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Does a Vanishing Twin Affect Perinatal Outcome?

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Abstract

Background: The impact of vanishing twin (VT) syndrome on obstetric outcome is currently unknown. The aim of this study was to compare obstetric and neonatal outcomes of VT with singleton and twin deliveries after assisted reproduction and to evaluate the impact of VT on pregnancy outcome.

Methods: We analyzed 130 births at our hospital between January 2000 and February 2012 that resulted from assisted reproduction. Among these, 96 were singleton, 10 were VT, and 24 were twin deliveries. Vanishing twin was defined as a first-trimester (≤ 12 gestational weeks) embryonic loss of one of the twins. We compared the obstetric and neonatal outcomes of VT with singletons and twins, respectively.

Results: The obstetric and neonatal outcomes were similar between VT and singleton deliveries, although there was a trend towards an increased rate of preterm delivery (9.4% vs. 20%, p=0.28), extremely preterm delivery (5.2% vs. 20%, p=0.13), and low birth weight <2500 g (30% vs. 73.3, p=0.023) in the VT group. Outcomes were significantly better in the VT group than in the twin group. The rate of preterm delivery was significantly higher in the twin group than in the VT group (20% vs. 70.8%). Furthermore, birth weight was significantly lower in the twin group than in the VT group (2798 ± 187 vs. 2046 ± 97), and the rate of low birth weight was higher in the twin group than in the VT group (30% vs. 73.3%).

Conclusion: Obstetric and neonatal outcome after assisted reproduction may deteriorate according to pregnancy status in the following order: singleton, VT and twin pregnancy.

Keywords: Vanishing twin; Neonatal outcomes; Assisted reproductive treatment; Preterm delivery; Low birth weight

Abbreviations

VT: Vanishing Twin; ART: Assisted Reproductive Technologies; IVF: *In Vitro* Fertilization; ICSI: Intracytoplasmic Sperm Injection

Introduction

Vanishing twin (VT) syndrome is defined as the first-trimester embryonic loss of one of the set of twins. The prevalence of this syndrome is reported in 4%–30% of all singleton deliveries after the use of assisted reproductive technologies (ART) [1-7]. The impact of VT on obstetric outcome till date has been unknown. Some studies state that VT is associated with lower birth weight and a high-rate of preterm deliveries [1-5] and that significant similarity are present between the obstetric outcome of VT and twin pregnancies. However, other studies have shown that there is no difference between the obstetric outcome of VT and singletons [6,7]. Despite the high incidence of VT, there has been little research on this topic.

The aim of this study was to compare the obstetric and neonatal outcomes in VT with singleton and twin deliveries after ART and to evaluate the impact of VT on pregnancy outcome.

Materials and Methods

We achieved 227 clinical pregnancies by *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) between January 2000 and February 2012 at the University of the Ryukyus Hospital (Okinawa, Japan). Of these pregnancies, we retrospectively analyzed 130 deliveries; miscarriages and on-going pregnancies were excluded. Of the 130 deliveries, 96 were singletons, 10 were VT, and 24 were twin deliveries. VT was defined as a first-trimester (≤ 12 gestational weeks) embryonic loss of one of the twins. The diagnosis was made by ultrasonography. No cases of VT after the first trimester or of VT from monochorionic twins were included in this study. Outcomes analyzed included gestational age at delivery, birth weight, rate of low and very low birth weight, rate of preterm and extremely preterm delivery, and rate of caesarian section. Low birth weight was defined as birth weight <2500 g, very low birth weight as birth weight <1500 g. Preterm delivery was defined as birth occurring before 37 weeks of gestational age and extremely preterm delivery as birth occurring before 28 weeks of gestational age. Outcomes of VT deliveries were compared with singleton and twin deliveries, respectively. This retrospective study was approved by the Institutional review board of our University (21st April 2015).

For IVF, we used a gonadotropin-releasing hormone-agonist long or short protocol, or a gonadotropin-releasing hormone-antagonist protocol for controlled ovarian stimulation. Oocyte pick-up was performed under intravenous anesthesia and fertilization was achieved by insemination or ICSI, depending on the analysis of the

spermatozoa. If there were >5 fertilized ova, all were cultured for 5 days and blastocyst embryo transfer or cryopreservation was performed. If there were ≤ 4 fertilized ova, early cleavage embryo transfer or cryopreservation was performed. From 2000 to 2008, multiple embryo transfer was performed. After 2008, single embryo transfer was predominantly performed; however, double embryo transfer was considered if the woman was >35 years old or had undergone unsuccessful IVF treatment more than twice. All frozen–thawed embryo transfers were performed during an artificial cycle.

For statistical analysis of maternal characteristics, categorical variables were assessed using the chi-square test and Fisher's exact test for a small sample. Differences in continuous variables were evaluated using Tukey's test. For statistical analysis in obstetric and neonatal outcomes, VT outcomes were compared with both singleton and twin deliveries. Categorical variables were assessed using the chi-square test and Fisher's exact test for a small sample size. Differences in continuous variables were evaluated using Student's t-test. A p value of <0.05 was considered statistically significant.

Results

A total of 130 deliveries were included in the study. There were 96 singleton, 10 VT, and 24 twin deliveries. The incidence of VT was 9.4% (10/106). Characteristics of the three groups are shown in Table 1. There were no significant differences in age, duration of infertility or population of primary infertility among the three groups. The number of embryos transferred was significantly higher in VT and twin pregnancies than singleton pregnancies. All twin pregnancies were achieved after fresh embryo transfer, and blastocyst transfer was lower in twin pregnancies compared with VT and singleton pregnancies.

	Singleton (n=96)	VT (n=10)	Twin (n=24)	p
Age				0.35
mean ± SD	35.7 ± 0.36	36.1 ± 1.1	34.6 ± 0.72	
range	26–43	33-41	26-43	
Number of embryos transferred	2.0 ± 0.08	2.6 ± 0.25	2.5 ± 0.16	0.008
Duration of infertility (years)	4.4 ± 0.34	3.4 ± 1.1	4.6 ± 0.66	0.63
primary infertility	43 (44.8%)	4 (40%)	7 (29.7%)	0.38
Frozen–thawed embryo transfer	26 (27.1%)	3 (30%)	0 (0%)	0.014
Blastocyst transfer	38 (39.6%)	3 (30%)	1 (4.2%)	0.004

Table 1: Characteristics and treatment data of the singleton, vanishing twins (VT), and twin groups.

Obstetric and perinatal outcomes are summarized in Table 2. The outcomes were similar between singleton and VT. There were no significant differences for all parameters between singleton and VT, although there was a trend towards an increased rate of preterm delivery (9.4% vs. 20%, p=0.28), extremely preterm delivery (5.2% vs. 20%, p=0.13) and low birth weight <2500 g (17.2% vs. 30.0%, p=0.39) in the VT group. Compared with twins, outcomes in the VT group were significantly better in gestational age at delivery and birth weight. Twins were delivered at earlier gestational ages (34.9 ± 0.73 weeks vs. 37.3 ± 0.84 weeks, p=0.064) and had a significantly higher rate of preterm delivery compared with that of VT (70.8% vs. 20%, p=0.0098). Birth weight was significantly lower in the group with twins compared with VT (2046 ± 97 g vs. 2798 ± 187 g, p=0.0017), and the rate of low birth weight in this group was higher than that in VT (73.3% vs. 30%, p=0.023). There was no difference in the rate of caesarean section.

	Singleton (n=96)	VT(n=10)	p[a]	Twin (n=24)	p[b]
Gestational week			0.22		0.064
mean ± SD	38.4 ± 0.28	37.3 ± 0.84		34.9 ± 0.73	
Range	28–41	28–41		26–39	
Preterm delivery <37-week-gestation	9 (9.4%)	2 (20%)	0.28	17 (70.8%)	0.0098
Extremely preterm delivery <34-week-gestation	5 (5.2%)	2 (20%)	0.13	5 (20.1%)	1
Caesarean section	39.7%	44%	1	79.1%	0.09
Birth weight (g)			0.7		0.0017
mean ± SD	2874 ± 61.7	2798 ± 187		2046 ± 97	
Range	1014–4280	1338–3538		430–3192	

Low birth weight <2500 g	16 (17.2%)	3 (30%)	0.39	33 (73.3%)	0.023
Very low birth weight <1500 g	3 (3.2%)	1 (10%)	0.34	9 (20%)	0.67

Table 2: Outcome of singleton, vanishing twin (VT), and twin pregnancies after *in vitro* fertilization (a: Singleton versus VT; b: VT versus twin).

Discussion

VT is defined as a first-trimester embryonic loss of one of a set of twins. Since the syndrome was first reported by Levi in 1976, the phenomenon has been widely observed. The frequency of diagnosis of VT has increased as twin pregnancies have risen in number following the use of ART and as the diagnostic tool, namely the transvaginal ultrasound, has been improved. The prevalence of VT has been reported at 4%-30% after ART, and the impact on obstetric and neonatal outcome has been discussed [1-7]. Almog et al. [1] compared 57 VT deliveries with 171 matched singleton deliveries after ART and observed lower birth weight, an increased rate of low birth weight <2500 g and an increased rate of delivery at <28 weeks of gestation in the VT group. Shebl et al. [2] compared 46 VT deliveries with 92 matched singletons after ART and showed that VT was associated with small size for gestational age and an increased rate of low birth weight <2500 g. The reasons for these poor VT outcomes are considered to be the direct impact of embryonic loss on the surviving twin, infection and the disturbed placental circulation of blood shunting through inter-twin vascular anastomoses, particularly in monochromatic twins [1,2,6].

Elsewhere, opposite outcomes have been described. La-Sala et al. [6] compared 84 VT births with 602 singleton births after IVF/ICSI and showed that the two groups had similar mean gestational age and birth weights as well as similar frequencies of preterm and extremely preterm (≤ 32 weeks gestation) birth, low birth weight, and very low birth weight. Mansour et al. [7] reviewed 206 VT and 1891 singleton pregnancies after ICSI and observed that there was no statistically significant difference in the mean gestational age at delivery. However, they did note that the live-birth rate and take-home-baby rate per pregnant woman were significantly higher and the miscarriage rate was significantly lower in the VT group. They speculated that the improved prognosis in VT pregnancies could be explained by the higher implantation rate in pregnancies associated with VT, which represented a better capacity of the uterus for early embryonic development. In our study, there was no significant difference in all parameters between VT and singleton deliveries, although there was a trend toward an increased rate of preterm delivery, extremely preterm delivery and low birth weight <2500 g in the VT group.

Of the 10 VT pregnancies in our study, one of the twins died between 8 and 12 gestational weeks in three cases after a fetal heart beat had been detected and at 5 gestational weeks in seven cases in which an empty gestational sac had been detected. Pinborg et al. [3,4] conducted a retrospective study, including the cases of VT into the third trimester, and showed higher rates of low birth weight, very low birth weight, preterm delivery, and infant mortality associated with VT. They also showed that these risks were almost entirely because of the demise at >8 weeks of gestation. In our study, there were only 3 cases with demise after 8 weeks and others were detected at relatively earlier dates. This could be a reason why there was no difference between the outcomes of VT and singletons in our study. However, the impact of VT on obstetric and neonatal outcome has been unknown to date, and studies with larger sample sizes are required to confirm the findings in this study.

Some researchers have compared obstetric and neonatal outcomes between VT and twin pregnancies. Almog et al. [1] reviewed VT and twin deliveries after IVF/ICSI and described that the outcomes were similar in terms of the rate of low birth weight <1500 g, preterm delivery, and extremely preterm delivery. Alternatively, Chasen et al. [5] showed that the median gestational age at delivery and birth weight were significantly lower, and the rate of preterm delivery was significantly higher in twin than in VT deliveries, concluding that the outcome in VT was better than that in twin deliveries in their study that compared 55 VT with 86 twin births after IVF/ICSI. In our study, when compared with twin deliveries, outcomes in the VT group were significantly better in almost all parameters, including the gestational age at delivery and birth weight.

Limitations of this study were that the sample size was small. We could not adjust patient characteristics and IVF treatments, including the number of embryo transferred, the method of controlling ovarian stimulation, the rate of fresh embryo transfer or the rate of blastocyst transfer; all these factors could have affected obstetric and neonatal outcomes. However, as there have been few studies regarding the impact of VT on neonatal outcome, and there have been few studies comparing VT with twin delivery, we believe that the current study could help evaluate the outcome of VT pregnancies.

Conclusion, the obstetric and neonatal outcomes were similar between VT and singleton deliveries, although there was a trend toward an increase rate of preterm delivery and low birth weight in the VT group. Compared with twin pregnancies, outcomes in the VT group were significantly improved. Obstetric and neonatal prognoses after ART may deteriorate according to pregnancy status in the following order: singleton, VT and twin pregnancy.

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