anastomoses, unequal placental sharing, and abnormalities in umbilical cord insertions are all associated with TTTS. It is believed that almost all monochorionic twins have intertwin vascular anastomoses. These vascular anastomoses can be either direct, superficial anastomoses between the twins' umbilical cord branch vessels on the chorionic plate surface; or ''deep'' anastomoses, wherein the arterial vessels from one twin's cord pierce the chorionic plate to supply a placental cotyledon drained by the venous system of its co-twin; or both.

In regard to type of anastomoses, vascular communications between the recipient and donor twin may be artery to artery, vein to vein, or artery to vein within a placental cotyledon. Depending on the number and type of anastomoses present, the exchange of blood may be balanced or unbalanced. Shifts in blood flow between the twins may be acute, as in the case of co-twin demise, or chronic. Artery-to-artery and vein-to-vein anastomoses are superficial anastomoses with bidirectional flow, but artery-to-vein anastomoses are deep anastomoses with unidirectional flow from one twin to the other. It is thought that TTTS is more likely to develop when there is a paucity of bidirectional artery-to-artery and veinto - vein anastomoses that can assist with regulation of intertwin circulatory imbalances. It has been suggested that artery-to-artery and vein-to-vein anastomoses when present are protective. The antenatal detection of artery-to-artery anastomoses with color Doppler ultrasound is associated with a nine-fold reduction in the

likelihood of developing chronic TTTS. The percent of each type of anastomoses ranges from 20 to 90 percent based on whether the vascular connection was determined by pathologic examination or from fetoscopic studies. Recent evidence suggests that vascular diameter, vascular resistance, and chorionic plate pattern may be as important as the number and type of anastomoses in development, timing, and severity of TTTS.

Several studies have reported that TTTS with unidirectional artery-to-vein anastomoses had a worse perinatal outcome. However, placental vascular anastomoses by themselves do not explain the patho-physiology of TTTS. Other factors, such as cord insertion and placental sharing, may also play an important role.

FETAL ADAPTIVE RESPONSES

The unbalanced blood shunting from donor to recipient has been reported to cause hormonal, hemodynamic, and biochemical fetal changes. This shunting creates a hydrostatic difference between the recipient and donor twins.

The recipient becomes hyperdynamic and hypervolumic. The donor becomes hypovolumic and hy-podynamic. This donor hypovolumia causes a decrease in renal perfusion, thus activating the renin-angiotensin-aldosterone system, which is a hormone system that regulates blood pressure and water (fluid) balance by increasing renin enzyme and angiotensin II (a vasconstrictor), which in turn stimulates the secretion of the hormone aldosterone (increases fluid volume) from the adrenal cortex. This donor hypovo-lumia is also associated with a number of renal structural and functional aberrations, especially in severe TTTS, including renal tubular degeneration and cellular apoptosis, loss of glomeruli or reduction in tubular number, and maldevelopmental progression to renal dysgenesis.

Thus, in TTTS, donors have an increase in renin-secreting cells with up-regulation of renin synthesis system and an increase in angiotensin II, aldosterone, and antidiuretic hormones as an adaptive mechanism to restore euvolumia. With progression of TTTS or in severe TTTS cases, further fetal vasoconstriction mediated by angiotensin II compromises renal and placental blood flow, leading to worsening oliguria, oligohydramnios, and growth restriction in the donor.

In contrast, recipient fetuses demonstrate down-regulation of renin expression with elevation in renin levels and glomerular and arterial lesions in the kidneys, suggestive of hypertension-induced microangiopathy. These findings suggest that hypertensive changes in the recipient twin may be due to vascular shunting of renin from the donor, leading to these hormonal changes.

DIAGNOSIS AND STAGING OF TWIN-TO-TWIN TRANSFUSION SYNDROME

Diagnosis of TTTS is one of exclusion based upon ultrasound findings. Although not all of the following sonographic criteria are necessary for a diagnosis of TTTS, the following findings are suggestive of the diagnosis:

1. monochorionicity, 2. discrepancy in amniotic fluid between the amniotic sacs with polyhydraminos of one twin deepest vertical pocket more than 8 cm and oligohydraminos of the other deepest vertical pocket less than 2 centimeter 3. discrepancy in size of the umbilical cords, 4. presence of cardiac dysfunction in the polyhydramniotic twin, 5. characteristically abnormal umbilical artery or ductus venosus Doppler velocimetry, and 6. less specifically, significant growth discordance often 20 percent.

The differential diagnosis of TTTS includes ute-roplacental insufficiency, growth disturbances due to abnormal cord insertions, discordant manifestation of intrauterine infection, preterm premature rupture of membranes of one twin, and discordant chromosomal or structural anomalies of one twin.

Table 1

Quintero staging system

Stages	Observations			
	Donor Bladder	Amniotic Fluid: Donor/Recipient	Doppler Wave Forms	Other
I	Visible	Oligohydramnios/ Polyhydramnios	Normal	
II	Not visible	Oligohydramnios/ Polyhydramnios	Normal	
III	Visible or not visible	Oligohydramnios/ Polyhydramnios	Abnormal	
IV				Fetal hydrops or abdominal ascites
V				Demise of either fetus

Abnormal Doppler waveform defined as absent or reverse end-diastolic flow in the umbilical artery, reverse flow in the ductus venosus, or pulsatile umbilical venous flow.

CHARACTERISTIC DOPPLER CHANGES IN TWIN-TO-TWIN TRANSFUSION SYNDROME

Several case series earlier reported that TTTS pregnancies have an abnormal pulsatility index of umbilical artery Doppler waveforms; abnormal middle cerebral artery systolic velocities; and pulsatile waveforms in the ductus venosus, hepatic vein, and umbilical veins. Early investigators concluded that Doppler waveforms of the umbilical artery, umbilical vein, ductus venosus, and middle cerebral artery may play a role in diagnosis, prognosis, survival, treatment selection, and follow up after treatment. In 1999, Doppler waveforms of the ductus venosus, umbilical artery, and umbilical vein were an integral part of the Quintero TTTS staging system. The investigator incorporated Doppler changes in severe stages of TTTS based on the natural history of the disease. These Doppler changes in TTTS pregnancies are clinically a reflection of the histo-pathologic placental vascular communication among the donor, the recipient, and the shared cardiac circulatory system. Thus, umbilical vein, umbilical artery, ductus veno-sus, and middle cerebral artery Doppler waveforms are reflective of the fetal circulatory and cardiac status. Since the advent of laser therapy as an acceptable primary treatment of TTTS, several investigators have reported changes in the Doppler waveforms after laser therapy as a clinical reflection of interruption of intervascular anastomoses between both twin placentas.

RECIPIENT ECHOCARDIOGRAPHIC FINDINGS

TTTS is a progressive disease secondary to interplacental vascular anastomoses leading to functional and structural cardiac changes in the recipient. For donor twins, Doppler echocardiographic changes are rare, and ventric-ular function and atrioventricular valve competence are usually preserved. Cardiovascular compromise occurs in most recipient twins, is a major cause of death for these fetuses, and contributes to morbidity and mortality in the donor co-twin. These abnormalities are tricuspid regurgitation, ventricular hypertrophy, increased cardiothoracic ratio, and pulmonary stenosis. An echocardiographic examination of the twins is thus an essential component of the initial workup of TTTS. Then, during the antenatal and postnatal periods, follow-up evaluation for progression of the disease is also necessary. The recipient twin manifests a cardiomyopathy that is progressive in nature. The most common recipient cardiovascular abnormalities in TTTS are unilateral or bilateral ventricular hypertrophy increased cardiothoracic ratio as high as 47 percent ventricular dilation tricuspid regurgitation and mitral regurgitation . These abnormalities are more common with advanced stages of disease. Finally, several cases of acquired pulmonary atresia/stenosis with intact ventricular septum have been described in the recipient twin.

TREATMENT

Numerous treatments for TTTS have been proposed, including selective feticide, cord coagulation, sectioparva that is re moving one fetus, placental blood letting, maternal digitalis, maternal indomethacin, serial amnioreduction, microseptostomy of the intertwin membrane, and nonselective or selective fetoscopic laser photocoagulation. For decades serial amnioreduction has been the most prevalent therapy for TTTS, but in recent years, selective fetoscopic laser photocoagulation has become more widely accepted and in many centers is the primary treatment offered.

AMNIOREDUCTION

Amnioreduction was employed initially for maternal comfort and as a means to control polyhydramnios in the hope of prolonging the pregnancy until the risks of extreme prematurity were lessened. The survival in more recent series, with more consistently aggressive serial amnioreduction to reduce amniotic fluid volume to normal, have ranged from as low as 37% to as high as 83%. Severity of TTTS and gestational age at diagnosis may have a profound impact on the observed mortality with any treatment strategy. The earlier in gestation that TTTS presents, the worse is the prognosis.

INTERTWIN SEPTOSTOMY

Septostomy was proposed specifically as a treatment for TTTS to restore amniotic fluid dynamics without the need for repeated amnioreduction. One objection to this approach is that it possibly results in a large septostomy, creating an essentially monoamniotic sac with the attendant risk of cord entanglement. The survival in each arm of the study was 65%, consistent with the concept that the effect of amnioreduction may be inadvertent septostomy.

FETOSCOPIC LASER PHOTOCOAGULATION

The first treatment for TTTS that attempted to treat the anatomic basis for the syndrome was reported by De Lia who described fetoscopic laser photocoagulation of vessels crossing the intertwine membrane. This treatment option should be superior, because it not only arrests shunting of blood between twins, but it also halts transfer of potentially vasoactive mediators . More recently, Quintero and colleagues described a selective approach to fetoscopic laser photocoagulation in TTTS that does not photocoagulate every vessel crossing the intertwine membrane. Only direct, artery-to-artery and vein-to-vein connections are photocoagulated, along with, more commonly, any unpaired artery going to a cotyledon drained by a corresponding unpaired vein (and vice versa) going to the opposite (co-twin's) umbilical cord

FETOSCOPIC CORD COAGULATION

Some centers have taken the view that the most definitive approach to treating TTTS is selective reduction using fetoscopic cord ligation or coagulation. The rationale is that cord occlusion and sacrifice of one twin arrests the syndrome, prolongs the gestation, and maximizes the outcome for the surviving twin. Cord coagulation preserves the vascular communications between the donor twin and the placenta in the recipient twin's domain.

CONCLUSION

Timely diagnosis of TTTS is crucial because delay in diagnosis and treatment increases the perinatal mortality and morbidity. At the moment the best treatment seems to be the fetoscopic lasercoagulation of placental vessel anastomosis which showed survival rate between 76-88%.

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