Vanishing twin syndrome: is it associated with adverse perinatal outcome?

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Objective: To evaluate whether vanishing twin syndrome (VTS) is associated with adverse perinatal outcome.
Design: A retrospective cohort study investigating the impact of VTS on perinatal outcome was conducted. Parturients were classified into three groups: those pregnancies that started with double fetal sacs and spontaneously reduced into one (VTS), those with dichorionic twins, and those with singleton pregnancies. Statistical analysis included multiple logistic regression models to control for possible confounders.
Setting: Tertiary university medical center.
Patient(s): The study involved 252,994 singleton deliveries between the years 1988 and 2012.
Intervention(s): None.
Main Outcome Measure(s): The impact of VTS on perinatal outcome.
Result(s): During the study period, 278 pregnancies with VTS were compared with 1,801 pregnancies of dichorionic twins and 252,994 pregnancies of singletons. A significant linear association was documented among the three groups and various adverse outcomes, including gestational diabetes mellitus (GDM), intrauterine growth restriction (IUGR), very low birth weight (VLBW), and perinatal mortality. The higher risk was noted in the VTS group, and the lowest in singletons. Using multivariable logistic regression models, while controlling for confounders such as fertility treatment and maternal age, VTS (as compared with singletons) was found to be an independent risk factor for several adverse perinatal outcomes including GDM, IUGR, VLBW, low Apgar scores, and perinatal mortality (adjusted odds ratios with their respective 95% confidence intervals, 1.4 [1.01–2.0], 2.7 [1.7–4.3], 6.9 [4.7–10.2], 1.9 [1.1–3.3], 2.4 [1.2–4.5]).
Conclusion(s): Pregnancies with VTS are associated with an adverse perinatal outcome, even after controlling for confounders such as fertility treatment and maternal age. (Fertil Steril® 2015;103:1209–14. ©2015 by American Society for Reproductive Medicine.)
Key Words: Vanishing twin syndrome, VTS, perinatal mortality, risk factors, congenital malformations

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In recent years, a substantial rise in the prevalence of twin pregnancies within the industrialized world has been noted (1). This increase may be attributed mainly to the wide use of fertility treatments that are available to patients today, in addition to advanced maternal age at the time of conception and delivery (1). In the year 2011, twin pregnancies made up roughly 3.3% of all live births in the United States (2). Out of all naturally conceived multiple pregnancies, twins make up approximately 96% of births, where roughly 69% are dizygotic twins and the remaining 31% are monozygotic twins (3).

High-order pregnancies are known to be associated with adverse pregnancy outcomes, including preterm delivery (PTD) (4). This is of main concern to caregivers and patients alike, as PTD was found to be one of the five leading causes of infant death within the United States, as of 2011 (5).

Vanishing twin syndrome (VTS) describes a spontaneous reduction of a

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fetus while still in utero, which dissipates either partially or completely during gestation (6). In more than 50% of all pregnancies that started with three gestational sacs or more, a spontaneous reduction of at least one fetus was noted before the 12th week of gestation (7). Spontaneous reduction also occurred in about 36% of twin gestations (7). Additionally, it is quite plausible that the prevalence of spontaneous reduction is in essence much higher, since VTS may often be undetected throughout the course of pregnancy and labor.

Similar rates of VTS were noted among pregnancies that were achieved solely through assisted reproductive technologies (ART) (6, 8). A retrospective cohort study that examined complications in ART pregnancies that had undergone spontaneous fetal reductions found that in comparison with singleton gestations, the loss of one or more fetuses significantly increased the risk for low birth weight (LBW) and PTD. Moreover, this study also found fetal reduction as a risk factor for perinatal mortality (9). Other studies have reconfirmed most of these findings as well (10–13). Luke et al. described how these risks tended to grow, in accordance with the amount of reduced fetuses noted (14). VTS has also been demonstrated to alter the results of first trimester biochemistry testing that is used to screen for aneuploidy (15, 16). Additionally, VTS was found to be associated with an increased risk for congenital anomalies (17), malformations of cortical development in monochorionic twins (18), vaginal bleeding (19, 20), and preterm premature rupture of membranes (20), as compared with other types of gestation.

Conversely, there is no uniform consensus as to whether any detrimental perinatal outcome concerning infants delivered after VTS exists at all (21). Moreover, another study that examined only IVF pregnancies compared the outcomes of singletons, twins, and VTS and found that indeed VTS was associated with poorer outcome when compared with singletons, although a better outcome was noted when compared with twins (22). Hence, there may be additional factors pertaining directly to the inherent underlying etiology of infertile couples seeking treatment that can account for the adverse outcomes noted above, regardless of whether spontaneous fetal reduction or other potentially confounding factors have concomitantly occurred (23, 24).

Although VTS is a quite common occurrence among high-order pregnancies, the existing studies relating to its potential maternal and perinatal outcomes are quite scarce. Additionally, there is no consensus within the literature regarding the outcomes of labor and delivery.

The purpose of this study was to evaluate whether VTS is associated with adverse perinatal outcome as compared with dichorionic twins and singleton pregnancies. This study was conducted to substantiate a more decisive standpoint regarding the phenomenon's natural course and effect.

MATERIALS AND METHODS

A retrospective population-based study comparing VTS pregnancies to singleton and dichorionic twin pregnancies was conducted, following appropriate Institutional Review Board approval. The study included all deliveries that occurred between the years 1988 and 2012 at the Soroka University Medical Center, which is the sole provider of services to the entire obstetrical population in the southern region of Israel. All deliveries occurring at this time were classified into three groups as follows: VTS, singleton pregnancies, and dichorionic twins.

Data were collected from the computerized perinatal database. Inclusive VTS pregnancies were defined as gestations that originally started with two gestational sacs, where one of them dissipated at some point during the pregnancy. Twin dichorionicity was guaranteed by selecting only pregnancies with different fetal gender.

Excluded from the analysis were all higher order pregnancies (three or more fetuses) and patients lacking prenatal care. Clinical characteristics that were noted include maternal age, parity, ethnicity (Jewish and Bedouin Arab), recurrent pregnancy loss, gestational diabetes mellitus (GDM), hypertensive disorders, and neonatal gender. The following labor characteristics and perinatal outcomes were assessed: premature rupture of membranes (PROM), labor induction, vasa previa, mode of delivery, low Apgar score (1 and 5 minutes), birth weight, macrosomia, congenital malformations, perinatal mortality, and maternal blood transfusion.

Statistical analysis was performed using the SPSS package, version 21. Categorical variables were compared using χ^2-tests. Continuous variables were calculated by one-way analysis of variance. We examined the differences among the three groups by using χ^2-tests for trends (linear by linear association test). Multivariable logistic regression models were constructed to study the association and impact of VTS on perinatal outcome, while controlling for the confounders that were found to be significant in the univariate analysis and that had biological plausibility (i.e., maternal age, ethnicity, primiparity, and fertility treatments). VTS was entered as a categorical variable (i.e., VTS vs. dichorionic twins vs. singletons, as a reference). The independent variables were considered using backward selection. Odds ratios (OR) and their 95% confidence intervals (CI) were computed. $P<.05$ was considered statistically significant.

RESULTS

Of the 255,073 parturients studied, 278 (0.1%) had vanished twins. Their obstetrical outcome was compared with 252,994 singletons (99.1%) and 1,801 first born dichorionic twins (0.8%). The different clinical and demographic characteristics of the women within these three groups are presented in Table 1. Women belonging to the VTS group were significantly older and also had a higher prevalence of recurrent pregnancy loss compared with the two comparison groups. The rates of fertility treatment were similar in the VTS and the twin groups alike (35.7% in the twins group vs. 34.5% in the VTS group; $P=.9$) and were notably higher compared with the singletons group (2%, $P<.001$).

Table 2 summarizes the pregnancy and labor complications of the three groups. GDM, chronic hypertension, and cervical insufficiency were all found to be more prevalent in a linear association in the VTS group, demonstrating the highest prevalence among the VTS group and the lowest among singletons. Intrauterine growth restriction (IUGR)