

# Neonatal Outcomes of Twin Pregnancies After Assisted Reproductive Techniques

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#### **Abstract**

Objective: To compare neonatal outcome of twin pregnancies after assisted reproductive techniques with twins conceived spontaneously.

Materials and Methods: This is a retrospective study. Twenty eight deliveries which were conceived after assisted reproductive techniques and 252 spontaneously conceived deliveries were investigated. Neonatal outcomes were the main outcome measures. Results: The mean maternal and gestational ages were similar in both groups. Cesarean delivery was more frequent in twin pregnancies conceived after assisted reproductive techniques (*P*<0.001). There was also no difference in birth-weight discordance and neonatal outcome measures. The incidence of monochorionicity were found to be higher in spontaneously conceived twin pregnancies (*P*<0.032).

**Conclusion:** The neonatal outcomes between spontaneous and assisted reproductive techniques conceived twins are similar except for greater number of cesarean deliveries in assisted reproductive techniques conceived twin pregnancies and higher monochorionicity in spontaneously conceived group.

Keywords: neonatal, outcome, assited reproductive technology

#### Özet

# Yardımla Üreme Teknikleri ile Elde Edilen İkiz Gebeliklerde Neonatal Sonuçlar

Amaç: Yardımla üreme teknikleri (YÜT) kullanımının yaygınlaşmasıyla çoğul gebelik insidansında artış görülmektedir. Kimi çalışmalarda YÜT ile oluşan gebeliklerde kötü perinatal ve neonatal sonuçlar bildirilmiştir. Bu olumsuzluğun gerekçeleri açık olarak belirlenmemiştir ancak çoğul gebeliklerdeki artışın sorumlu olma olasılığı yüksektir. Bu çalışmada YÜT ve spontan ikiz gebeliklerde perinatal ve neonatal sonuçları karşılaştırdık.

Materyal ve Metot: Çalışmaya 24 hafta üzerindeki tüm ikiz gebelikler dahil edildi. Yirmi sekiz YÜT ikiz gebeliğine karşılık, 252 spontan ikiz kontrol grubu olarak kullanıldı. Olgular YÜT ve spontan ikiz gebelikler olarak iki gruba ayrıldı. Gruplar ortalama maternal yaş, doğumda ortalama gebelik haftası, doğum şekli, cinsiyet, koryonisite, intrauterin fetal ölüm, neonatal mortalite, doğum ağırlığı diskordansı, yoğun bakım gereksinimi, hastanede kalış süresi, IVK, NEK, RDS, sepsis, fetal distres, mekanik ventilasyon ve fetal anomali yönünden karşılaştırıldı. İstatistiksel analiz Student's t-testi ve ki kare testi kullanılarak yapıldı.

Sonuçlar: YÜT grubunda parite spontan gruba oranla anlamlı şekilde düşüktü (*P*<0.001). YÜT grubunda sezaryen doğum oranları anlamlı olarak yüksek bulunurken (*P*<0.001), monokoryonik ikizlik spontan ikizlerde daha sık olarak görülmüştür (*P*<0.032).

Tartışma: İnfertilite ve YÜT prosedürlerinin kötü perinatal ve neonatal sonuçlara etkisi olabileceği tartışılmaktadır. Buna karşılık YÜT ve spontan ikiz gebeliklerde benzer perinatal ve neonatal sonuçlar bildiren birçok çalışma yapılmıştır. Bizim çalışmamızda da YÜT grubunda daha fazla olan sezaryen doğumlar dışında iki grup arasında neonatal parametreler yönünden belirgin fark görülmemiştir.

Anahtar sözcükler: neonatal, prognoz, yardımla üreme teknikleri

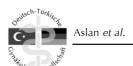
### Introduction

Twin pregnancies have been reported to have a natural incidence of 1/80. With more frequent use of assisted reproductive techniques (ART) the incidence of multiple pregnancies is

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rising substantially (1). Several studies have shown that pregnancies obtained by ART are associated with unfavorable perinatal and neonatal outcome (2-4). However some have indicated that twins from assisted conception have a similar risk of neurological sequelae as their naturally conceived peers and singletons from assisted conception (5). Although clear reasons for a less favorable outcome is unknown, a high incidence of multiple pregnancies seems to be one of the principal explanations (2). In this study we reviewed the perinatal and neonatal outcome of twin pregnancies conceived by ART with spontaneously conceived twins.



## **Materials and Methods**

Between January 2003 and February 2004; 388 twin pregnancies that were delivered in our hospital were retrospectively reviewed. All twin pregnancies >24 weeks were identified from computerized files. Twins were divided into two groups: pregnancies after ART and spontaneous. Gestational age for the ART conceived pregnancies was calculated from the date of embryo transfer and according to first trimester ultrasound estimation and/or last menstrual period for the spontaneously conceived pregnancies. Preterm birth was considered whenever labor occured before 36th weeks of gestation. Birthweight discordance was defined as intra-pair difference expressed as percentage of the larger twin >25%. Respiratory distress syndrome was defined by the presence of characteristic radiographic findings and an oxygen requirement at 24 hours. Intraventricular hemorrhage grade III was defined as hemorrhage with ventricular dilation, and grade IV as hemorrhage with parenchymal spread. Necrotizing enterocolitis was defined by characteristic clinical symptoms with radiographic findings of pneumatosis cystoides intestinalis (grade II) or pneumoperitoneum or portal air (grade III).

We compared the following variables between the two groups: maternal age, gravidity, parity, gestational age, fetal sex, mode of delivery, preterm delivery, chorionicity, birth weight discordance, intrauterine fetal death (IUFD) and neonatal morbidity and mortality. The continuous variables

were analyzed by Student's t test. Categorical data were analyzed by using chi-square. Differences were considered statistically significant when p<0.05.

#### Results

During the study period 388 twin pregnancies were recorded at our unit. Of the 388, 28 were ART pregnancies (including Clomiphene, IVF and ICSI) and 252 were eligible for the control group (cases with IUFD of both fetuses and incomplete neonatal data were excluded). Table 1 shows the demographic characteristics of the study group. The women concieved by ART were older than the spontaneously concieved women (28.8±4.95 vs 27.5±5.18) but the difference was not statistically significant. However both gravidity and parity were significantly different the women in the ART group and women with spontaneous pregnancies (1.30±0.69 vs 2.25±1.43 and

Table 1. Demographic data of the groups				
	ART (n=28)	Spontaneous (n=252)	P value	
Mean (± SD) maternal age (year)	28.8 ± 4.9	27.5 ± 5.1	0.054	
Gravidity	1.30	2.25	<0.001	
Parity	0.12	0.84	<0.001	

ART= assisted reproductive techniques; SD= standard deviation

	ART n=56 (%)	Spontaneous n=504 (%)	P value
Fetal sex			
Male	27 (48.2)	272 (53.9)	
Female	29 (51.8)	232 (46.0)	ns
Mode of delivery			
Vaginal	4 (7.1)	134 (26.5)	
Abdominal	52 (92.9)	370 (73.4)	<0.001
Mean (±SD) gestational age (wks)	34.6 ± 4.31	34.4 ± 3.50	ns
Chorionicity (n=486)			
Monochorionic	5 (10.8)	110 (25.0)	0.032
Dichorionic	41 (89.1)	330 (75.0)	
ntrauterine fetal death	4 (7.1)	37 (7.3)	ns
Neonatal mortality (n=447)	3/47 (6.3)	17/400 (4.2)	ns
Birthweight discordance	18 (32.1)	118 (23.4)	ns
NICU admission	15 (26.7)	135 (26.7)	ns
Duration of hospitalization (days)	5.1± 7.7	5.8 ± 8.6	ns
VH	-	2 (0.3)	-
NEC	-	7 (1.3)	-
RDS	2 (3.5)	20 (3.9)	ns
Sepsis	1 (1.7)	12 (2.3)	ns
Mechanical ventilation	1 (1.7)	21 (4.1)	ns
Fetal distress	4 (7.1)	30 (5.9)	ns
Fetal anomaly	4 (7.1)	13 (2.4)	ns

ART= assisted reproductive techniques; SD= standard deviation; IVH= intraventricular hemorrhage; NEC= necrotizing enterocolitis; RDS= respiratory distress syndrome; ns= no statistically significant difference.



0.12±0.44 vs 0.84±1.06) (p<0.001). Table 2 shows perinatal and neonatal outcome among twins. In our study we noted a non-significant increase in fetal anomaly in the ART group compared to the natural group. Cesarean section rate was higher for the study group. Compared with the ART group the ratio of monochorionic twins was significantly higher than the spontaneously conceived group (*P*=0.032). However the figures for the mean gestational age, mean duration of hospitalization and the incidences of IUFD, neonatal mortality, birthweight discordance, NICU admission, IVH, NEC, RDS, sepsis, mechanical ventilation and fetal distress were comparable between the two groups.

#### Discussion

The outcome of twin pregnancies resulting from ART has been a subject of controversy.

In the present study, we found that ART-conceived twin pregnancies are likely to have a comparable perinatal outcome with naturaly conceived twins. Twins conceived by ART were delivered predominantly by cesarean section. Some of the previous studies reported a shorter mean gestational age, higher incidences of preterm delivery, pregnancy complications, discordance, cesarean delivery, NICU admission, and a lower mean birth weight among the ART pregnancies compared with spontaneously conceived twin pregnancies (2,3,4,7,8). Several factors may account for the adverse perinatal outcomes. ART treated patients tend to be elderly nulliparous women who are known to be a high risk group for pregnancy complications, cesarean delivery and less favorable pregnancy outcome (9). In our study there was no difference in the mean age of the two groups but the proportion of primiparous women was significantly higher in the ART group as compared to naturally conceived twins. Several case-control studies that matched for age and parity also observed adverse outcomes for ART conceived pregnancies. This suggests that infertility status and ART procedure may have an effect on the pregnancy outcome in women who conceived by ART (10,11). Olivennes et al. observed the perinatal outcome of twin pregnancies conceived by IVF as being similar to those conceived spontaneously or after ovulation induction (12). We also have similar results and it is in accordance with some other studies. In their prospective study, Koudstaal et al found no difference with respect to perinatal morbidity and mortality (13). Bernasko et al concluded that the incidence of birth-weight discordance was higher for ART however overall perinatal outcomes was similar for the two groups. Elective cesarean deliveries were 4 times more likely to occur in twins conceived with ART (14). Fitzsimmons et al found that their spontaneously conceived twins pregnancies had higher mortality rates than ART pregnancies. It is mostly due to an increase in monochorionicity in spontaneous twins and the subsequent development of twin to twin transfusion syndrome. It is well known that compared with dichorionic placenta, monochorionic

placenta is associated with adverse perinatal and infantile outcomes, regardless of zygosity (15). We observed that nearly 90% of all placentas from ART conceived twin pregnancies are of the dichorionic type. In our study the incidence of birth-weight discordance and fetal anomaly was higher in the ART group as compared to spontaneously conceived group, but these differences did not reach statistical significance. There were some limitations in this study: small sample size, choice of the control group which is a major methodologic problem in similar studies and pooling clomiphene ovulation induction, IVF, and ICSI together as ART; are the ones to pronounce.

In conclusion, despite its limitations our current study suggests that neonatal outcomes between spontaneous and ART conceived twins are similar except for greater number of cesarean deliveries in ART conceived twin pregnancies.

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