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Obstetric and Perinatal Outcomes of Dichorionic Twin Pregnancies According to Methods of Conception: Spontaneous Versus In-Vitro Fertilization

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We have observed the inconsistent findings from various studies on twin pregnancy outcomes obtained by assisted reproductive technology and spontaneous conception. In most studies, however, the concrete chorionicity, regarded as a confounding factor for predicting the perinatal outcomes of twin pregnancies, has not been determined. The purpose of this study was to compare obstetric and perinatal outcomes of only the dichorionic twin pregnancies according to the methods of conception: spontaneous and in-vitro fertilization (IVF). The twin pairs with dichorionicity reported from 1995 to 2008 were investigated and we divided them into two groups which consisted of 286 and 134 twins by spontaneous conception and IVF, respectively. Odds ratios for associations between IVF and pregnancy outcomes were analyzed after adjustment for maternal age and parity. There were no risk differences between the two groups regarding the obstetric complications, which include preterm delivery, preterm labor, preterm premature rupture of membranes, preeclampsia, placenta previa, and abruption. Any differences were not shown in the two groups for the risk estimates of perinatal outcomes, such as low birthweight, very low birthweight, small for gestational age, Apgar scores of < 7 at 5 minutes, discordance in birthweights, congenital anomalies and mortality. However, twins conceived after IVF were less likely to be admitted to the neonatal intensive care unit than those conceived spontaneously (adjusted OR 0.488; 95% confidence interval 0.261–0.910). In the cases of dichorionic twins, IVF may not be associated with adverse perinatal and obstetric outcomes compared with spontaneous conception.

■ **Keywords:** IVF, twins, pregnancy, perinatal outcome, obstetric outcome

Lots of successful pregnancies conceived by assisted reproductive technology (ART) have resulted in a substantial increase of multiple pregnancies up to 15–30% (Kozinszky et al., 2003). Among many types of ART, in vitro fertilization (IVF) has become the standard treatment. Since the introduction of IVF in Korea, twin birth rates increased 38% between the 1980s and the 1990s (Park et al., 2001).

Although we have observed abundant evidence that perinatal outcomes of singleton births conceived using IVF were poorer than their spontaneously conceived counterparts (SC) (Helmerhorst et al., 2004; Jackson et al., 2004; Rimm et al., 2004), conflicting results remained in twin pregnancies between those two methods. It was demonstrated through many studies that IVF-obtained twin pregnancies were often subject to the risk of perinatal morbidity and obstetric complications (Daniel et al., 2000; Hansen et al., 2005; Hansen et al., 2009; French In Vitro National, 1995). In addition, some investigators suggested that these unfavorable outcomes were result of maternal characteristics of those treated with IVF, not the IVF technique per se (Bergh et al., 1999; Draper et al., 1999; Kessler et al., 1980; Li et al., 1991; Petersen et al., 1995; Williams et al., 1991).

Similar or even better perinatal outcomes in ART-conceived twins have been reported (Fitzsimmons et al., 1998;

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Kozinszky et al., 2003; Olivennes et al., 1996). A systematic meta-analysis of perinatal outcomes in assisted conception and spontaneous pregnancy demonstrated that the perinatal mortality rate of twins born following ART was reduced by 40% compared with SC method (Helmerhorst et al., 2004).

It is not easy to explain these observations due to the heterogeneous methodology among the studies, such as different proportions of maternal age, parity, and especially, chorionicity. The twins conceived by IVF are much less monochorionic than those conceived by SC, and many studies have demonstrated that monochorionic twins have poorer outcomes compared to dichorionic twins (Chitrit et al., 1999; Gruenwald, 1970; Nicolini & Poblete, 1999). Such observations have led to an opinion that chorionicity may be an important factor for making a prognosis of twin pregnancies. Although 'unlike-sex dizygotic twins' were usually used as a substitute for dichorionicity in most studies, few of them analyzed the pregnancy outcomes based on placental chorionicity.

The objective of this study is to investigate the obstetric and perinatal outcomes within the confines of dichorionic twin pregnancies after IVF or SC, controlling a major confounder, chorionicity, and to verify whether twin pregnancies conceived with IVF have adverse effects when compared to those of SC.

Materials and Methods

This retrospective study was conducted based on all twin births after IVF or natural conception in the Yonsei University Health System from January 1995 to December 2008. The data collected from the delivery suite medical records of mothers and neonates were analyzed. We excluded intrauterine fetal deaths, neonates with birthweight of < 500 grams or < 24 weeks of gestation at delivery, higher-order multiple pregnancies, singleton pregnancy deliveries complicated by early vanishing fetuses, twin pregnancies reduced to singleton, and lastly, triple pregnancy reduced to twin.

The estimated gestational age for the IVF group was calculated by adding two weeks to the day of oocyte retrieval. For the SC group, on the other hand, the gestational age was based on the first day of the last menstrual period if this was within 7 days of the first-trimester ultrasound-derived estimate and a single second trimester biparietal diameter measurement when the discrepancy was greater than 7 days (Waldenstrom et al., 1990). Although Carroll et al. showed the high reliability of ultrasound examination of twin pregnancies at 10–14 weeks of gestation as a predictor of chorionicity (Carroll et al., 2002), pathological examination of the placenta was undertaken for more accurate decision of the chorionicity and only dichorionic placentation was included in this study.

We compared the obstetric and perinatal outcomes between IVF and SC group. The maternal age, parity, gestational age at delivery, the respective incidence of delivery < 32 weeks', < 34 weeks' and < 37 weeks' gestation, and the difference ratio of twin sex were included as the variables of clinical data. Preterm labor, preterm premature rupture of membranes (PPROM), preeclampsia, placenta previa and placental abruption were involved for the variables of the obstetric complications. Preterm labor was defined as regular uterine contractions at a rate of eight in 1 hour or four in 20 minutes with progressive effacement and dilation of the cervix. Preeclampsia was diagnosed with persistent blood pressure above 140/90 mmHg after 20 weeks of gestation among previously normotensive women accompanied by proteinuria of ≥ 0.3g protein in a 24-hour urine specimen (American College of Obstetricians and Gynecologists, 2002). The perinatal outcomes were compared between two groups using variables such as low birthweight (LBW), very low birthweight (VLBW), small for gestational age (SGA), < 7 Apgar score at 5 minutes, rate of neonatal intensive care unit (NICU) admission, birthweight discordance, congenital anomalies and mortality. LBW and VLBW were explained as a birthweight of < 2500g and < 1500g, respectively. SGA was defined to birthweight below the tenth percentile for gestational age according to the twin nomograms (Ananth et al., 1998) and discordance was defined as interpair birthweight difference > 25% which is expressed as a percentage of the larger twin. Congenital anomalies referred to congenital malformations, deformations and chromosomal abnormalities according to the tenth edition of International Classification of Diseases (Q00-Q99); however, persistent ductus arteriosus in the case of premature birth was excluded. Neonatal mortality was defined as the death of a liveborn neonate during the first 28 days after birth.

The SAS (release 9.1; Institute Inc., Cary, NC, USA) program was used for statistical analysis. Means and proportions of two groups were compared by using independent two-sample *t* test and chi-square test, respectively. Since the maternal age and parity differed significantly between the two groups, all the results were presented as odds ratios (OR) with 95% confidence intervals (CIs) after multiple logistic regression analyses for the independent associations of IVF on each outcome. Because a number of outcomes including LBW, VLBW, SGA, Apgar < 7 at 5 minutes, NICU admission, congenital anomalies and mortality could appear in either one or both of the twin infants, ordinal logistic regression was applied to calculate adjusted cumulative ORs and 95% CIs for the relationship between IVF and the above outcomes. $P < 0.05$ was considered statistically significant.

This study was approved by the Institutional Review Boards at the Yonsei University Health System.

Results

Five hundred and thirty-two twins out of 664 twins delivered during this study period were available for analysis

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TABLE 1

Clinical Characteristics Among IVF and SC Groups

Variables	IVF group (n = 67)	SC group (n = 143)	P
Maternal age (y)	32.5 ± 3.5	30.7 ± 4.2	0.003
Nulliparity (%)	91.7	64.3	0.002
Mean gestational age at delivery (weeks)	35.3 ± 2.8	35.2 ± 3.0	0.817
Mean birthweight (g)	2,305 ± 590	2,286 ± 563	0.757
Sex differentiation			
Like-sex (%)	47.8	52.2	0.354
Unlike-sex (%)	53.1	46.1	

Note: IVF = in vitro fertilization; SC = spontaneously conceived
Data are represented as mean ± SD or percentage.

and among them, 164 (31%) twins were born after IVF and 368 (69%) twins were spontaneously conceived. Based on the placental pathology, 134 (81.7%) dichorionic twins and 30 (18.3%) monochorionic diamniotic (MD) twins were reported and monochorionic monoamniotic (MM) twins were not observed in the IVF group. In the SC group, the dichorionic twins were 286 (77.7%), MD twins were 72 (19.6%), and MM twins were 10 (2.7%).

The clinical characteristics of the IVF and SC groups were compared, and the results were summarized in Table 1. The dichorionic twins in the IVF group had a higher mean maternal age (32.5 ± 3.5 *vs* 30.7 ± 4.2, $P = .003$) and higher share of nulliparae (91.7% vs. 64.3% $P = .002$) than their counterparts in the SC group. There were no significant differences between two groups in terms of the mean gestational ages at delivery and mean birthweights. Although no statistical significance was observed, the proportions of the same sex pairs were 32 (47.8%) and 77 (52.2%) among the 67 IVF and 143 SC twin pairs, respectively. After controlling for maternal age and parity, IVF was not associated with the obstetric complications including deliveries before 32, 34, and 37 weeks' gestation, preterm labor, PPROM, preeclampsia, placenta previa and abruption (Table 2).

Table 3 showed the comparison of the perinatal outcomes from IVF and SC twins. None of statistically significant differences were observed in the rates of LBW, VLBW, SGA, Apgar score of < 7 at 5 minutes, discordant birthweights, congenital anomalies and mortality. However, the protective association between IVF and NICU admission was observed (adjusted OR 0.488; 95% CI [0.261–0.910]). The most frequent anomaly was congenital heart malformation in both groups (Table 4).

Discussion

Our study demonstrated that dichorionic twins conceived following IVF was not associated with the adverse perinatal or obstetric outcomes. There had been contradictory results for twin pregnancies according to the conception methods. Some investigators reported that twin pregnancies by IVF, as compared with SC corresponding cases, had a younger gestational age, a lower mean birthweight, and a higher rates in the characteristics such as prematurity, VLBW, discordance, NICU admission, and neonatal mortality (Bernasko et al., 1997; Moise et al., 1998; Nassar et al., 2003). Furthermore, the women who conceive after IVF are usually older than those who conceive naturally and in addition, they are almost primiparous, which is conferred as higher risks of the perinatal and obstetric outcomes. A matched control study with regard to age, gravidity and parity showed significantly increased mean birthweights in ART twins compared with SC twins (Kozinszky et al., 2003). And there were no differences in gestational age, or other neonatal outcomes including perinatal mortality, congenital malformations and neonatal hospital admissions. Although the IVF group had more primiparous and older women than SC group in this study, it was found that comparable pregnancy outcomes were observed in the two groups.

TABLE 2

Distribution and Adjusted OR for Associations Between IVF and Obstetric Complications Among Dichorionic Twin Births

	IVF twins (%) (n = 67)	SC twins (%) (n = 143)	P[a]	Adjusted OR[b]	95% CI
Gestational duration					
< 32 weeks	7.5	9.8	0.584	1.081	(0.321–3.639)
< 34 weeks	19.4	20.3	0.882	1.127	(0.493–2.574)
< 37 weeks	56.7	55.9	0.959	0.841	(0.437–1.617)
Preterm labor	26.9	21.7	0.71	1.045	(0.491–2.220)
PPROM	6	5.6	0.893	0.883	(0.233–3.347)
Preeclampsia	13.4	15.4	0.442	0.65	(0.263–1.606)
Placenta previa	3	0.7	0.239	7.228	(0.927–56.351)
Placental abruption	1.5	0.7	0.537	0.305	(0.012–7.759)

Note: IVF = in vitro fertilization; SC = spontaneously conceived; PPROM = preterm premature rupture of the membranes
[a] χ^2-test
[b] Adjusted for age and parity

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TABLE 3

Distribution and Adjusted OR for Associations Between IVF and Perinatal Outcomes Among Dichorionic Twins

Variables	IVF (%) (n = 134)	SC (%) (n = 286)	P[a]	Adjusted OR[b]	95% CI
LBW	59.0	61.9	0.566	0.696	0.378–1.280
VLBW	9.7	9.1	0.849	1.673	(0.578–4.842)
SGA	15.0	10.5	0.181	1.345	(0.642–2.818)
Apgar score < 7 at 5 min	9.7	10.1	0.889	1.080	(0.421–2.773)
NICU admission	50.8	64.7	0.008	0.488	(0.261–0.910)
Birthweight discordance	17.9	14.0	0.297	1.020	(0.527–1.973)
Congenital anomalies	7.5	8.0	0.837	1.858	(0.707–4.884)
Mortality	2.2	1.7	0.556	7.860	(0.626–98.737)

Note: IVF = in-vitro fertilization; SC = spontaneously conceived; LBW = low birthweight; VLBW = very low birthweight; SGA = small for gestational age; NICU = neonatal intensive care unit;
[a] χ2-testχ
[b] Adjusted for age and parity

The other studies showed that IVF might have a comparable or beneficial effects on the overall perinatal outcomes because the share of dichorionicity in the IVF-obtained pregnancies was higher than natural conception, regardless of zygosity (Derom et al., 1987; Dhont et al., 1999; Fitzsimmons et al., 1998; Helmerhorst et al., 2004; Malone, 2003; Minakami et al., 1999; Minakami et al., 1998). A population-based study reported that risks in terms of very preterm delivery, VLBW and infant death were lower in 1,446 ART twin deliveries than the 2,729 in the non-ART group (Boulet et al., 2008). Although the results showed that twins with dizygosity by restriction to 'unlike sex' had beneficial outcomes among the ART group, the authors indicated that it was doubtful to generalize this subset of dizygotic twins to all dizygotic twin deliveries. Most studies regarding chorionicity analyzed gender difference to define dizygosity because it was largely contributed to the dichorionic placentation, however, a possible explanation about dizygous monochorionic twinning has been propounded by several reports and dizygosity could not be determined by gender (Chan et al., 2007; Souter et al., 2003). In investigation to evaluate the gender mix of twin pregnancies, moreover, the gender combination might influence the length of gestation and birthweight independent of chorionicity (James, 2002; Luke et al., 2005). Therefore, exclusion of like-sex dizygotic twins may not lead to the full investigation into the effect of chorionicity on the twin pregnancy outcomes. Hansen et al. compared the perinatal outcomes between 700 ART and 1240 SC 'unlike-sex twins' in order to take account of the differing proportions of monochorionic placentation in the two groups, and found that the risks of preterm birth, LBW, perinatal death and NICU admission were increased in ART twins (Hansen et al., 2009). Recently, Kallen et al. showed that the neonatal outcomes for different-sex twins born after IVF were worse than those of non-IVF twins after adjustment for age and parity (Kallen et al. 2010). However, these cohort studies did not consider the accurate chorionicities as well.

Compared with dichorionic pregnancies, it was noted that monochorionic pregnancies had a higher rate of perinatal mortality, preterm delivery, growth discordance and LBW (Ananth et al., 1998; Leduc et al., 2005; Penava & Natale, 2004). In this study, dichorionic twins were identified after confirming placental pathology and accounted for 81.7% and 77.7% in the IVF and the SC group among all twin deliveries, respectively. The importance of the present study was that we analyzed only dichorionic twins in order to avoid possible adverse effects of monochorionicty itself. Our opinion was supported by previous study, of which the authors noted that dichorionic twins from IVF did not have an increased risk for preterm delivery, birthweight, birth discordance, Apgar score or pregnancy induced hypertension, and suggested clinicians should pay more attention to twin chorionicity versus the method of conception (Cai et al., 2006). Also, Joy et al. confirmed the chorionicity through combination of first trimester scan, sex determination of the twins and placental pathological examination, and showed that major factor for the increase of perinatal morbidity in twin pregnancies was

TABLE 4

Congenital Anomalies Among IVF and SC Twins

IVF (n)	SC (n)
Congenital heart malformation (8)	Congenital heart malformation (14)
Cleft lip (1)	Cleft lip (1)
Congenital muscular skeletal disease (1)	Congenital muscular skeletal disease (1)
	Congenital cystic adenomatoid malformation (1)
	Hydrocephalus (1)
	Spina bifida (1)
	Tuberous sclerosis (1)
	Congenital hydronephrosis (1)
	Undescended testicle (1)
	Down syndrome (1)

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the monochorionicity rather than conception mode (Joy et al., 2008). Consequently, these observations indicated that chorionicity might be the most confounding factor as to comparison of the perinatal outcomes in twin pregnancies between IVF and non-IVF group.

The subjects investigated in this study were racially homogeneous, which was different from the samples in many other literatures. They also had a similar level of access to medical services for ART or perinatal care because universal coverage of health services was provided in our country. This condition may have advantages to the analysis of the study because differences in perinatal outcomes are associated with disparities of race and accessibility to health care system (Fujimoto et al., 2008; Goldman et al., 2002).

We observed a higher rate of NICU admission in the SC group than in the IVF group. This finding, which was in line with those of previous study (Joy et al., 2008), might be the result of the selection bias according to our tertiary referral center. Moreover, one of the indications of the NICU admission in our unit was just the LBW infant without other problems, and a higher rate of LBW in the twins by SC was found despite no significant difference.

Since this study was performed in one tertiary hospital, it had an insufficient statistical power to investigate the risks of perinatal outcomes, especially rare complications such as mortality and congenital malformation. In addition, the duration of study, that is, more than 10 years, may be a confounding factor because perinatal care and ART are likely to have been evolved over the period of observation.

In conclusion, it was shown that the pregnancy outcomes were comparable between IVF and SC twins with dichorionicity in this study. Although there have been various arguments on the outcomes of twin pregnancies according to the conception modes in the literature, the implication was that IVF itself may not mainly contribute to perinatal and obstetric complications in twin pregnancies.

References

American College of Obstetricians and Gynecologists (2002). Diagnosis and management of preeclampsia and eclampsia: Practice bulletin number 33, January 2002. *International Journal of Gynaecology and Obstetrics, 77*, 67–75.

Ananth, C. V., Vintzileos, A. M., Shen-Schwarz, S., Smulian, J. C., & Lai, Y. L. (1998). Standards of birth weight in twin gestations stratified by placental chorionicity. *Obstetrics and Gynecology, 91*, 917–924.

Bergh, T., Ericson, A., Hillensjo, T., Nygren, K. G., & Wennerholm, U. B. (1999). Deliveries and children born after in-vitro fertilisation in Sweden 1982–95: a retrospective cohort study. *Lancet, 354*, 1579–1585.

Bernasko, J., Lynch, L., Lapinski, R., & Berkowitz, R. L. (1997). Twin pregnancies conceived by assisted reproductive techniques: Maternal and neonatal outcomes. *Obstetrics and Gynecology, 89*, 368–372.

Boulet, S. L., Schieve, L. A., Nannini, A., Ferre, C., Devine, O., Cohen, B., Zhang, Z., Wright, V., & Macaluso, M. (2008). Perinatal outcomes of twin births conceived using assisted reproduction technology: A population-based study. *Human Reproduction, 23*, 1941–1948.

Cai, L. Y., Izumi, S., Koido, S., Uchida, N., Suzuki, T., Matsubayashi, H., Sugi, T., Shida, N., Kikuchi, K., & Yoshikata, K. (2006). Abnormal placental cord insertion may induce intrauterine growth restriction in IVF-twin pregnancies. *Human Reproduction, 21*, 1285–1290.

Carroll, S. G., Soothill, P. W., Abdel-Fattah, S. A., Porter, H., Montague, I., & Kyle, P. M. (2002). Prediction of chorionicity in twin pregnancies at 10–14 weeks of gestation. *BJOG, 109*, 182–186.

Chan, O. T., Mannino, F. L., & Benirschke, K. (2007). A retrospective analysis of placentas from twin pregnancies derived from assisted reproductive technology. *Twin Research and Human Genetics, 10*, 385–393.

Chitrit, Y., Filidori, M., Pons, J. C., Duyme, M., & Papiernik, E. (1999). Perinatal mortality in twin pregnancies: A 3-year analysis in Seine Saint-Denis (France). *European Journal of Obstetrics, Gynecology and Reproductive Biology, 86*, 23–28.

Daniel, Y., Ochshorn, Y., Fait, G., Geva, E., Bar-Am, A., & Lessing, J. B. (2000). Analysis of 104 twin pregnancies conceived with assisted reproductive technologies and 193 spontaneously conceived twin pregnancies. *Fertility and Sterility, 74*, 683–689.

Derom, C., Vlietinck, R., Derom, R., Van den Berghe, H., & Thiery, M. (1987). Increased monozygotic twinning rate after ovulation induction. *Lancet, 1*, 1236–1238.

Dhont, M., De Sutter, P. Ruyssinck, G., Martens G., & Bekaert, A. (1999). Perinatal outcome of pregnancies after assisted reproduction: A case-control study. *American Journal Obstetrics and Gynecology, 181*, 688–695.

Draper, E.S. Kurinczuk, J.J., Abrams, K. R., & Clarke, M. (1999). Assessment of separate contributions to perinatal mortality of infertility history and treatment: A case-control analysis. *Lancet, 353*, 1746–1749.

Fitzsimmons, B. P., Bebbington, M. W., & Fluker, M. R. (1998). Perinatal and neonatal outcomes in multiple gestations: Assisted reproduction versus spontaneous conception. *American Journal of Obstetrics and Gynecology, 179*, 1162–1167.

Fujii, M., Matsuoka, R., Bergel, E., van der Poel, S., & Okai, T (2010). Perinatal risk in singleton pregnancies after in vitro fertilization. *Fertility and Sterility, 94,* 2113–2117.

Fujimoto, V.Y., Luke, B., Brown, M.B., Jain, T., Armstrong, A., Grainger, D.A., Hornstein, M.D. (2008). Racial and ethnic disparities in assisted reproductive technology outcomes in the United States. *Fertility and Sterility, 93,* 382–390.

Goldman, R.D., Mazkereth, R., & Blickstein, I. (2002). Twinning and birth weight in the Israeli Jewish versus Muslim maternities. *Twin Research*, 5, 15–18.

Gruenwald, P. (1970). Environmental influences on twins apparent at birth. A preliminary study. *Biologia Neonatorum, 15*, 79–93.

https://doi.org/10.1375/twin.14.1.98 Published online by Cambridge University Press

Hansen, M., Bower, C., Milne, E., de Klerk, N., & Kurinczuk, J. J. (2005). Assisted reproductive technologies and the risk of birth defects: A systematic review. *Human Reproduction, 20*, 328–338.

Hansen, M., Colvin, L., Petterson, B., Kurinczuk, J. J., de Klerk, N., & Bower, C. (2009). Twins born following assisted reproductive technology: perinatal outcome and admission to hospital. *Human Reproduction, 24,* 2321–2331.

Helmerhorst, F. M., Perquin, D. A., Donker, D., & Keirse, M. J. (2004). Perinatal outcome of singletons and twins after assisted conception: A systematic review of controlled studies. *BMJ, 328*, 261.

Jackson, R. A., Gibson, K. A., Wu, Y. W., & Croughan, M. S. (2004). Perinatal outcomes in singletons following *in vitro* fertilization: A meta-analysis. *Obstetrics and Gynecology, 103*, 551–563.

James, W. H. (2002). Gestation and birthweight in dizygotic twins. *Lancet, 359*, 171–172.

Joy, J., McClure, N., & Cooke, I. E. (2008). A comparison of spontaneously conceived twins and twins conceived by artificial reproductive technologies. *Journal of Obstetrics and Gynaecology, 28*, 580–585.

Kallen, B., Finnstrom, O., Lindam, A., Nilsson, E., Nygren, K.G., & Olausson, P.O. (2010). Selected neonatal outcomes in dizygotic twins after IVF versus non-IVF pregnancies. *BJOG, 117*, 676–682.

Kessler, I., Lancet, M., Borenstein, R., & Steinmetz, A. (1980). The problem of the older primipara. *Obstetrics and Gynecology, 56*, 165–169.

Kozinszky, Z., Zadori, J., Orvos, H., Katona, M., Pal, A., & Kovacs, L. (2003). Obstetric and neonatal risk of pregnancies after assisted reproductive technology: a matched control study. *Acta Obstetrica Gynecologica Scandinavia, 82*, 850–856.

Lambalk, C. B., & van Hooff, M. (2001). Natural versus induced twinning and pregnancy outcome: A Dutch nationwide survey of primiparous dizygotic twin deliveries. *Fertility and Sterility, 75*, 731–736.

Leduc, L., Takser, L., & Rinfret, D. (2005). Persistance of adverse obstetric and neonatal outcomes in monochorionic twins after exclusion of disorders unique to monochorionic placentation. *American Journal of Obstetrics and Gynecology, 193*, 1670–1675.

Li, T. C., MacLeod, I., Singhal, V., & Duncan, S. L. (1991). The obstetric and neonatal outcome of pregnancy in women with a previous history of infertility: A prospective study. *British Journal of Obstetrics and Gynaecology, 98*, 1087–1092.

Luke, B., Hediger, M., Min, S. J., Brown, M. B., Misiunas, R. B., Gonzalez-Quintero, V. H., Nugent, C., Witter, F. R., Newman, R. B., Hankins, G. D., Grainger, D. A., & Macones, G. A. (2005). Gender mix in twins and fetal growth, length of gestation and adult cancer risk. *Paediatric and Perinatal Epidemiology, 19 Suppl 1*, 41–47.

Malone, F. D. (2003). Monochorionic pregnancy — Where have we been? Where are we going? *American Journal Obstetrics and Gynecology, 189*, 1308–1309.

Minakami, H., Honma, Y., Matsubara, S., Uchida, A., Shiraishi, H., & Sato, I. (1999). Effects of placental chorionicity on outcome in twin pregnancies. A cohort study. *Journal of Reproductive Medicine, 44*, 595–600.

Minakami, H., Sayama, M., Honma, Y., Matsubara, S., Koike, T., Sato, I., Uchida, A., Eguchi, Y., Momoi, M., & Araki, S. (1998). Lower risks of adverse outcome in twins conceived by artificial reproductive techniques compared with spontaneously conceived twins. *Human Reproduction, 13*, 2005–2008.

Moise, J., Laor, A., Armon, Y., Gur, I., & Gale, R. (1998). The outcome of twin pregnancies after IVF. *Human Reproduction, 13*, 1702–1705.

Nassar, A. H., Usta, I. M., Rechdan, J. B., Harb, T. S., Adra, A. M., & Abu-Musa, A. A. (2003). Pregnancy outcome in spontaneous twins versus twins who were conceived through *in vitro* fertilization. *American Journal of Obstetrics and Gynecology, 189*, 513–518.

Nicolini, U., & Poblete, A. (1999). Single intrauterine death in monochorionic twin pregnancies. *Ultrasound in Obstetrics and Gynecology, 14*, 297–301.

Olivennes, F., Kadhel, P., Rufat, P., Fanchin, R., Fernandez, H., & Frydman, R. (1996). Perinatal outcome of twin pregnancies obtained after *in vitro* fertilization: Comparison with twin pregnancies obtained spontaneously or after ovarian stimulation. *Fertility and Sterility, 66*, 105–109.

Park, SH., Kim, TJ., Moon, SY., Kim, SH. (2001). Study on trends of multiple births in Korea: 1982–1998. *Korean Journal of Perinatology, 21*, 449–452.

Penava, D., & Natale, R. (2004). An association of chorionicity with preterm twin birth. *Journal of Obstetrics and Gynaecology Canada, 26*, 571–574.

Petersen, K., Hornnes, P. J., Ellingsen, S., Jensen, F., Brocks, V., Starup, J., Jacobsen, J. R., & Andersen, A. N. (1995). Perinatal outcome after *in vitro* fertilisation. *Acta Obstetrics and Gynecology Scandinavia, 74*, 129–131.

French In Vitro National (1995). Pregnancies and births resulting from *in vitro* fertilization: French national registry, analysis of data 1986 to 1990. *Fertility and Sterility, 64*, 746–756.

Rimm, A. A., Katayama, A. C., Diaz, M., & Katayama, K. P. (2004). A meta-analysis of controlled studies comparing major malformation rates in IVF and ICSI infants with naturally conceived children. *Journal of Assisted Reproduction and Genetics, 21*, 437–443.

Souter, V. L., Kapur, R. P., Nyholt, D. R., Skogerboe, K., Myerson, D., Ton, C. C., Opheim, K. E., Easterling, T. R., Shields, L. E., Montgomery, G. W., & Glass, I. A. (2003). A report of dizygous monochorionic twins. *New England Journal of Medicine, 349*, 154–158.

Waldenstrom, U, Axelsson, O, & Nilsson, S. (1990). A comparison of the ability of a sonographically measured biparietal diameter and the last menstrual period to predict the spontaneous onset of labor. *Obstetrics and Gynecology, 76*, 336–338.

Williams, M. A., Goldman, M. B., Mittendorf, R., & Monson, R. R. (1991). Subfertility and the risk of low birth weight. *Fertility and Sterility, 56*, 668–671.