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The vanishing twin: Diagnosis and implications

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A B S T R A C T

Vanishing twin syndrome (VTS), defined by first-trimester spontaneous loss of a twin, is a common phenomenon with a reported prevalence of 15–35% of twin pregnancies. The etiology of VTS is obscure. Still, several risk factors have been identified, including an increased number of embryos transferred in pregnancies conceived by in vitro fertilization, an initial increased number of gestational sacs and advanced maternal age.

The effect of VTS on obstetric and perinatal outcomes is controversial. Several studies have reported that pregnancies with VTS were associated with increased risk for preterm birth and small for gestational age neonates compared to singleton pregnancies, while others showed no difference in perinatal outcomes.

The prevalence of placental vascular and anatomic abnormalities such as small placentas was higher in VTS. These findings lay an essential foundation for understanding how this phenomenon affects obstetric and perinatal outcomes of the surviving pregnancy.

Introduction

The advances in ultrasound technology achieved over the years together with increasing routine clinical use of vaginal ultrasound in early pregnancy evaluation have confirmed the phenomenon

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known as the vanishing twin syndrome (VTS) first identified by Stoeckel in 1945, in which early spontaneous reduction from a twin to a viable singleton pregnancy occurs.

Diagnosis and prevalence

VTS is defined by first-trimester spontaneous loss of a twin, which is reabsorbed either partly or usually completely during pregnancy [1]. First-trimester vaginal bleeding is the only clinical sign described in the literature for VTS, but most cases are asymptomatic [2]. The diagnosis of VTS is based on two sequential ultrasonic examinations, the first at 6–7 weeks demonstrating a twin gestation and the second near the end of the first trimester presenting a single fetus with cardiac activity. The exact definition of VTS used in the literature is inconsistent and differs according to the utmost developmental stage documented in the first ultrasonic examination before identification of fetal reduction (only gestational sac, a gestational sac with a yolk sac, and fetal pole with and without cardiac activity).

VTS is a common phenomenon among multiple pregnancies with a reported prevalence of 15–35% of twin pregnancies [3–8]. It is assumed that the true prevalence of VTS is higher than reported in the literature, since many cases may be undetected if the patient is not monitored with sequential ultrasound exams during the first trimester. VTS is identified more often in pregnancies conceived by in vitro fertilization (IVF) than spontaneous pregnancies since multiple pregnancies are more common in IVF pregnancies, and especially since these pregnancies are monitored routinely by early and frequent ultrasound evaluations. However, the prevalence among IVF and spontaneous pregnancies is probably similar [1,3,5,6,9,10]. Since VTS is more commonly identified in pregnancies conceived by IVF, the vast majority of the existing literature regarding VTS focuses on this population.

Risk factors for the VTS

The etiology of VTS is still obscure, and several etiologies have been proposed, including placental degeneration, chromosomal abnormality in the vanishing embryo, inappropriate implantation site, placental "crowding," intrauterine bleeding and chronic maternal diseases. Vaginal bleeding in early gestation has been shown to be a risk factor for VTS [1,2,11]. Several studies have found a positive correlation between VTS and the initial number of gestational sacs or fetuses seen during the first-trimester ultrasound exam. Manzur et al. [12] reported a spontaneous reduction rate of approximately 50% in 38 triplet pregnancies achieved by assisted reproductive technology (ART). Similarly, Dickey et al. [3] reported on more than 50% spontaneous reduction rate in 155 triplet and higher-order pregnancies. Furthermore, the risk of spontaneous reduction in multiple pregnancies following IVF was shown to increase with the number of embryos transferred [5,13]. Sukur et al. [8] reported that the transfer of each additional embryo doubled the risk of spontaneous reduction in multiple pregnancies resulting from IVF. The positive association between the probability of early spontaneous fetal reduction and the number of gestational sacs or embryos transferred imply that placental crowding may play a role as an underlying cause of VTS.

Advanced maternal age is another well-established risk factor for VTS [3,4,7,8,13,14]. The fact that the VTS population seems to be older than women with singleton or twins can be explained by the age-related risk of pregnancy loss, mainly attributed to aneuploidy [15]. Evron et al. reinforced this explanation [16] by finding that pregnant women with VTS pregnancies also had a higher prevalence of a history of recurrent pregnancy loss than singleton and dichorionic twin pregnancies [14]. However, in a retrospective cohort study of ART pregnancies, La Sala et al. [5] did not find an association between early spontaneous multifetal reduction and maternal age.

Infertility and associated fertility treatments may influence the risk for VTS. Dickey et al. [3] reported that reduction was less frequent after ovulation induction and ART than spontaneous ovulation. Spontaneous reduction rates were 62% for unstimulated twins, 31% for clomiphene-citrate-induced twins, 38% for gonadotropins-induced twins without ART, and 33% for ART twins. There was a trend toward similar results in triplet and quadruplet pregnancies. The authors suggested that the lower spontaneous reduction rate in ovulation induction and ART twin pregnancies was due to equal size gestational sacs resulting from ovulation of a cohort of near equal-sized follicles. Marton et al. [4] further showed that IVF–ICSI procedures reduced the risk of VTS compared with spontaneous

pregnancies and suggested that the artificial selection procedure for morphologically normal embryos decreases the rate of chromosomal defects in the fetus and consequently the rate of VTS following IVF–ICSI. In agreement with this concept, it was shown that the transfer of intermediate versus top-quality embryos increases the risk for VTS [17]. Harris et al. [13] found that tubal factor infertility was also a risk factor for VTS while male factor infertility appeared to be protective, and Sukur et al. [8] have demonstrated that endometrial thickness on the day of ovulation induction was inversely related to an increased likelihood of spontaneous reduction in IVF pregnancies. Furthermore, chronic maternal diseases and history of intrauterine growth restriction (IUGR) and gestational diabetes mellitus (GDM) in previous pregnancies have also been reported as risk factors for VTS [4].

Adverse obstetric and perinatal outcomes associated with VTS

The effect of VTS on obstetric and perinatal outcomes is a subject of controversy with conflicting findings. These discrepancies may stem from several reasons. Most importantly, the definition of "vanished twin" used by different study groups has been inconsistent. In its pure sense, the VTS is a first-trimester missed abortion of one fetus in a twin pregnancy. However, several publications have included fetal losses occurring in the second or third trimester, which are associated with increased rate of adverse perinatal outcomes possibly due to absorption of necrotic fetoplacental tissues and release of cytokines and prostaglandins [14,18–20]. Furthermore, different studies used different developmental stages of the vanished twin before the documentation of fetal loss within the first trimester, ranging from only gestational sac to fetal pole with documented cardiac activity. In addition, most studies included pregnancies that originated in twins and resulted in singletons after early spontaneous reduction of a single fetus, whereas others included triplets and higher-order pregnancies [10,13]. Other reasons for inconsistency regarding the perinatal outcomes of VTS pregnancies include different exclusion criteria used by various studies regarding a lower gestational age limit at which the surviving twin was delivered, the inclusion of IVF pregnancies in some studies vs spontaneous pregnancies in others [21,22] and the different IVF techniques used in different studies, such as fresh versus cryopreserved embryos, five versus three-day embryos, and IVF versus IVF–ICSI procedures [23–25]. Lastly, some studies have excluded monochorionic twins while others incorporated them in their cohort, which may have influenced the results.

Several studies have reported that pregnancies with VTS were associated with increased risk for preterm birth and small for gestational age (SGA) neonates compared to singleton pregnancies [3,4,6,14,18,26–31], while others showed no difference [5,7,9,13,29] (Table 1). Dickey et al. reported that multifetal pregnancies that undergo first-trimester spontaneous reduction deliver earlier and have lower birth weights than unreduced pregnancies with the same number of fetuses at birth. Gestational age at delivery and birth weight were inversely related to the initial gestational sac number irrespective of the final birth number [3]. This observation has led to the hypothesis that the fate of a pregnancy in terms of fetal growth and the time of delivery is determined in its early stage by the number of embryos implanted.

On the other hand, La Sala et al. reported on similar mean gestational age at delivery and birth weights, as well as comparable rates of maternal and neonatal complications in singleton gestations that started as twins compared with singleton gestations that started as singletons, irrespective of the mode of conception [9]. Likewise, Romanski et al. [32] have showed that VTS pregnancies conceived by IVF had comparable perinatal outcomes including preterm birth rate and birth weight compared with singleton pregnancies. Furthermore, the timing of fetal loss during the first trimester was not associated with an increased risk for adverse perinatal outcomes. In a recent large retrospective cohort study, Harris et al. [13] evaluated the differences in perinatal outcome between VTS, singleton, and twin pregnancies conceived by fresh IVF cycles and showed that VTS pregnancies were not associated with worse perinatal outcomes compared to singleton pregnancies, including preterm birth and SGA neonates.

Several studies have demonstrated an increased mortality rate in VTS compared with singleton pregnancies [6,14,30]. In a Danish multicenter large cohort study, Pinborg et al. [6] found a 3.6-fold higher rate of infant mortality among singleton pregnancies with VTS than singleton pregnancies from the start conceived by IVF, even after adjustment for maternal age and parity. The risk increased the

Table 1
Summary of studies comparing obstetric and perinatal outcomes of vanishing twin pregnancies and singleton pregnancies.

Reference	Vanishing twin cohort size (n)	Cohort type	Preterm delivery[a] (%)			SGA[b] (%)			Hypertensive disorder (%)			Perinatal/neonatal mortality (%)		
			Vanishing twin	singleton	*P*/OR (95% CI)	Vanishing twin	singleton	*P*/OR (95% CI)	Vanishing twin	singleton	*P*/OR (95% CI)	Vanishing twin	singleton	*P*/OR (95% CI)
Harris (2020) [13]	73	IVF pregnancies	18	19	0.88	18	11	0.10	7 [c]	8 [c]	0.68	–	–	–
Chasen (2006) [30]	55	IVF pregnancies	12.7	8.9	0.44	14.5	9.6	0.32	9.3	2.4	0.04	–	–	–
Evron (2015) [14]	278	IVF/ovulation induction/ spontaneous pregnancies	32.4	7.7	<0.001	6.8	2.1	<0.001	9	5.5	<0.001	3.6	1.2	<0.001
La sala (2006) [9]	84	IVF pregnancies	16.7	15.9	NS	–	–	–	–	–	–	–	–	–
Marton (2016) [4]	78	IVF pregnancies	0	2.6	1.00	23.1	2.6	<0.001	6.4	4.3	0.24	–	–	–
Marton (2016) [4]	228	Spontaneous pregnancies	5.3	4.4	0.59	5.3	1.8	0.007	6.2	6.1	1.00	–	–	–
Romanski (2018) [7]	100	IVF pregnancies	17	14.8	1.18 (0.67 −2.06)	14	9.7	1.67 (0.88 −3.15)	9	9.2	1.01 (0.48 −2.11)	–	–	–
Almog (2010) [31]	57	IVF pregnancies	22.8	5.8	0.0003	14.0	17.5	NS	–	–	–	–	–	–
Pinborg (2005) [6]	642	IVF pregnancies	13.2	9.0	<0.001	–	–	–	–	–	–	1.09	0.3	–
Pinborg (2007) [18]	642	IVF pregnancies	–	–	–	5.3	3.6	1.50 (1.03 −2.20)	5.1	4.0	0.77 (0.53 −1.12)	–	–	–
Shebl (2008) [29]	46	IVF pregnancies	19.6	8.7	0.067	32.6	16.3	0.029	–	–	–	0	0	–

OR, adjusted odds ratio; CI, confidence interval; IVF, in vitro fertilization; SGA, small for gestational age; NS, not statistically significant.
[a] Delivery before 37 weeks of gestation, except in Almog et al. (before 34 weeks of gestation).
[b] Birth weight below the 10th percentile according to gestational age at delivery.
[c] Delivery for hypertensive disorders.

later in pregnancy spontaneous reduction occurred and was almost entirely due to reductions which occurred at greater than eight weeks gestation. Of note, this study also included cases of fetal loss occurring in the second or third trimester. In contrast, other smaller studies demonstrated no increased risk of perinatal mortality among VTS pregnancies [29]. Moreover, Mansour et al. [10] demonstrated that VTS pregnancies conceived by IVF–ICSI were associated with a lower miscarriage rate and a higher live birth rate than pregnancies without VTS of the exact final order. These findings can be explained by the higher implantation rate in pregnancies associated with VTS, which represents a better capacity of the uterus for early embryonic development.

Several studies also investigated the effect of VTS on maternal obstetric outcomes with conflicting results. In a recent large retrospective cohort study, Harris et al. [13] evaluated the differences in obstetric outcomes between VTS, singleton, and twin pregnancies conceived by fresh IVF cycles. They showed that VTS pregnancies were not associated with worse obstetric outcomes than singleton pregnancies, including cesarean delivery, delivery for fetal indications or hypertensive disorders. Romanski et al. [32] have also demonstrated that VTS pregnancies had comparable obstetric outcomes with singleton pregnancies conceived by IVF, including rates of gestational hypertensive disease, postpartum hemorrhage, and primary cesarean deliveries. On the other hand, an earlier retrospective cohort study by Chasen et al. [30] found that VTS pregnancies were associated with a higher pre-eclampsia rate than singleton pregnancies.

Various explanations for worse perinatal and obstetric outcomes in VTS pregnancies compared to singletons have been suggested, including early implantation crowding, leading to an unfavorable implantation site, abnormal trophoblast invasion, placental insufficiency, and subsequently adverse perinatal and obstetric outcomes, including IUGR and pre-eclampsia [30,33,34]. Depp et al. [35] found increasing frequency of IUGR with increasing initial number of fetuses in multifetal reduction pregnancies, and suggested that early implantation crowding might adversely affect fetal growth of surviving singletons and twins in higher-order pregnancies. An alternative mechanism in which the early demise of one twin affects the surviving co-twin by disturbed placental circulation of blood shunting through inter-twin vascular anastomoses, especially in monochorionic twins, has been proposed [9]. It was also hypothesized that fetal reduction in the first trimester might cause chronic inflammation leading to subsequent fetal growth restriction for the remaining fetus and preterm birth [29].

The timing of the co-twin loss as well as the mode of conception may influence the perinatal and obstetric outcomes of VTS pregnancies. Previous studies have shown that the risk of adverse perinatal outcomes, including SGA, preterm birth, and infant mortality increased with increasing gestational age at the time of vanishing [6,18]. On the other hand, Romanski et al. demonstrated that the timing of early VTS was not associated with increased risk for adverse perinatal outcomes [7].

Marton et al. compared obstetric and neonatal outcomes between VTS and singleton pregnancies after IVF–ICSI and natural conception. They found that VTS pregnancies had a worse perinatal outcome after IVF–ICSI than their spontaneously conceived counterparts [4].

As opposed to the conflicting data regarding the effect of VTS on perinatal and obstetric outcomes compared to singleton pregnancies, the evidence in the literature is mostly consistent regarding the increased perinatal and obstetric morbidity associated with twin pregnancies compared with VTS pregnancies [7,13,30]. These findings are in line with known risks of multifetal gestations compared with singleton pregnancies [21]. In contrast, a retrospective cohort study which compared VTS pregnancies to singleton and dichorionic twin pregnancies found the highest risk for adverse perinatal outcomes, including gestational diabetes, IUGR, very low birth weight and perinatal mortality in the VTS pregnancies and the lowest in singletons [14]. These findings were surprising as they defied logical reasoning, which would expect to see a linear pattern regarding adverse obstetrical outcomes in such a fashion that the highest prevalence should be noted among twins and the lowest among singletons. Furthermore, Almog et al. [31] compared VTS pregnancies to twin pregnancies conceived by IVF and found no significant differences in adverse obstetric outcomes between these two groups of pregnancies, including a similar gestational age at delivery and rate of preterm birth. However, with respect to birth weight, the VTS group was in the middle between twin pregnancies and singletons. Those results support the hypothesis that the delivery time is determined early by the number of embryos implanted while birth weight is influenced to a lesser degree.

Higher-order pregnancies and the VTS

VTS is more common among triplets and higher-order multiple pregnancies compared to twins, with a prevalence of more than 50% [3,5,8,12,36]. La Sala et al. [5] found that at least one early spontaneous reduction occurred in 59.3% of triplets, similar to the rate reported by Dickey et al. (53%) [3]. Similarly, high rates of VTS in the range of 47–65% were reported for quadruplets as well.

Despite the high incidence of VTS in higher order pregnancies, the literature on this topic is scarce. Several studies suggested that high-order multiple pregnancies after fetal reduction are still associated with an increased risk of premature delivery and low birth weight compared with non-reduced twin pregnancies [30,37,38]. Luke et al. have reported that ART pregnancies that started as triplets and subsequently were spontaneously reduced to twins in the first trimester were associated with significantly lower birth weight and a higher rate of preterm birth compared with pregnancies that started as twins from the start [33]. Another study compared between singleton gestations that started as singleton, twins, and higher-order gestations (triplets, quadruplets, and quintuplets) and found a higher risk for preterm birth and low birth weight in singleton pregnancies that started with a higher number of fetal heartbeats on an early ultrasound [28]. Interestingly, the risk was positively correlated with the number of reduced fetuses.

Neurological sequelae of the VTS

Several studies have investigated the risk of neurological impairment in VTS survivors and reported controversial results. A case-control study evaluating VTS as a risk factor for cerebral palsy of unknown etiology including 86 cases of cerebral palsy without a known cause and 381 controls found that among mothers of cases, one of 86 had evidence of vanishing twin on ultrasound, as compared to two of 381 control mothers (odds ratio [OR] 2.2, 95% confidence interval [CI] 0.2–24.8; $P = 0.05$). It was not possible to determine whether the vanishing twins and surviving infants were mono- or bichorionic. The authors have concluded that VTS was unlikely to account for a high proportion of cerebral palsy cases, but there was insufficient statistical power to draw firm conclusions [39].

Pinborg et al. studied 642 VTS pregnancies and found no excess risk of neurological sequelae in survivors of a vanishing co-twin versus the singleton cohort. However, the risk of neurologic sequelae appeared to be dependent on the timing of spontaneous reduction during pregnancy as spontaneous fetal loss until eight weeks was not related to elevated risk of neurologic sequelae, whereas a significant association was noted for losses occurring after that and neurologic sequelae. However, this cohort was not restricted to the classical definition of VTS and included cases of fetal reduction that also occurred in the second and third trimesters [6].

The literature regarding VTS in monochorionic twins is scarce since most studies regarding VTS excluded monochorionic twins from their cohorts. However, the impact of VTS on the surviving twin is especially intriguing in monochorionic pregnancies since monochorionic twins share one placenta with inter-twin vascular placental anastomoses and consequently the loss of one twin can cause concomitant death or neurological injury to the surviving co-twin. However, the lowest gestational age at which a single loss in monochorionic twins may cause damage to the surviving co-twin is unknown.

Placental characteristics of the VTS

In VTS pregnancies, the reduced fetus is rarely recognized as embryonic remnants incorporated into the placenta of the survivor, owing to the early gestational age at fetal loss [13,40]. However, as opposed to its name, VTS is often evidenced by placental pathological findings. Jauniaux et al. [2] examined placentas from pregnancies with VTS and described focal degenerative changes composed of well-delineated plaques of perivillous fibrin deposition. These placental lesions, which represent abnormalities in vascular perfusion, also exist in about 25% of placentas from uncomplicated term pregnancies. In a recent large retrospective cohort study of fresh autologous IVF pregnancies, Harris et al. [13] evaluated the differences in placental pathology between VTS, singleton, and twin pregnancies. They found that the prevalence of placental anatomic abnormalities, such as small placentas (less than the 10th percentile), velamentous cord insertion, and accessory placental lobes was higher in vanishing

twin pregnancies than singleton and twin pregnancies. The authors hypothesized that the disappearance of one fetus might affect the placental development of the surviving twin, which may lead to an adverse perinatal outcome of the ongoing pregnancy. As anatomical placental pathologies have been linked to placental insufficiency, growth restriction, and non-reassuring fetal status [41,42], these findings lay an essential foundation for understanding how VTS may affect obstetric and perinatal outcomes.

VTS and aneuploidy screening

When interpreting the values of serum biochemical analytes used for aneuploidy screening in the first and second trimesters, adjustments are made for twin pregnancies, as different ranges of serum analytes are associated with multifetal pregnancies [43,44]. However, data about biochemical changes in VTS pregnancies are scarce.

Several studies reported changes in the second-trimester biochemistry screening for aneuploidy associated with VTS. A slower rising rate of human chorionic gonadotropin (hCG) than that seen in normally progressing twin pregnancies has been described [45]. Moreover, following multifetal pregnancy reduction, high levels of maternal serum alpha-fetoprotein in the second trimester have been described [46].

Likewise, several studies have reported that first-trimester biochemical values in VTS pregnancies is also altered compared with non-reduced singleton pregnancies [47,48]. Chasen et al. reported that spontaneous fetal reduction from twins to singleton within four weeks of biochemical measurement was associated with higher pregnancy-associated plasma protein A (PAPP-A) and free β-hCG compared with singleton pregnancies without fetal reduction [47]. In pregnancies in which spontaneous reduction has occurred, there might be a residual trophoblastic function from the nonviable gestation, resulting in higher levels of the biochemical markers. Another explanation for the elevated free β-hCG observed is that aneuploidy is likely to account for a high proportion of early embryo reduction, similar to early spontaneous abortion.

Differences in biochemical values can potentially affect risk assessment for fetal aneuploidy, leading to less accurate risk assessment in these pregnancies. If these findings are confirmed in subsequent extensive studies, laboratories may consider adjustments in the risk assessment algorithm when there is evidence of VTS.

Cell-free DNA (cfDNA)-based noninvasive prenatal testing (NIPT) is a more accurate method for detecting fetal aneuploidies than traditional serum screening methods [49]. However, this approach cannot determine the source of DNA and cannot detect additional fetal haplotypes associated with vanishing twins. A study of a large general screening population [50] showed that using single-nucleotide polymorphism (SNP)-based NIPT, pregnancies with VTS can be identified by its ability to detect the presence of additional fetal haplotypes. The ability to detect vanished twins is clinically essential. First, chromosomal abnormalities, common in vanished twins, are likely to generate false-positive results when using methods that can only assess total DNA and cannot detect additional haplotypes. Indeed, studies using counting-based methods attributed a significant proportion of false positive results to vanishing twins. In one study, 15% of NIPT false-positive results were shown to involve vanished twins [51], whereas another study showed that 33% of trisomy 21 false-positive results were attributed to vanishing twins [52]. Second, a vanished twin with discordant fetal sex may lead to the incorrect NIPT-based identification of fetal sex compared with ultrasound. Both circumstances may lead to unnecessary invasive testing. The ability of this method to identify additional fetal haplotypes is expected to result in fewer false-positive calls and prevent incorrect fetal sex identification.

Summary

VTS is a common phenomenon among multiple pregnancies, with a reported prevalence of 15–35% of twin pregnancies [3–8]. Couples diagnosed with a multiple gestation and consider the option of multifetal pregnancy reduction procedure should be informed regarding the relatively high rate of VTS

[3,5], as it enables them to delay their decision to the end of the first trimester and avoid an invasive procedure if VTS occurs by then.

The etiology of VTS is obscure, but several risk factors have been reported in the literature, including an increased number of embryos transferred in IVF pregnancies [5,13] and an initial increased number of gestational sacs [3,8,12]. Advanced maternal age is another well-established predictor of VTS [3,4,7,8,13,14], suggesting aneuploidy as a reason for VTS [15].

The effect of VTS on the perinatal outcome of the continuing pregnancy compared to singleton pregnancies is a subject of controversy. Several studies have demonstrated that pregnancies with VTS were associated with increased risk for an adverse perinatal outcome, including preterm birth, fetal growth restriction, and perinatal mortality [3,4,6,14,18,26–31], while others were reassuring and showed no difference [5,7,9,13,29]. Further large prospective studies are needed to reach a more decisive conclusion and settle this ongoing debate. Clinicians managing these pregnancies should inform parents of this controversy and consider a tighter prenatal care regimen, including fetal growth monitoring. No data exist regarding VTS in monochorionic pregnancies and its risk for neurological impairment in the surviving co-twin, and large prospective studies are urgently needed to elucidate this issue.

Placentas from VTS pregnancies were associated with vascular and anatomic pathologic findings [2,13]. These findings lay an essential foundation for understanding how VTS may affect obstetric and perinatal outcomes. Further investigation in larger cohorts of vanishing twin pregnancies is required.

Practice points

- The etiology of vanishing twin syndrome (VTS) is obscure, but several risk factors have been reported in the literature, including an increased number of embryos transferred in IVF pregnancies, an initial increased number of gestational sacs and advanced maternal age.
- The effect of VTS on the perinatal outcome compared to singleton pregnancies is a subject of controversy but appears to be related to adverse perinatal outcome.
- Placentas from VTS pregnancies were shown to be associated with placental vascular and anatomic pathologic findings.

Research agenda

- The effect of vanishing twin syndrome (VTS) on perinatal and obstetric outcomes of the continuing pregnancy is a subject of controversy. Further large prospective cohorts are needed to reach a more decisive conclusion.
- The risk of neurological impairment in survivors of VTS and specifically in monochorionic twins.
- Further research on placental pathologies in VTS may clarify if and how the disappearance of one fetus may affect the perinatal outcomes of the surviving fetus.

Declaration of competing interest

The authors have no conflicts of interest.

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