Vanishing Twin Syndrome: A Comprehensive Review

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Abstract*— Vanishing twin syndrome is a condition in which one of a set of twins or multiple embryos dies in utero, disappear, or gets resorbed, resulting in a spontaneous reduction of a multi-fetus pregnancy to a singleton pregnancy. This phenomenon typically occurs in the first trimester and can often go unnoticed due to common obstetric complications. The pathophysiology involves abnormalities present from early development, as demonstrated in studies showing flattened placental sacs and fragmented products of conception. Avoid creating or sharing content involving sensitive topics and substances. This article reviews the scientific literature discussing the vanishing twin phenomenon. Information pertaining to frequency, etiology, and potential complications, as well as the impact of sonographic technology on our growing understanding of the events in early multiple pregnancy is provided.

Index Terms- Multiple Pregnancy, Perinatal Outcomes, Spontaneous Reduction, Twin Pregnancy, Vanishing Twin Syndrome, Twin Resorption, VTS.

I. INTRODUCTION

A vanishing twin, also known as twin resorption, is a fetus in a multigestation pregnancy that dies in utero and is then partially or completely reabsorbed. [1][2] In some instances, the dead twin is compressed into a flattened, parchment-like state known as fetus papyraceus. [3]

Vanishing twin syndrome, as the name depicts, is a condition in which one of a set of twins or multiple embryos dies in utero, disappear, or gets resorbed partially or entirely, with an outcome of a spontaneous reduction of a multi-fetus pregnancy to a singleton pregnancy, portraying the image of a vanishing twin. In simple words, the number of embryos conceived, as observed via ultrasonographic examination in early pregnancy, differs from the number of fetuses delivered. This phenomenon occurs in multi-fetus pregnancies, commonly during the first trimester.

Twin loss can happen in the form of miscarriage, of which the mother is aware or in the form of vaginal bleeding or spotting in the first trimester without any knowledge of the mother, as vaginal bleeding is instead a frequent obstetric complication during the first trimester of pregnancy so that the twin loss may go unnoticed. This phenomenon can range from the disappearance of an early empty gestational sac to a sac that had developed a fetal pole to a fetus with documented heart activity. [4]

II. PATHOPHYSIOLOGY

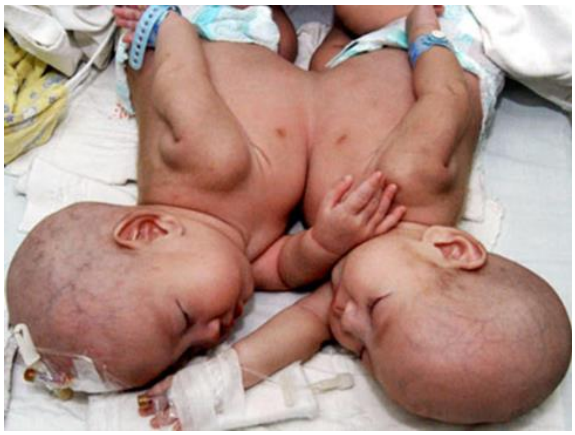
Vanishing twin syndrome is a type of miscarriage that occurs when one or more embryos in a multiple pregnancy die or are reabsorbed in the uterus. Abnormalities that brings about the vanishing of the fetus are usually present from right off the early development as opposed to happening from an intense acute insult [5]. A study including 30 patients performed by Robinson and Caines demonstrated the fetal surface of the placenta as an empty and flattened sac, as pathological evidence of the disappearing twin. Another study conducted by Finberg and Birnholz found a small area containing 30 ml of dark brown blood in the pathological specimen of abortion; this observation was followed by the appearance of a hemorrhagic second sac seen on ultrasonography, which made the patient opt for elective abortion. As per Finberg and Birnholz, if the pregnancy ends in abortion, the results are that the product of conception is commonly fragmented. On the contrary, if the pregnancy continues to term, the subsequent sac may have been removed or expelled, resorbed or fragmented, or may persevere as a little atretic section neglected considerably even after careful examination of the placenta and the membranes.

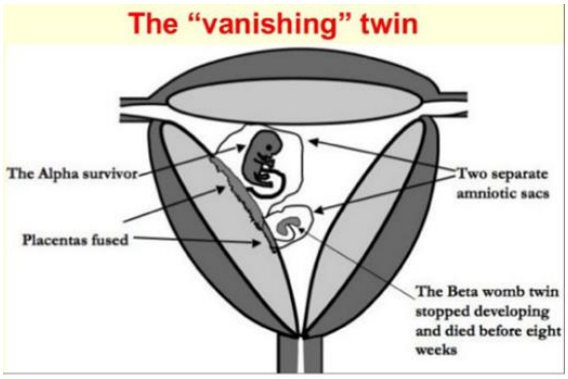
The vanishing twin may have the following physiologic outcomes:

- Resorption: Even though resorption is the most likely physiologic explanation for the vanishing of

the specific proportion of the gestational sac, the valid incidence of resorption is still unknown. Different study results show that resorption can be observed from as early as the seventh week to as late as the twelfth week of gestations. It is evident in any case that resorption of gestational sacs during pregnancy happens without affecting the co-twin. Regardless of the resorption of the vanishing twin, there are excellent chances of the survival of the other twin, as resorption mostly occurs in the first trimester. [6]

- Blighted Ovum: By definition, a blighted ovum is the gestational sacs inside which no embryo can be visualized via ultrasonography. According to some studies, most of the pregnancies that ended up with the vanishing of a fetus were subsequently found to be anembryonic pregnancy co-existing with normal pregnancy. The result could be in the form of vaginal bleeding in the first trimester, indicating the expulsion of the anembryonic sac. It is advisable, therefore, to undergo a thorough ultrasonographic examination before opting for dilation and curettage, as the process of dilation and curettage may end up in the accidental abortion of the other surviving twin. [6]
- Fetus papyraceous: Fetus papyraceous is a mummified, compressed or flattened fetus associated with the other viable fetus. This is very rare and most commonly occurs in multiple gestations. The deceased fetus gets flattened in between the membranes of the other viable fetus and the uterine wall. The demise of the fetus usually occurs right off in the early second trimester. The early demise of the twin may result in complete resorption, but as the pregnancy continues to term, the twin may become macerated and may affect the other viable twin as well, as the pregnancy continues. This course of events can be well observed via regular ultrasonographic examinations. [6] [7]





III. ETIOLOGY

Vanishing twin syndrome, or disappearing twin syndrome, is a type of miscarriage that happens when there's a loss of one baby in utero in a multiple's pregnancy. The other twin usually survives. The fetal tissue from the vanishing twin is usually absorbed by the mother and the surviving baby. In very rare cases, the surviving baby takes on some of the lost twin's cells and becomes a chimera – one person with two sets of DNAs.

Factors that may increase the likelihood of vanishing twin syndrome include:

- Advanced maternal age (over 35), though this may simply be because multiples pregnancies are more likely in older women
- Chromosomal abnormalities in the vanished twin
- Use of assisted reproductive techniques
- Small placenta or other placental abnormalities
- Genetics and teratogenic factors
- Increase the incidence of multiple gestations

Symptoms

Most of the time, there aren't symptoms of vanishing twin syndrome. Sometimes, though, there may be other miscarriage symptoms, such as:

- Cramping
- Bleeding
- Pelvic pain

IV. EPIDEMIOLOGY

Before the advent of ultrasound, little was known about the phenomenon of vanishing twin syndrome (VTS). It was disclosed in 1945 by Stoeckel that the rate of multiple gestations is greater than the rate of their birth, i.e., a twin or even multiple can be lost during multi-fetus pregnancy before the mother is even aware of the loss or the fact that she was carrying multiple fetuses. Since ultrasonography and transvaginal sonography in early pregnancy, vanishing twin syndrome is more frequently diagnosed. Vanishing twin syndrome is evaluated to happen in 36% of twin pregnancies and in half of the pregnancies that begins with at least three or more gestational sacs. With respect to assisted reproductive techniques (ART), it is assessed to occur in 20-30% pregnancies. This phenomenon is progressively predominant with the utilization of the assisted conceptive methods, as more than one embryo is transferred to the uterus; the rate of multiple gestations also increases. [10][5] The vanishing twine syndrome was seen to be associated with very low birth weight (VLBV) and low APGAR scores.

Here are some other statistics about VTS:

- In vitro fertilization (IVF): VTS occurs in 12–30% of IVF pregnancies.
- Advanced maternal age: Research suggests that VTS is more common in pregnant people over 30.
- Risk factors: Other risk factors for VTS include placental degeneration, chromosomal abnormalities, inappropriate implantation site, and placental crowding.
- Symptoms: Most cases of VTS are asymptomatic, but some patients report mild vaginal bleeding.
- Long-term outcomes: If a twin dies in the second or third trimester, the surviving fetus may be at a higher risk of cerebral palsy.

V. COMPLICATIONS

Depending upon the trimester of pregnancy, if the fetus is lost during the first trimester of pregnancy, i.e., in the embryonic stage, the mother is most likely to experience the complication of the vanishing twin in the form of vaginal bleeding or spotting, pelvic cramps or back pain. The chances of survival of the viable co-twin are good in such cases. [12]

On the other hand, chances of complications are higher in the existing co-twin if the demise of the twin occurs later in gestation, which may include cerebral palsy of the viable twin, intrauterine growth retardation (IUGR) of the viable twin, premature labor, and other congenital anomalies accompanied by a fetus papyraceous. [7]

A study was performed recently among singleton pregnancies, twin pregnancies, and women with vanishing twin pregnancies. The results of the study revealed adverse maternal and neonatal outcomes among vanishing twin pregnancies compared to the other two. Among maternal complications, gestational diabetes, premature rupture of membranes, oligohydramnios, cervical insufficiency, labor induction, and preterm labor were higher in vanishing twin pregnancies than singleton and twin pregnancies. [13]

Among neonatal outcomes, fetal malformations were recorded more in vanishing twin pregnancies than singleton and twin pregnancies. [13] Although cerebral palsy has no specific etiology, it is known through general consensus, that the death of a twin in late gestation is associated with higher chances of surviving twin to have cerebral palsy. [14] The pregnancies diagnosed with the vanishing twine syndrome after in-vitro fertilization compared with those were originally singleton carried a higher rate of obstetric complications with regards to preterm deliveries and low birth weight. [15]

It is advisable to have regular prenatal follow up and have the pregnancy assessed with the help of ultrasonographic examinations, to have knowledge about the fetal anomalies associated with the demise of the twin. However, most of the vanishing twin

pregnancies will end up uncomplicated throughout gestation and birth. However, studies show that the birth weight was found to be slightly lower in the co-twin in vanishing twin pregnancy as compared to non-vanishing twin pregnancy. [12]

VI. EVOLUTION

Examination via ultrasound during pregnancy confirms the presence of the vanishing twin phenomenon. Additionally, the examination of the placenta after giving birth provides morphological details about the vanishing twin that was established following an ultrasonographic examination. [16]

Moreover, a study performed to compare the rise of human chorionic gonadotrophin (hCG) between normally progressing twin pregnancies and pregnancies with vanishing twins demonstrated a slower rise of human chorionic gonadotrophin (hCG) in vanishing twin pregnancies as compared to the normal twin pregnancies. The reason for the slower rate of human chorionic gonadotrophin rise could be the result of poor trophoblastic activity due to embryonic causes. These findings indicate that the abnormality in the human chorionic gonadotrophin in vanishing twin syndrome is present from the earliest days of implantation and not due to some acute insult. [17]

A recent study, including a large series of pregnancies with a vanishing twin, was performed to determine the use of maternal serum pregnancy-associated plasma protein-A (PAPP-A) and serum-free B-human chorionic gonadotrophin (B-HCG) in first-trimester screening for trisomy's in relation to the interval between embryonic death and blood sampling. Compared to the previous studies, this study revealed that multiples of the median (MoM) values of maternal serum free B-human chorionic gonadotrophin (B-HCG) were not altered, but that of PAPP-A (MoM) was increased in both pregnancies with an empty gestational sac or a dead embryo. [18]

If the pregnancy is conceived via an assisted reproductive technique, complicated by advanced maternal age, chances of vanishing twin phenomenon to occur get higher, most probably due to the increased chances of chromosomal abnormalities in the fetus associated with advanced maternal age. [19] The regular prenatal examination is highly advisable in such cases, which includes: ultrasonographic examinations and first and second-trimester maternal serum markers. [20] [21]

VII. TREATMENT

There is no special medical care necessary for an uncomplicated vanishing twin pregnancy when the twin is lost during the first trimester of pregnancy. The mother may experience vaginal bleeding or spotting or pelvic pain, which needs regular medical care. The other fetus has higher chances of survival and could be delivered normally. [4]

On the other hand, if the disappearance of a twin complicates the pregnancy during the second or third trimester, then the pregnancy could be treated as high-risk pregnancy, as the outcomes of such pregnancies through later gestational ages might affect the other twin adversely. Regular prenatal visits to assess any signs of complications and keep a check on both maternal and fetal health is necessary to avoid adverse outcomes and their effect on both maternal and fetal health. [22]

VIII. DIFFERENTIAL DIAGNOSIS

Careful ultrasonographic assessment is required to diagnose a vanishing twin in early pregnancy, as any artifact may incorrectly indicate the presence of an additional gestational sac or any pathology of the placenta, such as; placental cysts may incorrectly imply multiple gestations. Histologic examination of the placenta by the experts after delivery is necessary in such cases. [2]

IX. MORTALITY/MORBIDITY

First Trimester Morbidity: When vanishing twin syndrome occurs during the first trimester is limited. The mother is most likely to develop mild vaginal bleeding and cramping.

Second and Third Trimesters Maternal Complications Include

- Premature labour

- Infection from a retained fetus
- Severe puerperal haemorrhage
- Consumptive coagulopathy and
- Obstruction of labour by a low-lying fetus papyraceus causing dystocia and leading to a caesarean delivery.
- The diagnosis of vanishing twin in a pregnancy significantly increases both preterm (<37 gestational weeks) and very preterm (<32 gestational weeks) births.

Fetal Morbidity and Mortality

- In addition to loss of a twin, the surviving fetus has an increased risk of cerebral palsy, particularly if vanishing twin syndrome occurred during the second half of pregnancy.
- Other forms of morbidity reported in the surviving twin are aplasia cutis or areas of skin necrosis.
- In twins connected through vascular connection by placental anastomoses, temporary hypotension in the surviving twin at the time of fetal demise of the vanishing twin leads to poor perfusion and skin necrosis.

X. CASE REPORTS

Case 1:
Objective: To report a case of “Vanishing Twin” syndrome.
Design: Case report.
Methods: Clinical presentation, examination and ultrasound were consistent with diagnosis “Vanishing Twin “syndrome.

CLINICAL CASE:
The Patient in our case is a 40 year- old woman with a secondary infertility with two unsuccessful preceding IVF procedures: first unsuccessful and the second - a spontaneous abortion in the eight gestational weeks, with reduced ovarian reserve (reduced FSH and AMH). The result of the sperm gram is Normozoospermia. The ovulation induction has been done via Flare Up protocol with an initial dose of 450 E FSH and triggering of ovulation with 10000E of hCG. On the 12th day of the COH a function and aspiration of four oocytes was performed, as three of them were in a metaphase II and another one in a GV-stage. The embryo transfer (ET) was performed on the 72nd hour after the function with 20µl culture (Blast Assist™, Origin, Denmark) via Wallace catheter (Smith Medical International, UK) and transabdominal ultrasound control. Three embryos were transferred 1-2 cm from the fundus uteri. The luteal support was performed with micronized progesterone, administrated vaginally (Utrogestan 200mg, 3x/day). On day 14, a quality pregnancy test was done, and it resulted as positive. The first transvaginal ultrasonography was done on day 21st after the ET and an intrauterine pregnancy and three gestational sacs (trihorionic and triamnionic) with CA were visualized (fig:1). A selective embryo reduction was suggested to the patient, but she refused to go through it. The pregnancy continued undisturbed, without fetuses discordant reported, until the 13-14th gestational week. During a routine sonography by the 15th week, one of the fetuses was found without CA. On the 21st of October 2014 a planned Cesarean delivery was performed. Two live infants were delivered with Apgar score 9-10: one male with 2900g and a female with 2400g weight. During the routine examination of the placentas, a mummified fetus (fetus papyraceus) was found (Figure 2, Figure 3). Although no significant differences in the outcomes were noted, many obstetricians prefer Cesarean delivery to reduce the risk for the mother and the fetus in case of multifetal pregnancy.

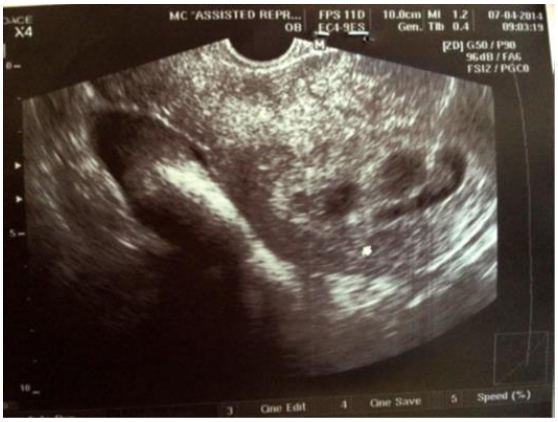


Figure: 1 Triplet pregnancy in early gestational week

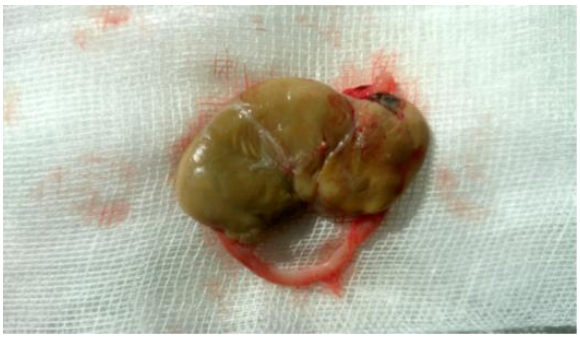


Figure:2: fetus papyraceus

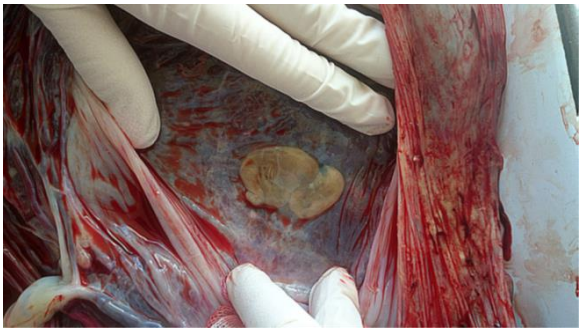


Figure 3: This fetus papyraceus is compressed against the fetal membranes (our case)

Case 2:

A 29-year-old primigravid woman with spontaneous conception without any assisted pregnancy or IVF was diagnosed with VTS. Her last menstrual period (LMP) was on 18 April 2021. The expected date of delivery (EDD) was 25 January 2022. She confirmed her pregnancy after 45 days of amenorrhea through the urine pregnancy Beta-HCG test. During the early confirmation (Five weeks of gestation) ultrasonography scan showed conception was di-chorionic di-amniotic twin pregnancy (two gestational sacs) but no evidence of cardiac activities. She was advised to take regular progesterone support. At ten weeks of gestation, she had light spotting. At 11 weeks, the dual test report showed an early positive risk of preeclampsia and hence she was advised to take a tablet of Aspirin 75 mg daily up to 34 weeks of gestation. After 12 weeks, the ultrasound showed that one co-twin was missing. There was no family history of twin pregnancy, no significant medical comorbidity, or any surgical intervention. At 16 weeks of gestation, her blood serum test result showed TSH: 0.020 mlU/L, T4: 14.95 mcg/dl, was diagnosed with gestational thyrotoxicosis. She took two complete doses of Tdap (Tetanus toxoid, Diphtheria and Pertussis) prophylaxis. An anomaly scan (at 19 weeks of pregnancy) showed no abnormal detection in the survived fetus, and also foetal echo was normal. The biophysical profile showed normal reading, adequate amniotic fluid index (AFI), and the growth scan showed a regular growth interval maintained. She was receiving routine pregnancy care such as regular antenatal care follow-up, iron and calcium supplement, nutritional advice, antenatal exercise, advice on self-care, monitoring and assessing the risk of developing pregnancy-related complications, regular foetal assessment, advice on daily foetal movement count (DFMC) record, close foetal surveillance and conservative management provided by Obstetrician of the tertiary hospital. She was very cooperative and well-compliant with the treatment. Written informed consent was obtained from the patient to publish the report.

Case 3:

A 24-year-old primigravida lady came to our department for her routine first trimester scan. This was her first pregnancy with spontaneous conception. She gave no prior history of any miscarriage. No prior antenatal ultrasound scans were done. On ultrasound, it was found that alongside a normal fetus corresponding to 13 weeks 3 days of gestation, an amorphous mass (2.4 × 2.1 cm) having umbilical vein, fundic bubble, liver and few echogenic bony rib and vertebrae like structures were noted; however, no detectable heart like structure or internal cardiac activity was evident on color Doppler. The amorphous mass was showing surface vascularity in the region of site of attachment of umbilical cord which on spectral Doppler tracing showed reversal of flow in the umbilical artery. There was a single placenta with normal attachments of both the umbilical cords. The other fetus had normal nuchal translucency of 1.6 mm, a normal nasal bone length for gestation, 3 vessel umbilical cord and normal Ductus venosus Doppler parameters with no signs of hemodynamic decompensation.

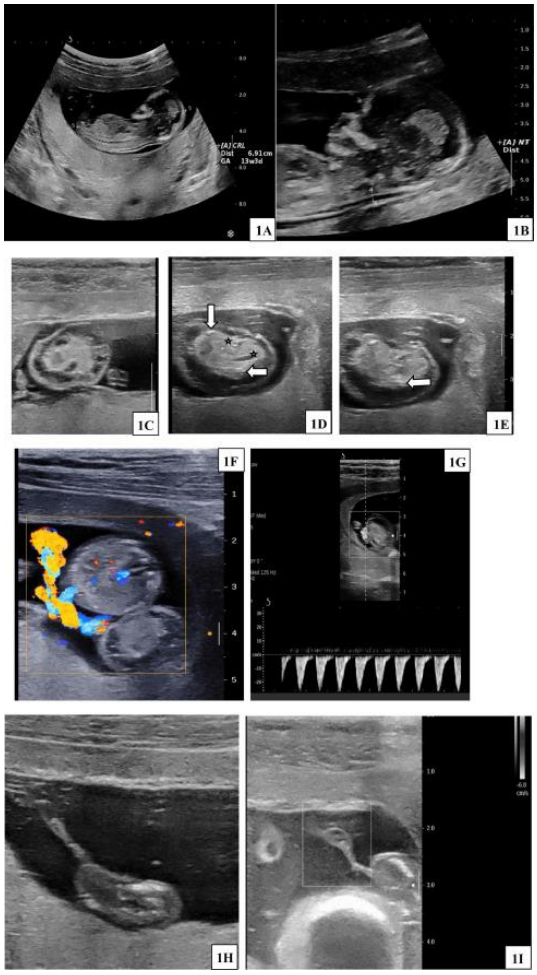


Fig: (A and B) showing normal twin with a crown rump length corresponding to 13 weeks 3 days normal nuchal translucency for gestation age. Figure (C, D, & E) showing an amorphous solid cystic mass (white arrow in figure C & D) separate from the normal twin measuring approximately 2.4 × 2.1 cm in size. Umbilical vein, liver (star in Fig. D) along with few echogenic bony structures were noted within the amorphous mass (white arrows in Fig D & E) suggesting amorphous acardiac twin. Figure (F and G) showing color and spectral Doppler images of the amorphous mass with surface vascularity near the attachment site of umbilical cord which on spectral (Fig G) Doppler showed persistent reversed flow in the umbilical artery. Figure (H and I) Subsequent USG done after 1 month showed reduction in size of the acardiac twin (1.8 × 1 cm) with absence of flow within umbilical cord on color Doppler (Fig I).

A provisional diagnosis of monochorionic pregnancy with acardiac twin with twin reversed arterial perfusion (TRAP) was given and the patient was referred to dedicated fetal medicine unit for further management. The patient was managed expectantly since no ominous signs of heart failure or growth restriction were noted in the normal fetus. The patient was kept under weekly sonographic surveillance.

On subsequent ultrasound done 1 month later, no structural anomaly was noted in the normal fetus, however there was significant reduction in size of acardiac twin (1.8 × 1 cm) with no detectable internal or surface vascularity implying spontaneous demise of the acardiac twin without any intervention.

CONCLUSION

The cause of VTS is not known, but the likelihood of having low birth weight in the survived fetus is high. An assisted or IVF pregnancy is associated with an increased risk of vanishing twins compared to spontaneous pregnancies. Hence, early screening and detection of the cause of the loss of co-twin are necessary steps for preventing the risk of surviving co-twin. It is also essential to provide education about pregnancy care and explain possible complications caused by VTS, counselling and support to pregnant women with VTS.

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